NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of mechanical clot retrieval for treating acute ischaemic stroke

An ischaemic stroke happens when the normal blood supply to part of the brain is cut off. This can be caused by a blood clot blocking an artery supplying the brain. The brain cells in the affected area are starved of oxygen, and become damaged or die. Symptoms may include problems with speech and weakness on one side of the body. Mechanical clot retrieval aims to restore normal blood flow by using a special device such as a stent retriever, which is passed into the blocked artery in the brain through an artery in the neck. This traps the clot so that it can be removed from the artery.

Introduction

The National Institute for Health and Care Excellence (NICE) has prepared this interventional procedure (IP) overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This IP overview was prepared in June 2015.

Procedure name

- Mechanical clot retrieval for treating acute ischaemic stroke

Specialist societies

- British Society of Neuroradiologists
- British Association of Stroke Physicians (BASP).

Description

Indications and current treatment

Ischaemic stroke is characterised by the sudden loss of blood circulation to an area of the brain, resulting in a corresponding loss of neurological function. This may lead to symptoms such as numbness or weakness of the face, arm or leg on one side of the body, and often problems with speech and swallowing. Severity of stroke can be measured using scales such as the National Institutes of Health Stroke scale and the Modified Rankin scale. Broadly, strokes are classified as either haemorrhagic or ischaemic. Acute ischaemic stroke refers to stroke caused by arterial thrombosis or embolism and is more common than haemorrhagic stroke.

Patients suspected to have an acute ischaemic stroke should have rapid assessment and early intervention with specialist care according to Stroke: diagnosis and initial management of acute stroke and transient ischaemic attack (NICE guideline CG68). Recanalisation strategies, such as thrombolysis, attempt to re-establish blood flow so that cells starved of oxygen can be rescued before they are irreversibly damaged. Effective stroke care also includes specialised supportive care and rehabilitation when appropriate.

Mechanical clot retrieval for treating acute ischaemic stroke aims to remove the obstructing blood clot or other material from large arteries to the brain, thereby restoring blood flow to the brain and minimising brain tissue damage.

Acute ischaemic stroke causes high mortality and morbidity, and neurological outcome may be improved by early recanalisation.

What the procedure involves

Mechanical clot retrieval for treating acute ischaemic stroke is carried out on patients with a stroke due to blockage of a main cerebral blood vessel. Immediately after they are admitted to hospital patients have a CT scan along with a CT or MR angiogram to confirm the presence of a major vessel occlusion. The procedure is usually done with the patient under sedation with local anaesthesia, sometimes general anaesthesia is used. Conventional cerebral angiography is done to show the exact location of arterial occlusion. A delivery catheter is inserted, usually through the femoral artery at the groin, and advanced using X-ray guidance to the occluded artery. A clot-retrieval device attached to a guidewire is introduced through the delivery catheter to the site of the occlusion to remove the clot and re-establish blood flow to the affected part of the brain.

Several types of device and different techniques have been used for clot retrieval in the past. Most recent clinical trial evidence is based on the use of stent-retrievers, which are currently the most commonly used type of device. The stent

retriever is a self-expanding metal mesh tube that is introduced through a catheter and partially deployed within the clot. The stent retriever traps the clot within its mesh and is then withdrawn through the catheter.

The aim is to perform the procedure as soon as possible after the onset of stroke symptoms.

Outcome measures

The National Institutes of Health Stroke scale (NIHSS)

The NIHSS is used to measure the severity of a stroke. It scores areas such as level of consciousness, vision, sensation, movement, speech and language with a maximum of 42 points representing the most severe symptoms.

The levels of stroke severity on the NIHSS are categorised as:

- 0: no stroke
- 1–4: minor stroke
- 5–15: moderate stroke
- 16–20: moderate/severe stroke
- 21–42: severe stroke.

Modified Rankin scale (mRS)

This is a functional assessment scale that measures the degree of disability or dependence of people who have suffered a stroke.

The scale runs from perfect health without symptoms to death:

- 0: No symptoms.
- 1: No significant disability. Able to carry out all usual activities, despite some symptoms.
- 2: Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.
- 3: Moderate disability. Requires some help, but able to walk unassisted.
- 4: Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
- 5: Severe disability. Requires constant nursing care and attention, bedridden, incontinent.

- 6: Dead.

Thrombolysis in myocardial infarction (TIMI)

TIMI grade flow is a system that scores the level of coronary blood flow, but has also been applied to intracranial thrombolysis.

- TIMI 0 flow (no perfusion): Absence of any antegrade flow beyond a coronary occlusion.
- TIMI 1 flow (penetration without perfusion): Faint antegrade coronary flow beyond the occlusion, with incomplete filling of the distal coronary bed.
- TIMI 2 flow (partial reperfusion): Delayed or sluggish antegrade flow with complete filling of the distal territory.
- TIMI 3 flow (complete perfusion): Normal flow that fills the distal coronary bed completely.

Thrombolysis in cerebral infarction (TICI)

TICI scores are based on modified TIMI criteria to define cerebral perfusion.

- Grade 0: No perfusion beyond the occlusion.
- Grade 1: Penetration but not perfusion. Contrast penetration exists past the initial obstruction but with minimal filling of the normal territory.
- Grade 2a: Partial perfusion with incomplete distal branch filling of under 50% of the expected territory.
- Grade 2b: Partial perfusion with incomplete distal branch filling of 50–99% of the expected territory.
- Grade 2c: Near complete perfusion without clearly visible thrombus but with delay in contrast run-off.
- Grade 3: Full perfusion with normal filling of all distal branches of expected territory in a normal haemodynamic fashion.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to mechanical clot retrieval for treating acute ischaemic stroke. The following databases were searched, covering the period from their start to 28 May 2015: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with acute ischaemic stroke.
Intervention/test	Mechanical clot retrieval.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on 1511 patients from 6 randomised controlled trials, 1 case series and 4 case reports [1–12].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on mechanical clot retrieval for treating acute ischaemic stroke

Study 1 Berkhemer OA (2015)

Details

Study type	**Randomised controlled trial (MR CLEAN)**
Country	The Netherlands (16 centres)
Recruitment period	2010–4
Study population and number	**n=500** (233 intra-arterial treatment [intra-arterial thrombolysis, mechanical treatment, or both] plus usual care versus 267 usual care alone) Adult patients with acute ischaemic stroke caused by an intracranial occlusion in the anterior circulation artery.
Age and sex	Mean age 65 years; 58% (292/500) male
Patient selection criteria	Age 18 years or older; acute ischaemic stroke caused by an intracranial occlusion in the anterior circulation artery; occlusion of the distal intracranial carotid artery, middle cerebral artery (M1 or M2), or anterior cerebral artery (A1 or A2), established with CT angiography, magnetic resonance angiography or digital subtraction angiograph; score of 2 or higher on the National Institutes of Health Stroke Scale (NIHSS); initiation of intra-arterial treatment had to be possible within 6 hours after stroke onset. Inclusion of patients with an additional extracranial internal-carotid-artery occlusion or dissection was left to the judgement of the treating physician.
Technique	Intra-arterial treatment consisted of arterial catheterisation to the level of the occlusion and delivery of a thrombolytic agent (alteplase or urokinase), mechanical thrombectomy, or both. Mechanical treatment could involve thrombus retraction, aspiration, wire disruption, or use of a retrievable stent. General anaesthesia was used for 38% (88/233) of patients in the intervention group. Retrievable stents were used in 82% (190/233) of patients and other devices were used in 2% (5/233) of patients. Control patients were treated by 'usual care', which could include intravenous alteplase.
Follow-up	**90 days**
Conflict of interest/source of funding	Supported by the Dutch Heart Foundation and by unrestricted grants from AngioCare Covidien/ev3, Medac/Lamepro, and Penumbra.

Analysis

Follow-up issues: Data on the primary outcome were complete.

Study design issues: Randomised treatment group assignments, open-label treatment, and blinded end-point evaluation. Randomisation was computerised, with the use of permuted blocks. The primary outcome was the score on the modified Rankin scale at 90 days (7-point scale ranging from 0 [no symptoms] to 6 [death]; a score of 2 or less indicates functional independence). All analyses were based on the intention-to-treat principle. One patient received intra-arterial treatment after being assigned to the control group. Intra-arterial treatment was never initiated in 7% (17/233) of patients assigned to the intervention group. The outcome values were adjusted for age, NIHSS score at baseline, time from stroke onset to randomisation, status with respect to previous stroke, atrial fibrillation, and diabetes mellitus, and occlusion of the internal carotid artery terminus (yes versus no). Activities of daily living were assessed using the Barthel index (scores range from 0 to 20, with 0 indicating severe disability and 19 or 20 indicating no disability that interferes with daily activities). Health status was measured using the EuroQol Group 5-Dimension self-report questionnaire (EQ-5D), scores range from -0.33 to 1.00 with higher scores indicating a better quality of life.

Study population issues: Risk factors for a poor outcome, clinical risk factors for stroke, and aspects of pre-randomisation treatment were evenly distributed between the 2 treatment groups. Randomisation was slightly unbalanced, with more patients in the control group than in the intervention group.

Other issues: 89% (445/500) of patients were treated with intravenous alteplase before randomisation. An additional 2 patients were randomised to the control group but consent was withdrawn immediately and they were not included in the analysis. A total of 30 patients assigned to intra-arterial treatment had a simultaneous second revascularisation procedure (acute cervical carotid stenting).

Key efficacy and safety findings

Efficacy

Number of patients analysed: 500 (233 versus 267)

Primary and secondary outcomes and treatment effects

Outcome	Intervention n=233	Control n=267	Effect variable	Unadjusted value (95% CI)	Adjusted value (95% CI)
Primary outcome: median modified Rankin scale score at 90 days (IQR)	3 (2 to 5)	4 (3 to 5)	Common odds ratio	1.66 (1.21 to 2.28)	1.67 (1.21 to 2.30)
Secondary outcomes – clinical outcomes					
Modified Rankin score of 0 or 1 at 90 days, no. (%)	27 (11.6)	16 (6.0)	Odds ratio	2.06 (1.08 to 3.92)	2.07 (1.07 to 4.02)
Modified Rankin score of 0–2 at 90 days, no. (%)	76 (32.6)	51 (19.1)	Odds ratio	2.05 (1.36 to 3.09)	2.16 (1.39 to 3.38)
Modified Rankin score of 0–3 at 90 days, no. (%)	119 (51.1)	95 (35.6)	Odds ratio	1.89 (1.32 to 2.71)	2.03 (1.36 to 3.03)
NIHSS score after 24 hours, median (IQR)	13 (6 to 20)	16 (12 to 21)	Beta	2.6 (1.2 to 4.1)	2.3 (1.0 to 3.5)
NIHSS score at 5–7 days or discharge, median (IQR)	8 (2 to 17)	14 (7 to 18)	Beta	3.2 (1.7 to 4.7)	2.9 (1.5 to 4.3)
Barthel Index of 19 or 20 at 90 days, no. (%)	99/215 (46.0)	73/245 (29.8)	Odds ratio	2.0 (1.3 to 2.9)	2.1 (1.4 to 3.2)
EQ-5D score at 90 days, median (IQR)	0.69 (0.33 to 0.85)	0.66 (0.30 to 0.81)	Beta	0.08 (0.00 to 0.15)	0.06 (-0.01 to 0.13)
Imaging outcomes					
No intracranial occlusion on follow-up CT angiography, no. (%)	141/187 (75.4)	68/207 (32.9)	Odds ratio	6.27 (4.03 to 9.74)	6.88 (4.34 to 10.94)
Final infarct volume at 3–9 days on CT, median (IQR) ml	49 (22 to 96), n=138	79 (34 to 125), n=160	Beta	20 (3 to 36)	19 (3 to 34)

The NIHSS score was determined for survivors only; 56 patients died before assessment was finished and 18 had missing scores.

Data for follow-up CT angiography were not available for 106 patients because of imminent death or death (n=24), decreased kidney function (n=13), insufficient scan quality (n=5), and other reasons (n=64).

Data on final infarct volume were missing for 202 patients because of death (n=52), hemicraniectomy (n=21), technical errors (n=14), insufficient scan quality (n=5), other reasons (n=110).

Median time from stroke onset to groin puncture=260 minutes (IQR, 210–313)

Safety

Safety variables and serious adverse events within 90 days after randomisation, n(%)

Variable	Intervention n=233	Control n=267
Death		
Within 7 days	27 (11.6)	33 (12.4)
Within 30 days	44 (18.9)	49 (18.4)
Hemicraniectomy	14 (6.0)	13 (4.9)
Any serious adverse event	110 (47.2)	113 (42.3)
Symptomatic intracerebral haemorrhage		
Any type	18 (7.7)	17 (6.4)
Parenchymal haematoma type 1	0	2 (0.7)
Parenchymal haematoma type 2	14 (6.0)	14 (5.2)
Haemorrhagic infarction - type 1	1 (0.4)	0
Haemorrhagic infarction - type 2	1 (0.4)	1 (0.4)
Subarachnoid haemorrhage	2 (0.9)	0
New ischaemic stroke in a different vascular territory*	13 (5.6)	1 (0.4)
Progressive ischaemic stroke	46 (19.7)	47 (17.6)
Pneumonia	25 (10.7)	41 (15.4)
Other infection	16 (6.9)	9 (3.4)
Cardiac ischaemia	1 (0.4)	4 (1.5)
Extracranial haemorrhage	0	2 (0.7)
Allergic reaction	1 (0.4)	0
Other complication	22 (9.4)	33 (12.4)

*p<0.001

Procedure-related complications in the intervention group: embolisation into new territories, 8.6% (20/233); vessel dissection, 1.7% (4/233); vessel perforation, 0.9% (2/233).

Abbreviations used: CI, confidence interval; EQ-5D, EuroQol Group 5-Dimension self-report questionnaire; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale

Study 2 Campbell BCV (2015)

Details

Study type	**Randomised controlled trial (EXTEND-IA)**
Country	Australia and New Zealand (10 centres)
Recruitment period	2012–4
Study population and number	**n=70** (35 endovascular therapy versus 35 alteplase only) Patients with anterior circulation ischaemic stroke with occlusion of the internal carotid artery or of the first or second segment of the middle cerebral artery.
Age and sex	Mean age 69 years; 49% (34/70) male
Patient selection criteria	Patients were eligible if they could receive intravenous alteplase within 4.5 hours after the onset of anterior circulation ischaemic stroke and had occlusion of the internal carotid artery or of the first or second segment of the middle cerebral artery, as seen on CT angiography. CT perfusion imaging was used to identify potentially salvageable brain tissue. Endovascular therapy had to be initiated within 6 hours after stroke onset and completed within 8 hours after onset. Patients were required to have functional independence before the stroke episode.
Technique	The use of conscious sedation or general anaesthesia for endovascular treatment was at the discretion of the neurointerventionist. A Solitaire FR retrievable stent (Covidien) was used for all patients in the intervention group.
Follow-up	**90 days**
Conflict of interest/source of funding	Supported by grants from the Australian National Health and Medical Research Council of Australia, Royal Australasian College of Physicians, Royal Melbourne Hospital Foundation, and the National Heart Foundation of Australia, and by infrastructure funding from the state government of Victoria. The Solitaire FR device and trial infrastructure were provided under an unrestricted grant from Covidien.

Analysis

Follow-up issues: No losses to follow-up were described.

Study design issues: Randomised, open-label, blinded-end-point study. The plan was to enrol 100 patients but recruitment into the trial was suspended after the release of the results of the MR CLEAN study. Data for the 70 enrolled patients were analysed and the trial was stopped for efficacy. The early termination of the trial creates potential for overestimation of the effect size, but the authors noted that details of the statistical stopping rule were highly conservative. All analyses were based on the intention-to-treat principle. The coprimary outcomes were reperfusion (defined as the percentage reduction in the perfusion-lesion volume between initial imaging and imaging at 24 hours) and early neurological improvement (defined as a reduction of 8 points or more on the NIHSS, which ranges from 0 [normal] to 42 [death] or a score of 0 or 1 at 3 days).

Study population issues: There were no significant differences between the 2 groups with regard to baseline characteristics. The majority of the thrombus had been lysed before angiography in 11% (4/35) of patients in the endovascular treatment group. Four other patients in the endovascular treatment group did not have thrombectomy because they had major clinical improvement, deterioration, stenting of the extracranial internal carotid artery to obtain access achieved an adequate flow, or the procedure was terminated before deployment of the stent retriever because of vessel perforation.

Other issues: All patients received alteplase as standard care.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **70 (35 vs 35)**

	Endo-vascular therapy group	Control group	Effect size (95% CI)			
			Adjusted odds ratio	p value	unadjusted odds ratio	p value
Primary outcomes						
Median reperfusion at 24 hours (IQR), %	100 (100 to 100)	37 (-0.5 to 96)	4.7 (2.5 to 9.0)	<0.001	4.9 (2.5 to 9.5)	<0.001
Early neurological improvement (8 points or more reduction on NIHSS or a score of 0 or 1 at day 3), no. (%)	28 (80)	13 (37)	6.0 (2.0 to 18.0)	0.002	6.8 (2.3 to 20)	<0.001
Secondary outcomes						
Median modified Rankin scale score at 90 days (IQR)	1 (0 to 3)	3 (1 to 5)	2.0	0.02	2.1 (1.2 to 3.8)	0.006
Independent outcome, no. (%)	25 (71)	14 (40)	4.2 (1.4 to 12)	0.01	3.8 (1.4 to 10.0)	0.009
Excellent outcome, no. (%)	18 (51)	10 (29)	2.4 (0.87 to 6.6)	0.09	2.6 (1.0 to 7.1)	0.05
Tertiary outcomes						
Reperfusion of >90% at 24 hours without symptomatic intracerebral haemorrhage, no. (%)	31 (89)	12 (34)	27.0 (5.5 to 135.0)	<0.001	15.0 (4.0 to 52.0)	<0.001
Recanalisation at 24 hours (partial or complete restoration of flow at the site of occlusion), no. (%)	33 (94)	15 (43)	29.0 (5.4 to 155.0)	<0.001	22.0 (4.5 to 106.0)	<0.001
Median infarct growth at 24 hours (IQR), ml	10.9 (0 to 23.6)	35.3 (6.3 to 73.4)	-0.44 (-0.76 to -0.13)*	0.007	-	-
Median home time (IQR) (adjusted for NIHSS score and age at baseline), days	73 (47 to 86)	15 (0 to 69)	64 (28 to 90)*	0.001	58 (17 to 90)*	0.006

* Effect size is the median difference rather than odds ratio

Median time from stroke onset to groin puncture=210 minutes (IQR, 166–251)

Safety

Safety outcomes

Death

- Endovascular therapy=9% (3/35) (2 of the 3 patients had a deterioration in their condition during the initial alteplase infusion before angiography because of a second cerebral embolism)
- Control=20% (7/35), p=0.31 (adjusted)

Symptomatic intracerebral haemorrhage

- Endovascular therapy=0% (0/35)
- Control=6% (2/35) (both patients died), p=0.49 (unadjusted)

Parenchymal haematoma

- Endovascular therapy=11% (4/35)
- Control=9% (3/35), p=0.99 (unadjusted)

Embolisation into a different vascular territory occurred in 6% (2/35) of patients treated by endovascular therapy but did not cause any clinical symptoms.

1 patient treated by endovascular therapy had a groin haematoma needing transfusion.

Abbreviations used: CI, confidence interval; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale

Study 3 Goyal M (2015)

Details

Study type	**Randomised controlled trial (ESCAPE)**
Country	Canada, US, South Korea, Ireland, UK (22 centres)
Recruitment period	2013–4
Study population and number	**n=315 (165 endovascular treatment plus standard care versus 150 standard care alone)** Adults with acute ischaemic stroke with a small infarct core, a proximal intracranial occlusion in the anterior circulation, and moderate-to-good intracranial collateral circulation.
Age and sex	Median 71 years (interquartile range 60–81); 48% (150/315) male
Patient selection criteria	Adults with a disabling ischaemic stroke who had been functioning independently in the community (Berthel Index score [range 0–100, with higher scores indicating a greater ability to complete activities of daily living] of 90 or above before the stroke. Enrolment could occur up to 12 hours after the onset of stroke symptoms. Non-contrast CT and CT angiography were done to identify patients with a small infarct core (defined as an Alberta Stroke Program Early Computed Tomography Score [ASPECTS] of 6 to 10), an occluded proximal artery in the anterior circulation, and moderate-to-good collateral circulation.
Technique	The neurointerventionist used available thrombectomy devices to achieve reperfusion. Retrievable stents were used in 86% (130/151) of patients who had endovascular treatment (100 patients received a Solitaire stent [Covidien]). During thrombus retrieval, suction through a balloon guide catheter in the relevant internal carotid artery was also recommended. General anaesthesia was used in 15 patients (9%) who had endovascular treatment. The control group received the current standard of care.
Follow-up	**90 days**
Conflict of interest/source of funding	Supported by Covidien through an unrestricted grant to the University of Calgary. Also supported by the University of Calgary, Alberta Innovates-Health Solutions, the Heart and Stroke Foundation of Canada, and Alberta Health Services.

Analysis

Follow-up issues: 4 (1.3%) patients were lost to follow-up; missing data on outcomes in these patients were not imputed.

Study design issues: Multicentre, prospective, randomised, open-label, controlled trial with blinded outcome evaluation. The primary outcome was the modified Rankin score (range 0 [no symptoms] to 6 [death]), at 90 days, using the intention-to-treat population. A sample size of 500 patients was anticipated, with a formal interim analysis planned after enrolment of 300 patients. The stopping rule for efficacy was defined with the use of O'Brien-Fleming boundaries on the binary outcome of a modified Rankin score at 90 days of 0 to 2 versus 3 to 6. An unplanned interim analysis was done after the release of the MR CLEAN results. The ESCAPE trial was stopped early on the advice of the data and safety monitoring board because the prespecified boundary for efficacy had been crossed. Outcome estimates were adjusted for age, sex, baseline NIHSS score, baseline ASPECTS, occlusion location, and status with respect to intravenous alteplase treatment. Activities of daily living were assessed using the Barthel index (scores range from 0 to 100, with 0 indicating severe disability and 95 or 100 indicating no disability that interferes with daily activities). Health status was measured using the EuroQol Group 5-Dimension self-report questionnaire (EQ-5D), scores range from 0 to 100 with higher scores indicating a better quality of life.

Study population issues: Baseline characteristics were similar in the 2 groups. Imaging protocol violations occurred in 26 patients: 11 patients in whom the ASPECTS score could be evaluated had a score of less than 6 on the ASPECTS scale, 20 patients had poor collateral circulation and 14 patients had inappropriate target-vessel occlusion (a new technique of collateral assessment, multiphase CT angiography, was used in a majority of patients).

Other issues: All patients received intravenous alteplase within 4.5 hours after the onset of stroke symptoms if they met accepted local guidelines for intravenous alteplase treatment. The authors note that a majority of patients were enrolled at selected endovascular centres that are capable of implementing efficient workflow and imaging processes.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **315 (165 versus 150)**

Primary and secondary efficacy outcomes

Outcome	**Intervention n=165**	**Control n=150**	**Effect variable**	**Unadjusted value (95% CI)**	**Adjusted value (95% CI)**
Primary outcome: modified Rankin scale score at 90 days*			Common odds ratio	2.6 (1.7 to 3.8)	3.1 (2.0 to 4.7)
Secondary outcomes – clinical outcomes					
Modified Rankin score of 0–2 at 90 days (indicating functional independence), no. (%)	87/164 (53.0)	43/147 (29.3)	Rate ratio	1.8 (1.4 to 2.4)	1.7 (1.3 to 2.2)
NIHSS score of 0–2 at 90 days, no. (%)	79/153 (51.6)	31/134 (23.1)	Rate ratio	2.2 (1.6 to 3.2)	2.1 (1.5 to 3.0)
Barthel Index score of 95–100 at 90 days, no. (%)	94/163 (57.7)	49/146 (33.6)	Rate ratio	1.7 (1.3 to 2.2)	1.7 (1.3 to 2.2)
TICI score of 2b or 3 at final angiogram (indicating successful reperfusion), no. (%)	113/156 (72.4)				
Modified AOL score of 2 or 3 (indicating partial or complete recanalisation), no. (%)		43/138 (31.2)			
NIHSS score at 24 hours, median (IQR)	6 (3 to 14)	13 (6 to 18)	Beta coefficient	4.0 (2.2 to 5.8)	4.1 (2.6 to5.6)
NIHSS score at 90 days, median (IQR)	2 (1 to 8)	8 (3 to 19)	Beta coefficient	6.5 (3.2 to 9.8)	6.5 (3.5 to 9.6)
EQ-5D score at 90 days, median (IQR)	80 (60–90)	65 (50–80)	Beta coefficient	9.4 (3.5 to 15.2)	9.9 (3.8 to 16.0)

* Odds ratio calculated with the use of multiple regression analyses and indicates the odds of improvement of 1 point on the modified Rankin scale, with a common odds ratio greater than 1 favouring the intervention.

Median time from stroke onset to first reperfusion (defined as the first visualisation of reflow in the middle cerebral artery, usually on deployment of a retrievable stent)=241 minutes (IQR, 176–359)

A total of 49 patients underwent randomisation 6 or more hours after stroke onset; in the analysis of a modified Rankin score of 0 to 2 at 90 days, the direction of effect favoured the intervention in these patients (rate ratio 1.7, 95% CI: 0.7 to 4.0), but the between-group difference was not significant.

Safety

Reported serious adverse events

Death
- Intervention=10.4% (17/164)
- Control=19.0% (28/147),

Rate ratio=0.5 (95% CI 0.3 to 1.0)
Adjusted rate ratio=0.5 (95% CI 0.3 to 0.8)

Large or malignant middle-cerebral-artery stroke
- Intervention=4.8% (8/165)
- Control=10.7% (16/150),

Rate ratio=0.5 (95% CI 0.2 to 1.0)
Adjusted rate ratio=0.3 (95% CI 0.1 to 0.7)

Symptomatic intracerebral haemorrhage
- Intervention=3.6% (6/165)
- Control=2.7% (4/150),

Rate ratio=1.4 (95% CI 0.4 to 4.7)
Adjusted rate ratio=1.2 (95% CI 0.3 to 4.6)

Haematoma at access site
- Intervention=1.8% (3/165)
- Control=0

Perforation of the middle cerebral artery
- Intervention=0.6% (1/165)
- Control=0

Device–related or procedural complications were observed in 18 patients: 4 had a serious adverse event and 14 had a non-serious adverse event.

2 patients were treated by hemicraniectomy: 1 patient in the control group with middle-cerebral-artery ischaemic stroke and 1 patient in the intervention group with symptomatic intracerebral haemorrhage.

Abbreviations used: AOL, Arterial Occlusive Lesion; CI, confidence interval; EQ-5D, EuroQol Group 5-Dimension self-report questionnaire; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; TICI, Thrombolysis in Cerebral Infarction score

Study 4 Saver JL (2015)

Details

Study type	**Randomised controlled trial (SWIFT PRIME)**
Country	US, Canada, France, Germany, Switzerland (39 centres)
Recruitment period	2012–4
Study population and number	**n=196** (98 intravenous tissue plasminogen activator [tPA] and endovascular thrombectomy with a stent retriever versus 98 intravenous tPA alone) Patients with acute ischaemic stroke, with confirmed occlusions in the proximal anterior intracranial circulation and an absence of large ischaemic-core lesions.
Age and sex	Mean 65 years; 51% (99/194) male
Patient selection criteria	Acute ischaemic stroke with moderate-to-severe neurological deficits; imaging-confirmed occlusion of the intracranial internal carotid artery, the first segment of the middle cerebral artery, or both; receiving or had received intravenous tPA; able to undergo initiation of endovascular treatment within 6 hours after the time that they were last known to be well before the onset of stroke symptoms. At trial launch, the entry criteria regarding imaging selection required patients to have a target-mismatch penumbral profile, with a small core of tissue that was likely to be irreversibly injured and a large region of hypoperfused tissue that was likely to be salvageable. The criteria were subsequently revised to use a small-to-moderate core-infarct strategy to accommodate study sites with limited perfusion-imaging capability.
Technique	Mechanical thrombectomy was done with the Solitaire FR or Solitaire 2 stent retriever (Covidien). Concomitant stenting of the cervical internal carotid artery was not permitted, although angioplasty could be done to permit intracranial access. The study target for the time from qualifying imaging to groin puncture was within 70 minutes.
Follow-up	**90 days**
Conflict of interest/source of funding	The trial was funded by Covidien.

Analysis

Study design issues: Multicentre, prospective, randomised, open clinical trial. Primary outcome was the severity of global disability at 90 days, as assessed by the modified Rankin scale with scores ranging from 0 (no symptoms) to 6 (death). Missing final scores on the modified Rankin scale were handled with the use of the last-observation-carried-forward approach when a score was available from the 30-day visit or the visit at 7–10 days. After the preliminary results of the MR CLEAN and the ESCAPE trials were reported, an interim efficacy analysis was done including 196 patients. The study was stopped in February 2015 when the interim efficacy analysis showed that the prespecified stopping-criteria boundary for efficacy had been crossed.

Study population issues: The demographic and clinical characteristics of the 2 groups at baseline were well balanced.

Other issues: All study centres were required to have done at least 40 mechanical thrombectomy procedures, including at least 20 procedures with the Solitaire stent retriever, annually. Study conduct included a continuous quality-improvement programme to improve endovascular workflow efficiency at participating sites.

Key efficacy and safety findings

Efficacy

Number of patients analysed: 196 (98 versus 98)

The stent retriever was deployed in 89% (87/98) of patients in the intervention group.

Primary and secondary outcomes

Outcome	Stent retriever plus intravenous tPA n=98	Intravenous tPA alone n=98	Risk ratio (95% CI)	p value
Modified Rankin scale at 90 days, median score (IQR)	2 (1–4) n=98	3 (2–5) n=93		<0.001
Functional independence at 90 days (score 0 to 2 on the modified Rankin scale)	60% (59/98)	35% (33/93)	1.70 (1.23 to 2.33)	<0.001
Mean change in NIHSS score at 27 hours	-8.5±7.1 n=97	-3.9±6.2 n=92		<0.001
Death at 90 days*	9% (9/98)	12% (12/97)	0.74 (0.33 to 1.68)	0.50
Substantial reperfusion immediately after thrombectomy (defined as reperfusion of at least 50% and a modified TICI score of 2b (50 to 99% reperfusion) or 3 (complete reperfusion).	88% (73/83)	NA	NA	NA
Successful reperfusion at 27 hours (reperfusion of at least 90%, as assessed with the use of perfusion CT or MRI)	83% (53/64)	40% (21/52)	2.05 (1.45 to 2.91)	<0.001

* 1 patient in the control group requested the deletion of all data, including vital status.

Median time from stroke onset to groin puncture=224 minutes (IQR, 165–275)

No evidence of heterogeneity of treatment effect was detected in any of the 8 prespecified subgroups (sex, age, NIHSS score, occlusion location, geographic location, Alberta Stroke Program Early CT score, site of initial administration of tPA [study hospital vs outside hospital], time from onset to randomisation).

Safety

Primary safety outcomes

Any serious adverse event at 90 days

- Stent retriever=36% (35/98)
- Control=31% (30/97)

Risk ratio=1.15 (95% CI: 0.78 to 1.72, p=0.54)

Symptomatic intracranial haemorrhage at 27 hours

- Stent retriever=0
- Control=3% (3/97)

p=0.12

Additional safety outcomes at 27 hours

Parenchymal haematoma

- Stent retriever=5% (5/98)
- Control=7% (7/97)

Risk ratio=0.71 (95% CI: 0.23 to 2.15, p=0.57)

Type 1 parenchymal haematoma

- Stent retriever=4% (4/98)
- Control=3% (3/97)

Risk ratio=1.32 (95% CI: 0.30 to 5.74, p=1.00)

Type 2 parenchymal haematoma

- Stent retriever=1% (1/98)
- Control=4% (4/97)

Risk ratio=0.25 (95% CI: 0.03 to 2.17, p=0.21)

Subarachnoid haemorrhage

- Stent retriever=4% (4/98)
- Control=1% (1/97)

Risk ratio=3.96 (95% CI: 0.45 to 34.79, p=0.37)

No serious adverse events and 7 nonserious adverse events were considered to be device-related. The most common nonserious device-specific adverse event was transient, intraprocedural vasospasm without clinical sequelae.

Abbreviations used: CI, confidence interval; IQR, interquartile range; NA, not applicable; NIHSS, National Institutes of Health Stroke Scale; TICI, Thrombolysis in Cerebral Infarction score

Study 5 Jovin TG (2015)

Details

Study type	**Randomised controlled trial (REVASCAT)**
Country	Spain (4 centres)
Recruitment period	2012–4
Study population and number	**n=206 (103 medical therapy and endovascular treatment with the Solitaire stent retriever versus 103 medical therapy alone)** Patients with acute ischaemic stroke and an occlusion in the proximal anterior circulation that could be treated within 8 hours after symptom onset.
Age and sex	Mean 66 years; 53% (109/206) male
Patient selection criteria	Age between 18 and 80 years; an occlusion in the proximal anterior circulation that could be treated within 8 hours after symptom onset; prestroke functional ability of 1 or less on the modified Rankin scale (ranging from 0=no symptoms to 6=death); baseline score of at least 6 points on the National Institutes of Health Stroke scale (ranging from 0 to 42, with higher values indicating more severe deficit). The main exclusion criteria on imaging were evidence of a large ischaemic core, as indicated by an Alberta Stroke Programme Early Computed Tomography Score (ASPECTS, range 0–10 with higher values indicating less infarct burden) of less than 7 on CT without the use of contrast material or a score of less than 6 on diffusion-weighted MRI. After the enrolment of 160 patients, the inclusion criteria were modified to include patients up to the age of 85 years with an ASPECTS score of more than 8.
Technique	Thrombectomy device – Solitaire stent retriever (Covidien)
Follow-up	**90 days**
Conflict of interest/source of funding	The study was funded by an unrestricted grant from Covidien (the manufacturer of the stent retriever).

Analysis

Follow-up issues: All patients had an available evaluation at 90 days for the primary outcome.

Study design issues: Multicentre, prospective, randomised, sequential, open-label phase 3 study with blinded evaluation. Thrombectomy was compared with medical therapy alone in eligible patients who had received intravenous alteplase within 4.5 hours after the onset of symptoms without revascularisation after 30 minutes of alteplase transfusion or who had a contraindication to intravenous alteplase. The primary outcome was the severity of disability at 90 days, according to the modified Rankin scale. All analyses were done in the intention-to-treat population. The study aimed to enrol 690 patients for a power of 90% to detect a difference in the distribution of scores on the modified Rankin scale with a 1-sided significance level of 0.025, assuming an expected result of an odds ratio of 1.615. The first interim analysis was done as planned after 25% of patients had completed 90 days of follow-up. Recruitment to the study was stopped because of loss of equipoise after the results from 3 other studies were released. One patient withdrew consent immediately after randomisation and was not included in the analysis. Symptomatic intracranial haemorrhage was defined as parenchymal haemorrhage type 2 and neurological deterioration ≥4 points on NIHSS, according to the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST) criteria, or any symptomatic intracranial haemorrhage and neurological deterioration ≥4 points on NIHSS, according to the European-Australasian Acute Stroke Study (ECASS II) criteria.

Study population issues: There were no significant differences in baseline characteristics between the 2 groups. Intravenous alteplase was given to 68% of patients in the thrombectomy group and 78% of those in the control group.

Other issues: Study sites were stroke centres that treat more than 500 patients with acute stroke and do more than 60 mechanical stroke thrombectomy procedures annually and are staffed by trained neurointerventionalists who are required to have done at least 20 thrombectomies with the Solitaire device.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **206 (103 vs 103)**

Primary and secondary clinical and imaging outcomes

Outcome	Thrombectomy n=103	control n=103	Effect variable	Unadjusted value (95% CI)	Adjusted value (95% CI)
Modified Rankin scale score at 90 days			Common odds ratio	1.7 (1.04 to 2.7)	1.7 (1.05 to 2.8)
Score of 0–2 on modified Rankin scale at 90 days	43.7%	28.2%	Odds ratio	2.0 (1.1 to 3.5)	2.1 (1.1 to 4.0)
Dramatic neurological improvement at 24 hours (reduction of ≥8 points on NIHSS or score of 0–2)	59% 59/100	20% 20/100	Odds ratio	5.5 (2.9 to 10.3)	5.8 (3.0 to 11.1)
Median NIHSS score at 90 days (IQR)	2.0 (0.0 to 8.0)	6.0 (2.0 to 11.0)	Beta	-2.7 (-4.4 to -0.9)	-2.4 (-4.1 to -0.8)
Barthel Index score of 95-100 at 90 days (range 0–100, higher scores indicate good performance of daily living activities)	57.3% 47/82	26.4% 23/87	Odds ratio	3.7 (2.0 to 7.1)	4.2 (2.1 to 8.4)
Median EQ-5D score at 90 days (IQR) (range -0.33–1 with higher scores indicating a better quality of life)	0.65 (0.21 to 0.79)	0.32 (0.13 to 0.70)	Beta	0.13 (0.03 to 0.23)	0.11 (0.02 to 0.21)
Infarct volume at 24 hours, median (IQR), ml	16.3 (8.3 to 58.5)	38.6 (11.9 to 86.8)	p value		0.02

The median time from stroke onset to randomisation was 225 minutes.

Safety

Serious adverse events within 90 days

Death at 90 days
- Thrombectomy=18.4% (19/103)
- Control=15.5% (16/103)

Risk ratio=1.2 (95% CI: 0.6 to 2.2)

Death at ≤7 days
- Thrombectomy=9.7% (10/103)
- Control=4.9% (5/103)

Risk ratio=2.0 (95% CI: 0.7 to 5.6)

Symptomatic intracranial haemorrhage – SITS-MOST criteria
- Thrombectomy=1.9% (2/103)
- Control=1.9% (2/103)

Risk ratio=1.0 (95% CI: 0.1 to 7.0)

Symptomatic intracranial haemorrhage – ECASS II criteria
- Thrombectomy=4.9% (5/103)
- Control=1.9% (2/103)

Risk ratio=2.5 (95% CI: 0.5 to 12.6)

Asymptomatic intracranial haemorrhage
- Thrombectomy=16.5% (17/103)
- Control=10.7% (11/103)

Risk ratio=1.5 (95% CI: 0.7 to 3.1)

Subarachnoid haemorrhage
- Thrombectomy=4.9% (5/103)
- Control=1.9% (2/103)

Risk ratio=2.5 (95% CI: 0.5 to 12.6)

Parenchymal haematoma
- Thrombectomy=5.8% (6/103) (3 type 1, 3 type 2)
- Control=5.8% (6/103) (4 type 1, 2 type 2)

Neurological worsening
- Thrombectomy=15.5% (16/103)
- Control=12.6% (13/103)

Risk ratio=1.2 (95% CI: 0.6 to 2.4)

Malignant cerebral oedema
- Thrombectomy=10.7% (11/103) (treated by decompressive hemicraniectomy in 3 patients)
- Control=9.7% (10/103) (treated by decompressive hemicraniectomy in 6 patients)

Risk ratio=1.1 (95% CI: 0.5 to 2.5)

Recurrent stroke
- Thrombectomy=3.9% (4/103)
- Control=2.9% (3/103)

Risk ratio=1.3 (95% CI: 0.3 to 5.8)

Procedure-related complications
- Distal embolization in a different territory=4.9% (5/103)
- Arterial dissection=3.9% (4/103)
- Arterial perforation=4.9% (5/103)
- Groin haematoma=10.7% (11/103)
- Groin pseudoaneurysm=1.0% (1/103)
- Vasospasm needing treatment=3.9% (4/103)

Abbreviations used: CI, confidence interval; ECASS-II, European-Australasian Acute Stroke Study; EQ-5D, EuroQol Group 5-Dimension self-report questionnaire; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; SITS-MOST, Safe Implementation of Thrombolysis in Stroke-Monitoring Study

Study 6 Ahmad N (2013)

Details

Study type	**Case series (prospective register)**
Country	UK
Recruitment period	2009–13
Study population and number	**n=106** Patients with acute ischaemic stroke.
Age and sex	Mean 64 years; 60% (64/106) male
Patient selection criteria	Mechanical thrombectomy was considered in patients under the age of 80 who were previously fit and well and who have an occlusion of a treatable intracranial artery. Patients should be within 4.5 hours of onset of anterior circulation symptoms and within 10.5 hours of posterior circulation symptoms. Patients older than 80 years were considered on an individual basis.
Technique	Mechanical thrombectomy was done under general anaesthesia or sedation, using a stent-based thrombus retrieval device. Suction by hand aspiration or using the Penumbra Aspiration Pump (Penumbra Inc., Alameda, USA) was used in more proximal lesions. Devices used for thrombectomy were Solitaire AB/FR™ (EV3, Covidien, USA) (n=63), Acandis APERIO (Pforzheim, Germany) (n=20), Revive SE™ (Codman & Shurtleff Inc., USA) (n=14), pRESET (Phenox, Bochum, Germany) (n=1) and aspiration via a distal catheter (n=13). More than 1 type of device was used in 18 interventions.
Follow-up	**90 days**
Conflict of interest/source of funding	The authors had no support or funding to report. One author received free thrombectomy devices for in-vitro experiments from device manufacturers, honoraria for lectures and sponsorship for conferences and lectures from Boehringer, the manufacturer of alteplase. One author advised on device design and had a consultant contract with Covidien, Codman and Acandis. One author received travel expenses and honoraria for lectures and sponsorship for conferences and lectures from Boehringer. One author received travel expenses and accommodation for one conference from Boehringer. One author was once sponsored for an animal lab educational workshop by EV3 for stroke thrombectomy.

Analysis

Study design issues: Data recorded included the National Institutes for Health Stroke Scale (NIHSS), with a score of 35 used for unconscious and ventilated patients and 42 for patients who were no longer alive at the time of assessment, the Thrombolysis in Myocardial Infarction (TIMI) score (0=no recanalisation of the primary occlusive lesion; I=minimal recanalisation; II=incomplete or partial recanalisation; III=complete recanalisation), and the Thrombolysis in Cerebral Infarction (TICI) score (0=no perfusion or antegrade flow; 1=penetration with minimal perfusion; 2a=partial reperfusion in <50% of the vascular territory; 2b=partial reperfusion in >50% of the vascular territory; 3=complete reperfusion).Symptomatic intracranial haemorrhage included contrast extravasation because of the difficulty in distinguishing contrast extravasation and haemorrhage on plain CT head scan. The modified Rankin score was assessed at 90 days by telephone or in person by a member of the research team not involved in the intervention to establish functional outcome.

Study population issues: Most of the patients had severe strokes (median NIHSS 18, IQR 13–23) before the intervention; 63% had a total anterior circulation syndrome; 8% had a brain stem stroke, were unconscious, and needed ventilation before the procedure. 78% of occlusions were in the anterior circulation.

Other issues: Bridging intravenous thrombolysis with alteplase was given as soon as eligibility was confirmed as a 10% bolus and 90% infusion up to 6 hours after symptom onset for major vessel occlusion in the anterior circulation and up to 12 hours after basilar artery occlusion. An additional 3 patients were prepared for thrombectomy but recovered after intravenous thrombolysis alone and were not included in the register. Intraarterial thrombolysis without thrombectomy was done in 14 patients, usually when the only occluded vessel was more distal. It was impossible to gain access to the carotid artery for endovascular treatment in 4 patients and in 2 patients, the vessel had recanalised with intravenous

thrombolysis at the time of the catheter angiogram and no visible occlusion remained. 20 patients needed angioplasty and/or stenting.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **106** 83% of patients had thrombectomy with or without intraarterial thrombolysis, 13% had intraarterial thrombolysis alone and 4% of patients had neither. Intravenous bridging thrombolysis was done in 81% of patients. **Outcomes** • Partial/full recanalisation (TICI 2b or 3)=84% (89/106) • Partial/full recanalisation (TIMI 2 or 3)=89% (94/106) • Median change in NIHSS at 1 week (higher score indicates more severe symptoms)=-10 • Mortality at 1 week=6% (6/106) • Mortality at 90 days=15% (16/106) • Modified Rankin score ≤2 at 90 days=48% (51/106) • Modified Rankin score ≤3 at 90 days=58% (62/106) Median time from stroke onset to end of procedure=363 minutes (IQR, 307–422)	**Procedure-related complications** • Vasospasm in the internal carotid artery=9% (10/106) • Vasospasm in other vessels=8% (9/106) • Distal clot propagation=8% (8/106) • Dissection of the access vessel=4% (4/106) • Dissection of the target vessel=5% (5/106) (all 5 patients also had subarachnoid haemorrhage) • Subarachnoid haemorrhage=6% (6/106) • Device malfunction=3% (3/106) (unintended stent detachments) • Transient contrast leak without subarachnoid haemorrhage=1% (1/106) **Complications within the first week after the procedure** • Asymptomatic intracranial haemorrhage=25% (27/106) • Symptomatic intracranial haemorrhage=9% (10/106) • Cerebral oedema with midline shift=14% (15/106) • Transient asymptomatic contrast nephropathy=2% (2/106) **Complications within 90 days** • Deep vein thrombosis=7% (7/106) • Pulmonary embolism=4% (4/106)
Abbreviations used: IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; TICI, Thrombolysis in Cerebral Infarction score; TIMI, Thrombolysis in Myocardial Infarction score	

Study 7 and 8 Akins PT (2014), Saver (2012) (study included in 2013 overview)

Details

Study type	**Randomised controlled trial (SWIFT)**
Country	USA (18 centres)
Recruitment period	2010–1
Study population and number	**n=113** (58 Solitaire [stent retriever device] group vs 55 Merci [coil retrieval device] group) + 31 patients treated by Solitaire (non-randomised roll-in phase) Patients with acute ischaemic stroke.
Age and sex	Mean age: 67 years (randomised groups), 65 years (Solitaire non-randomised group) Sex: 48% vs. 51% males (Solitaire vs Merci group), 42% male (Solitaire non-randomised group)
Patient selection criteria	Patients who had acute ischaemic stroke with moderate to severe neurological deficits, harboured angiographically confirmed occlusions of proximal cerebral arteries, and were treatable by thrombectomy within 8 hours of stroke symptom onset. Key inclusion criteria included age (22–85 years), NIHSS score (≥8 and ≤30), and ineligibility for or failure to respond to intravenous rtPA. Key exclusion criteria included uncontrolled hypertension, serious sensitivity to radiographic contrast agents, and CT or MRI evidence of intracranial haemorrhage or major ischaemic infarction (acute ischaemic change in more than a third of the middle cerebral artery territory or more than 100 mL of tissue in other territories).
Technique	A neurointerventionalist attempted recanalisation using the assigned device type, continuing until successful recanalisation was achieved or until 3 passes of the study group device through any vessel has been done. After the primary end point outcome angiogram was done, rescue treatment (using another approved thrombectomy device/intra-arterial fibrinolysis) was permitted in patients in whom adequate recanalisation had not been achieved. Devices: Solitaire Flow Restoration Device (Covidien/ev3, Ireland), Merci Retriever (Stryker, USA)
Follow-up	**90 days**
Conflict of interest/source of funding	Funding was received from Covidien/eV3, BrainsGate, CoAxia, Grifols/Talecris, Ferrer, Mitsubishi, Genervon, Benechill, Asubio, and Sygnis.

Analysis

Study design issues: The focus of the study was to compare the efficacy and safety of 2 different devices used for clot removal in acute ischaemic stroke. The primary endpoint was Thrombolysis in Myocardial Ischaemia (TIMI) scale 2 or 3 flow in all treatable vessels without symptomatic intracranial haemorrhage, after up to 3 passes of the assigned device, as assessed by an independent core laboratory that was blinded to study assignment. Primary analysis was done by intention to treat. A prespecified efficacy stopping rule triggered an early halt to the trial. Symptomatic intracranial haemorrhage was defined as any parenchymal haematoma, subarachnoid haemorrhage, or intraventricular haemorrhage associated with a worsening of the NIHSS score by ≥4 within 24 hours.

Study population issues: There were more patients with atrial fibrillation, history of previous visual disturbance, and presentation with confusion in the Merci group (before adjustment for multiple comparisons).

Other issues: All the study sites were experienced in Merci procedures but 17 of the 18 centres had not used the Solitaire device before the brief roll-in phase of the study. The efficacy data were extracted from Saver JL (2012) and safety data were extracted from Akins PT (2014), which included more details of the major periprocedural complications.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **113 (58 stent retriever vs 55 coil retriever), 31 (stent retriever group non-randomised)**

Efficacy endpoints

	Stent retriever, roll-in n=31	Stent retriever n=58	Coil retriever n=55	Odds ratio (95% CI)	non-inferiority p value	superiority p value
Successful recanalisation without symptomatic ICH	55% (16/29)	61% (34/56)	24% (13/54)	4.87 (2.14 to 11.10)	<0.0001	0.0001
Angiographic efficacy endpoints						
Successful recanalisation with study device (assessed by core laboratory)	63% (17/27)	69% (37/54)	30% (16/53)	5.03 (2.22 to 13.66)	<0.0001	0.0001
Successful recanalisation with study device (assessed at study site)	77% (24/31)	83% (45/54)	48% (26/54)	5.38 (2.21 to 13.15)	<0.0001	0.0002
Use of rescue treatment	23% (7/31)	21% (12/58)	44% (24/55)	0.34 (0.15 to 0.77)	<0.0001	0.015
Successful recanalisation at end of procedure (assessed at study site)	94% (29/31)	89% (48/54)	67% (37/55)	3.89 (1.41 to 10.78)	<0.0001	0.01
Clinical efficacy endpoints at 90 days						
Good neurological outcome	63% (17/27)	58% (32/55)	33% (16/48)	2.78 (1.25 t0 6.22)	0.0001	0.017
Independent	44% (12/27)	36% (20/55)	29% (14/48)	1.39 (0.61 to 3.18)	0.0312	0.53
Modified Rankin scale score, median (IQR)	3 (1–4)	3 (1–4)	4 (2–6)			0.035
Activities of daily living (Barthel index), median (IQR)	80 (10 to 100)	70 (15 to 100)	22.5 (0 to 100)			0.054
Neurological deficit (NIHSS), median (IQR)	3.0 (1.0 to 15.0)	4.5 (1.0 to 12.5)	30.0 (2.0 to 42.0)			0.007

Safety

Major procedural complications

	Stent retriever	Coil retriever	p value
SAH symptomatic	1.1% (1/89)	7.3% (4/55)	0.07
SAH asymptomatic	3.4% (3/89)	5.5% (3/55)	0.67
IVH symptomatic	0	1.8% (1/55)	0.38
ICH symptomatic	1.1% (1/89)	10.9% (6/55)	0.013
ICH asymptomatic	27.0% (24/89)	27.3% (15/55)	1.00
Ischaemic stroke symptomatic	3.4% (3/89)	12.7% (7/55)	0.044
Air emboli	1.1% (1/89)	1.8% (1/55)	1.00
Emboli to same vascular territory	4.5% (4/89)	5.5% (3/55)	1.00
Emboli to new vascular territory	0	1.8% (1/55)	0.38
Device detachment	0	0	1.00
Vessel dissection*	4.5% (4/89)	1.8% (1/55)	0.65
Vessel vasospasm on angiography	22.5% (20/89)	16.4% (9/55)	0.40
Vessel vasospasm symptomatic	0	0	1.00
Major access site issues	7.9% (7/89)	3.6% (2/55)	0.48
Study device related adverse event	10.1% (9/89)	16.4% (9/55)	0.31
Ancillary device related adverse event	7.9% (7/89)	3.6% (2/55)	0.48
Technical difficulty with device	10.1% (9/89)	7.3% (4/55)	0.77

1 of the air emboli was determined to be a serious adverse event.
6 patients were treated by hemicraniectomy.
* 3 were managed conservatively, 1 was treated by balloon angioplasty and 1 was treated by stent placement.

Death from any cause by 90 days
- Stent (roll-in)=16% (5/31)
- Stent (randomised)=17% (10/58)
- Coil=38% (21/55)

Odds ratio=0.34 (95% CI 0.14 to 0.81), p=0.02

Abbreviations used: CI, Confidence interval; ICH, intracranial haemorrhage; IVH, intraventricular haemorrhage; PH, parenchymal haematoma; SAH, subarachnoid haemorrhage

Study 9 Geuzebroek GSC (2015)

Details

Study type	**Case report**
Country	The Netherlands
Recruitment period	Not reported
Study population and number	**n=1** Patient with acute ischaemic stroke treated by mechanical thrombectomy.
Age and sex	65 year old male
Patient selection criteria	Not applicable
Technique	Device: Trevo retrievable stent (Concentral Medical Inc.)
Follow-up	**6 days**
Conflict of interest/source of funding	None

Key efficacy and safety findings

Trapped cerebral thrombectomy device

The patient presented with a gaze preference towards the left, aphasia and a right-sided hemiparesis. CT angiography showed an occluded middle cerebral artery, and intravenous thrombolysis was initiated within 1.5 hours of stroke onset. The patient was included in the MR CLEAN trial and mechanical intra-arterial thrombectomy was started within 4 hours of symptom onset.

Angiography showed 99% stenosis of the proximal left internal carotid artery with insufficient space to pass with the catheter for the retrieval device. A stent was implanted to overcome the stenosis and a micro-catheter was positioned in the middle cerebral artery distal to the thrombus. The thrombus was mechanically extracted using a retrievable stent (Trevo device). As the retriever was being pulled out, the patient became agitated and moved his head. The Trevo device was trapped in the carotid stent and surgical removal was necessary. A carotid endarterectomy was done and the carotid stent was removed with the trapped Trevo device inside. The patient showed no clinical deterioration and was discharged from hospital 6 days later.

Study 10 Macke JJ (2014)

Details

Study type	**Case reports**
Country	USA
Recruitment period	Not reported
Study population and number	**n=2** Patients with acute ischaemic stroke treated by a stent retriever.
Age and sex	Both patients were in their 50s.
Patient selection criteria	Not applicable
Technique	Device: Solitaire stent retriever and penumbra aspiration system
Follow-up	**8 and 13 months**
Conflict of interest/source of funding	None

Key efficacy and safety findings

Delayed stenosis

2 cases of delayed post-embolectomy stenosis (a new stenosis in the vascular bed of a previous endovascular embolectomy). The first case was discovered incidentally in a patient returning after embolectomy for evaluation of cerebral aneurysms. The patient had an upper basilar artery occlusion that was treated by mechanical clot retrieval using a stent retriever. There was complete recanalisation after 2 passes of the device and the patient was discharged home without deficits on day 7. An angiogram was done 5 months later to evaluate cerebral aneurysms that were seen on the initial angiograms. A severe concentric stenosis of the basilar artery was seen, proximal to the level of the initial occlusion.

The second case was discovered on an MR angiogram obtained to screen for stenosis. The patient had a distal left vertebral artery occlusion and a hypoplastic distal right vertebral artery. Mechanical clot retrieval was done using a stent retriever and an aspiration system. After the procedure, the left vertebral artery was widely patent with no evidence of intimal injury. The patient had an MR angiogram 6 months later, which showed a severe (70+%) stenosis of the left vertebral artery at the vertebrobasilar junction.

Both patients were asymptomatic at follow-up, and being treated medically.

Study 11 Backaus R (2014)

Details

Study type	**Case report**
Country	Germany
Recruitment period	Not reported
Study population and number	**n=1** Patients with acute ischaemic stroke treated by a stent retriever.
Age and sex	78- year old woman
Patient selection criteria	Not applicable
Technique	Device: retractable stent (Solitaire)
Follow-up	**7 days**
Conflict of interest/source of funding	None

Key efficacy and safety findings

Hyperperfusion syndrome

A 78-year old woman with acute ischaemic stroke was treated by mechanical clot retrieval using a stent retriever (Solitaire), which resulted in complete and successful recanalisation of middle cerebral artery about 210 minutes after symptom onset. There was partial dislocation of thrombotic material into the anterior cerebral artery and treatment using tirofiban was initiated for 24 hours. After frustrated weaning from ventilation, MRI was done 6 days later and showed corticol swelling of the complete left middle cerebral artery territory sparing the lateral insula, strong diffusion weighted lesions in the anterior cerebral artery and slightly attenuated diffusion abnormality in the left middle cerebral artery territory, and dilated left internal carotid artery and middle cerebral artery vessels. The T2-weighted sequences demonstrated dilated middle cerebral artery branches indicative of compromised vasoreactivity. In absence of severe atherosclerosis and other risk factors, stroke was classified as cardioembolic due to intermittent atrial fibrillation. 7 days after onset, left sided middle cerebral artery flow was still increased to 2m/sec, tracheotomy was done and the patient transferred to neurological rehabilitation with severe left hemispheric deficits.

Study 12 Hui FK (2012)

Details

Study type	**Case reports**
Country	USA
Recruitment period	Not reported
Study population and number	**n=2** Patients with acute ischaemic stroke
Age and sex	Age: '70s' and '80s'
Patient selection criteria	Not applicable
Technique	Device: Penumbra 054 system
Follow-up	**48 hours**
Conflict of interest/source of funding	None

Key efficacy and safety findings

Extravasation

Two patients presenting with acute ischemic stroke were treated via mechanical thrombectomy using the Penumbra 054 system. The first was a tandem occlusion with a high grade narrowing and occlusion of the internal carotid artery (ICA) origin and an ICA terminus thrombus. The second was a long segment, high volume thrombus extending from the cavernous segment to the ICA terminus

Conventional access techniques were utilized to position the Penumbra 054 catheter in the ICA in both cases. Intraprocedurally, angiography through the 054 catheter within the closed segment resulted in contrast extravasation adjacent to the tentorium, originating from the communicating segment of the ICA, both of which cleared within 48 h. Due to the extravasation, the interventions were both terminated, and the infarcts went on to complete.

Efficacy

Functional outcomes

A randomised controlled trial (RCT) of 500 patients treated by intra-arterial treatment (intra-arterial thrombolysis, mechanical clot retrieval, or both) and usual care or usual care alone reported that the median modified Rankin scale score (7-point scale ranging from 0 [no symptoms] to 6 [death]) was significantly lower in the intervention group compared with the control group at 90 days (3 compared with 4, odds ratio 1.67, 95% confidence interval [CI] 1.21 to 2.30)[1]. In the same study, 33% (76/233) of patients in the intervention group had a modified Rankin score of 0 to 2, indicating functional independence, compared with 19% (51/267) of patients in the control group (odds ratio 2.16, 95% CI 1.39 to 3.38). An RCT of 70 patients treated by mechanical clot retrieval with a retrievable stent or thrombolysis alone reported that 80% (28/35) of patients treated by clot retrieval had an improvement of 8 points or more or a score of 0 or 1 at day 3, on the National Institutes of Health Stroke Scale (NIHSS, scores range from 0 [normal] to 42 [death]) compared with 37% (13/35) of patients in the control group (odds ratio 6.0, 95% CI 2.0 to 18.0, p<0.001)[2]. The median modified Rankin scale score at 90 days was 1 compared with 3, p=0.02. An RCT of 315 patients treated by mechanical clot retrieval and standard care or standard care alone reported that 53% (87/164) of patients in the intervention group had a modified Rankin score of 0 to 2, compared with 29% (43/147) of patients in the control group (rate ratio 1.8, 95% CI 1.4 to 2.4)[3]. An RCT of 196 patients treated by intravenous tissue plasminogen activator [tPA] and mechanical clot retrieval with a stent retriever or intravenous tPA alone reported that the median modified Rankin scale score was significantly lower in the intervention group compared with the control group at 90 days (2 compared with 3, p<0.001)[4]. In the same study, 60% (59/98) of patients in the intervention group had a modified Rankin score of 0 to 2 at 90 days, compared with 35% (33/93) of patients in the control group (risk ratio 1.70, 95% CI 1.23 to 2.33, p<0.001)[4]. An RCT of 206 patients treated by mechanical clot retrieval with a stent retriever and medical therapy or medical therapy alone reported that 44% of patients in the intervention group had a modified Rankin score of 0 to 2, compared with 28% of patients in the control group (odds ratio 2.1, 95% CI 1.1 to 4.0)[5]. A case series of 106 patients reported that 48% (51/106) of patients had a modified Rankin score of 2 or less at 90 days[6].

Imaging outcomes

The RCT of 500 patients treated by intra-arterial treatment (intra-arterial thrombolysis, mechanical clot retrieval, or both) and usual care or usual care alone reported that 75% (141/187) and 33% (68/207) of patients respectively had no intracranial occlusion on follow-up CT angiography (odds ratio 6.88, 95% CI 4.34 to 10.94)[1]. The RCT of 70 patients reported the median reperfusion at 24 hours was 100% for patients treated by mechanical clot retrieval with a retrievable stent compared with 37% for patients treated by thrombolysis alone

(odds ratio 4.7, 95% CI 2.5 to 9.0, p<0.001)[2]. 89% (31/35) of patients in the intervention group had reperfusion of more than 90% at 24 hours without symptomatic intracranial haemorrhage compared with 34% (12/35) of patients in the control group. The RCT of 196 patients reported at least 90% reperfusion at 27 hours in 83% (53/64) of patients treated by intravenous tPA and mechanical clot retrieval compared against 40% (21/52) of patients treated by intravenous tPA alone (risk ratio 2.05, 95% CI 1.45 to 2.91, p<0.001)[4]. The RCT of 206 patients treated by mechanical clot retrieval with a stent retriever and medical therapy or medical therapy alone reported median infarct volumes at 24 hours of 16.3 ml and 38.6 ml respectively (p=0.02)[5].

Death

The RCT of 196 patients reported death within 90 days for 9% (9/98) of patients treated by intravenous tPA and mechanical clot retrieval compared against 12% (12/97) of patients treated by intravenous tPA alone (risk ratio 0.74, 95% CI 0.33 to 1.68, p=0.50)[4]. The RCT of 206 patients treated by mechanical clot retrieval with a stent retriever and medical therapy or medical therapy alone reported death within 90 days of 18% (19/103) and 16% (16/103) respectively (risk ratio 1.2, 95% CI 0.6 to 2.2)[5]. The case series of 106 patients reported that 15% (16/106) of patients died within 90 days[6].

Safety

Death

Death within 7 days was reported in 12% (27/233) of patients treated by intra-arterial treatment (intra-arterial thrombolysis, mechanical clot retrieval, or both) with usual care and in 12% (33/267) of patients treated by usual care only in a RCT of 500 patients[1]. Death within 30 days was reported in 19% (44/233) and 18% (49/267) of patients respectively. Death within 7 days was reported in 10% (10/103) of patients treated by mechanical clot retrieval with medical therapy and in 5% (5/103) of patients treated by medical therapy alone in a RCT of 206 patients (risk ratio 2.0, 95% CI 0.7 to 5.6)[5]. Death was reported in 9% (3/35) of patients treated by mechanical clot retrieval with a retrievable stent compared with 20% (7/35) for patients treated by thrombolysis alone (p=0.31) in a RCT of 70 patients[2]. Death was reported in 10% (17/164) of patients treated by mechanical clot retrieval with standard care and in 19% (28/147) of patients treated by standard care alone in a RCT of 315 patients[3]. Death within 1 week was reported in 6% (6/106) of patients in a case series of 106 patients[6].

Symptomatic intracerebral haemorrhage

Symptomatic intracerebral haemorrhage was reported in 8% (18/233) of patients treated by intra-arterial treatment (intra-arterial thrombolysis, mechanical clot retrieval, or both) with usual care and in 6% (17/267) of patients treated by usual care only in the RCT of 500 patients[1]. Hemicraniectomy was done in 6% (14/267) and 5% (13/267) of patients respectively. Symptomatic intracerebral haemorrhage was reported in no patients treated by mechanical clot retrieval with

a retrievable stent and in 6% (2/35) of patients treated by thrombolysis alone (p=0.49) in the RCT of 70 patients: both patients died[2]. Symptomatic intracerebral haemorrhage was reported in 4% (6/165) of patients treated by mechanical clot retrieval with standard care and in 3% (4/150) of patients treated by standard care alone in the RCT of 315 patients (rate ratio 1.2, 95% CI 0.3 to 4.6); 1 patient in the intervention group was treated by hemicraniectomy[3]. Symptomatic intracranial haemorrhage at 27 hours was reported in no patients treated by intravenous tPA with mechanical clot retrieval and in 3% (3/97) of patients treated by intravenous tPA alone (p=0.12) in a RCT of 196 patients[4]. Subarachnoid haemorrhage was reported in 4% (4/98) and 1 patient respectively (p=0.37) and parenchymal haematoma in 5% (5/98) and 7% (7/97) of patients respectively, in the same study. Symptomatic intracranial haemorrhage diagnosed using the SITS-MOST criteria was reported in 2% (2/103) of patients both in the mechanical clot retrieval with medical therapy group and in the patients treated by medical therapy alone in the RCT of 206 patients; when ECASS II criteria were used, the rates were 5% (5/103) and 2% (2/103) respectively (risk ratio 2.5, 95% CI 0.5 to 12.6)[5]. Subarachnoid haemorrhage was reported in 5% (5/103) and 2% (2/103) of patients respectively and parenchymal haematoma was reported in 6% (6/103) of patients in both groups, in the same study. Symptomatic intracranial haemorrhage within the first week after the procedure was reported in 9% (10/106) of patients in the case series of 106 patients; subarachnoid haemorrhage was reported in 6% (6/106) of patients[6]. Symptomatic intracranial haemorrhage was reported in 1 patient treated by mechanical clot retrieval using a stent retriever and in 11% (6/55) of patients treated by mechanical clot retrieval using a coil retriever in a RCT of 113 patients (p=0.013). In the same study, symptomatic subarachnoid haemorrhage was reported 1 patient and 7% (4/55) of patients respectively (p=0.07)[7].

New ischaemic stroke

New ischaemic stroke in a different vascular territory was reported in 6% (13/233) of patients treated by intra-arterial treatment (intra-arterial thrombolysis, mechanical clot retrieval, or both) with usual care and in 1 patient treated by usual care only in the RCT of 500 patients (p<0.001)[1]. Large or malignant middle cerebral artery stroke was reported in 5% (8/165) of patients treated by mechanical clot retrieval with standard care and in 11% (16/150) of patients treated by standard care alone in the RCT of 315 patients (rate ratio 0.3, 95% CI 0.1 to 0.7); 1 patient in the control group was treated by hemicraniectomy[3]. Recurrent stroke was reported in 4% (4/103) of patients treated by mechanical clot retrieval with medical therapy and in 3% (3/103) of patients treated by medical therapy alone in the RCT of 206 patients (risk ratio 1.3, 95% CI 0.3 to 5.8)[5]. Symptomatic ischaemic stroke was reported in 3% (3/89) of patients treated by mechanical clot retrieval using a stent retriever and in 13% (7/55) of patients treated by mechanical clot retrieval using a coil retriever in the RCT of 113 patients (p=0.04)[7].

Embolisation into new territories

Embolisation into new territories was reported in 9% (20/233) of patients treated by intra-arterial treatment (intra-arterial thrombolysis, mechanical clot retrieval, or both) with usual care in the RCT of 500 patients[1]. Asymptomatic embolisation into a different vascular territory occurred in 6% (2/35) of patients treated by mechanical clot retrieval in the RCT of 70 patients[2]. Distal embolisation in a different territory was reported in 5% (5/103) of patients treated by mechanical clot retrieval with medical therapy in the RCT of 206 patients[5].

Vessel dissection or perforation

Vessel dissection and vessel perforation were reported in 2% (4/233) and 1% (2/233) of patients respectively treated by intra-arterial treatment (intra-arterial thrombolysis, mechanical clot retrieval, or both) with usual care in the RCT of 500 patients[1]. Perforation of the middle cerebral artery was reported in 1 patient treated by mechanical clot retrieval in the RCT of 315 patients[3]. Arterial dissection and arterial perforation were reported in 4% (4/103) and 5% (5/103) of patients treated by mechanical clot retrieval in the RCT of 206 patients[5]. Dissection of the access vessel was reported in 4% (4/106) of patients in a case series of 106 patients; dissection of the target vessel was reported in 5% (5/106) – all patients also had subarachnoid haemorrhage[6]. Vessel dissection was reported in 4% (4/89) of patients treated by mechanical clot retrieval using a stent retriever and in 1 patient treated by mechanical clot retrieval using a coil retriever in the RCT of 113 patients (p=0.65): 3 patients were managed conservatively, 1 patient was treated by balloon angioplasty and 1 patient was treated by stent placement[7].

Malignant cerebral oedema

Malignant cerebral oedema was reported in 11% (11/103) of patients treated by mechanical clot retrieval with medical therapy and in 10% (10/103) of patients treated by medical therapy alone in the RCT of 206 patients (risk ratio 1.1, 95% CI 0.5 to 2.5): 3 patients in the intervention group and 6 patients in the control group were treated by decompressive hemicraniectomy[5].

Cerebral hyperperfusion syndrome

Cerebral hyperperfusion syndrome was reported in a case report: the patient deteriorated after successful recanalisation and needed a tracheotomy 7 days after the procedure. The patient was transferred to neurological rehabilitation with severe left hemispheric deficits[11].

Asymptomatic delayed stenosis

Asymptomatic stenosis in the vascular bed of a previous endovascular embolectomy was reported in 2 patients in a case report[10]. In both patients the stenosis was diagnosed on follow-up MR angiogram after 5 and 6 months respectively. Both patients were asymptomatic and were being treated medically at follow-ups of 13 and 8 months respectively.

Device related events

Unintended stent detachment was reported in 3% (3/106) of patients in the case series of 106 patients[6]. Technical difficulty with the device was reported in 10% (9/89) of patients treated by mechanical clot retrieval using a stent retriever and in 7% (4/55) of patients treated by mechanical clot retrieval using a coil retriever in the RCT of 113 patients (p=0.77)[7]. A trapped cerebral thrombectomy device was reported in a case report: the patient was treated by carotid endarterectomy to remove a carotid stent with the trapped clot retrieval device inside. The patient showed no clinical deterioration and was discharged from hospital 6 days later[9].

Validity and generalisability of the studies

- The 5 RCTs only include patients with proximal artery occlusions.
- One of the RCTs used 'intra-arterial treatment' as the intervention, which included intra-arterial thrombolysis, mechanical treatment, or both[1]. In the majority of patients a stent retriever was used.
- One of the RCTs notes that patients were treated early with the use of combined alteplase and mechanical clot retrieval rather than waiting to assess the clinical response to alteplase. This reduced the time lag between stroke onset and initiation of the clot retrieval procedure[2].
- All or most patients received alteplase as standard care in 5 studies[1,2,3,5,6] .
- There are different devices available for mechanical clot retrieval and they are likely to have different safety and efficacy profiles. Most of the patients included in the recent trials described in table 2 were treated by stent retrievers.
- Neuroimaging techniques are evolving and this may have improved patient selection in the more recent trials.
- All of the RCTs were multi-centre and some included centres with different levels of expertise. One RCT enrolled the majority of patients at selected endovascular centres that were capable of implementing efficient workflow and imaging processes[3]. In another RCT, all study centres were required to have done at least 40 mechanical thrombectomy procedures, including at least 20 procedures with the Solitaire stent retriever, annually[4].
- Several of the trials were stopped early and have a reduced sample size, which creates the potential to overestimate the effect size. The trials were all stopped because predetermined efficacy criteria had been reached.
- There is a case series from the UK and 1 of the RCTs included a UK centre[6, 3].

Existing assessments of this procedure

A consensus statement on mechanical thrombectomy in acute ischaemic stroke was released in February 2015 by the European Stroke Organisation in collaboration with the European Society of Minimally Invasive Neurological Therapy and the European Society of Neuroradiology. The statement includes a number of recommendations on treatment, patient selection, implementation, registries and further trials. These include:

- Mechanical thrombectomy, in addition to intravenous thrombolysis within 4.5 hours when eligible, is recommended to treat acute stroke patients with large artery occlusions in the anterior circulation up to 6 hours after symptom onset.
- Mechanical thrombectomy should not prevent the initiation of intravenous thrombolysis where this is indicated, and intravenous thrombolysis should not delay mechanical thrombectomy.
- Mechanical thrombectomy should be performed as soon as possible after its indication.
- For mechanical thrombectomy, stent retrievers approved by local health authorities should be considered.
- Other thrombectomy or aspiration devices approved by local health authorities may be used upon the neurointerventionalists discretion if rapid, complete and safe revascularisation of the target vessel can be achieved.
- If intravenous thrombolysis is contraindicated (e.g. Warfarin-treated with therapeutic international normalised ratio) mechanical thrombectomy is recommended as first-line treatment in large vessel occlusions.
- 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; alternatively they may be treated within a RCT for thrombectomy approved by the local ethical committee.
- The decision to undertake mechanical thrombectomy should be made jointly by a multidisciplinary team comprising at least a stroke physician and a neurointerventionalist and performed in experienced centres providing comprehensive stroke care and expertise in neuroanesthesiology.
- Mechanical thrombectomy should be performed by a trained and experienced neurointerventionalist who meets national and/or international requirements.
- The choice of anaesthesia depends on the individual situation; independently of the method chosen, all efforts should be made to avoid thrombectomy delays.

- Health authorities are strongly encouraged to implement access to thrombectomy within a reasonable time range in a network including stroke centres.
- It is encouraged to perform and include patients in a RCT addressing unresolved thrombectomy questions such as thrombectomy for basilar artery occlusion, treatment in late and unknown time windows, treating patients with imaging findings not sufficiently covered in recent trials, comparing new devices with widely-used stent retrievers, thrombectomy with or without intravenous thrombolysis, and different types of anesthesia.
- Non-randomised trials comparing centres not yet having access to mechanical thrombectomy with others should continue (such as SITS OPEN).
- Ischemic stroke patients undergoing any type of acute revascularisation treatment should be included systematically in national or international registries (such as SITS or SITS-TBY).

The American Heart Association and the American Stroke Association have produced an update of the 2013 Guidelines for the Early Management of Patients with Acute Ischaemic Stroke Regarding Endovascular Treatment. The updated recommendations state that patients should receive endovascular therapy with a stent retriever if they meet all the following criteria:
(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.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Mechanical clot retrieval for treating acute ischaemic stroke. NICE interventional procedure guidance 458 (2013). This guidance is currently under review and is expected to be updated in 2016. For more information, see http://www.nice.org.uk/guidance/indevelopment/gid-ip2807

Technology appraisals

- Alteplase for treating acute ischaemic stroke (review of technology appraisal guidance 122). NICE technology appraisal 264 (2012). Available from http://www.nice.org.uk/guidance/TA264

NICE guidelines

- Stroke: Diagnosis and initial management of acute stroke and transient ischaemic attack (TIA). NICE clinical guideline 68 (2008). Available from http://www.nice.org.uk/guidance/CG68

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Seven Specialist Advisor Questionnaires for mechanical clot retrieval for treating acute ischaemic stroke were submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme was unable to gather patient commentary for this procedure.

Issues for consideration by IPAC

Ongoing trials

- **Pragmatic Ischaemic Stroke Thrombectomy Evaluation (PISTE) trial** (NCT01745692), Glasgow, UK. A Randomised Controlled Clinical Trial of

Adjunctive Mechanical Thrombectomy Compared With Intravenous Thrombolysis in Patients With Acute Ischaemic Stroke Due to an Occluded Major Intracranial Vessel. Estimated enrolment=800. Estimated study completion date August 2017.

- **SITS (Safe Implementation of Treatments in Stroke) Open Artery by Thrombectomy in Acute Occlusive Stroke Study (SITS Open)** (NCT02326428), Sweden (non-randomised). SITS Open Artery by Thrombectomy in Acute Occlusive Stroke Study: an Open Prospective International Multicentre Controlled Study of Safety and Efficacy of Thrombectomy in Acute Occlusive Stroke Following IV Thrombolysis With Alteplase. Estimated enrolment=600. Estimated study completion date July 2015.

- **Trevo and Medical Management Versus Medical Management Alone in Wake Up and Late Presenting Strokes (DAWN)** (NCT02142283), US (randomised). Estimated enrolment=500. Estimated study completion date July 2017.

- **Endovascular Acute Stroke Intervention Trial - the EASI Trial** (NCT02157532), Canada (randomised). Intra-arterial Thrombectomy as an Acute Treatment Intervention for Stoke: the Endovascular Acute Stoke Intervention (EASI) Trial. Estimated enrolment=480. Estimated study completion date January 2020.

- **RECO Flow Restoration Device Versus Intravenous t-PA for Stroke Within 4.5h of Symptom Onset (RESTORE)** (NCT01983644), China (randomised). RECO Flow Restoration Device Versus Intravenous t-PA for Stroke Within 4.5h of Symptom Onset: a Prospective Randomised Control Trial (RESTORE). Estimated enrolment=130. Estimated study completion date November 2015.

- **Endovascular Therapy for Acute Ischemic Stroke Trial (EAST)** (NCT02350283), China. A Multicenter, Prospective, Non-randomized Pilot Control Study to Evaluate of Thrombectomy With Solitaire in Patients With Acute Ischemic Stroke. Estimated enrolment=150. Estimated study completion date October 2016.

- **POSITIVE Stroke Clinical Trial** (NCT01852201), US (randomised). POSITIVE: PerfusiOn Imaging Selection of Ischemic STroke PatIents for EndoVascular ThErapy. Estimated enrolment=750. Estimated study completion date May 2016.

- **Trevo® Retriever Registry Post Market Surveillance** (NCT02040259). Stryker Neurovascular Trevo® Retriever Registry. Estimated enrolment=300. Estimated study completion date December 2015.

- **A Randomized, Concurrent Controlled Trial to Assess the Safety and Effectiveness of the Separator 3D as a Component of the Penumbra System in the Revascularization of Large Vessel Occlusion in Acute Ischemic Stroke** (NCT01584609), US. A Randomized, Concurrent Controlled Trial to Assess the Safety and Effectiveness of the Separator 3D as a Component of the Penumbra System in the Revascularization of Large Vessel Occlusion in Acute Ischemic Stroke. Estimated enrolment=230. Estimated study completion date December 2016.

- **Efficacy and Security of an Endovascular Treatment as First Choice Procedure Compared With a Standard Intravenous Thrombolytic Therapy Treatment for Patients With Acute Ischemic Stroke Within 4.5 Hours After Onset (FUN-TPA)** (NCT02164357), Spain. Efficacy and Security of an Endovascular Treatment as First Choice Procedure Compared With a Standard Intravenous Thrombolytic Therapy Treatment for Patients With Acute Ischemic Stroke Within 4.5 Hours After Onset: A Prospective Cohorts Study. Estimated enrolment=124. Estimated primary completion date March 2015.

- **Embolectomy in Acute SYlvian Thrombosis in Refractory or Ineligible Patients to ALteplase (EASYTRAL)** (NCT02216565), France. Benefits of the Endovascular Treatment in the Early Management of Proximal Sylvian Artery Thrombosis in Patients Refractory or Ineligible to Intravenous Fibrinolysis : a Multicenter Controlled Randomized Trial. Estimated enrolment=270. Estimated study completion date March 2017.

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Appendix A: Additional papers on mechanical clot retrieval for treating acute ischaemic stroke

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies. Case series with fewer than 35 patients were excluded.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Abilleira S, Ribera A, Davalos A et al. (2014) Functional outcome after primary endovascular therapy or IV thrombolysis alone for stroke. An observational, comparative effectiveness study. Cerebrovascular Diseases 38: 328-336	Prospective registry data n=1832 (250 mechanical thrombectomy)	Patients undergoing endovascular thrombectomy within 180-270 min (OR: 2.89; 95% CI: 1.17-7.15) and patients with severe strokes (OR: 1.84; 95% CI: 1.02-3.35) did better than their intravenous thrombolysis counterparts. The propensity score-matched analyses with and without adjustment by additional covariates showed that endovascular thrombectomy was as effective as intravenous thrombolysis alone in achieving functional independence (OR for unadjusted propensity score matched: 1.35; 95% CI: 0.9-2.02, OR for adjusted propensity score matched: 1.45; 95% CI: 0.91-2.32)	More recent RCTs are included.
Abilleira S, Cardona P, Ribo M et al. (2014) Outcomes of a contemporary cohort of 536 consecutive patients with acute ischemic stroke treated with endovascular therapy. Stroke 45: 1046-1052	Case series (registry data) n=536 FU=3 months	Overall, revascularization (modified Thrombolysis In Cerebral Infarction scores, 2b and 3) occurred in 74%, 6% developed symptomatic intracerebral haemorrhages, 43% achieved good functional outcome, and 22% were dead at 90 days. Multivariate analyses confirmed the independent protective effect of revascularisation. Additionally, age >80 years, stroke severity, hypertension (deleterious), atrial fibrillation, and onset-to-groin puncture <6 hours (protective) also predicted good outcome, whereas lack of previous disability and anterior circulation strokes (protective) as well as and hypertension (deleterious) independently predicted mortality.	More recent RCTs are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Abou-Chebl A (2010) Endovascular treatment of acute ischemic stroke may be safely performed with no time window limit in appropriately selected patients. Stroke 41(9): 1996–2000	Case series n=55 FU=90 days	Procedural success=84% (46/55), Mortality at 30 days=27% (15/55), and 42% (23/55) of patients had modified Rankin Scale score ≤2 at 90 days. Symptomatic intracranial haemorrhages=9% (5/55)	Retrospective study. Mixed methods with variation in combinations of treatments used.
Abou-Chebl A, Zaidat OO, Castonguay AC et al. (2014) North American SOLITAIRE stent-retriever acute stroke registry: Choice of anesthesia and outcomes. Stroke 45: 1396-1401	Case series (registry data) n=281 FU=90 days	The NASA Registry has demonstrated that clinical outcomes and survival are significantly better in patients treated with local anaesthesia, without increased symptomatic intracranial haemorrhage risk. Future trials should prospectively evaluate the effect of general anaesthesia on outcomes.	Study focuses on type of anaesthesia.
Adamczyk P, Attenello F, Wen G et al. (2013) Mechanical thrombectomy in acute stroke: utilization variances and impact of procedural volume on inpatient mortality. Journal of Stroke & Cerebrovascular Diseases 22: 1263-1269	n=not reported in abstract	Significant allocation differences existed for mechanical thrombectomy procedures according to hospital size ($p<0.001$), location ($p<0.0001$), control/ownership ($p<0.0001$), geography ($p<0.05$), and teaching status ($p<0.0001$). Substantial procedural volume was independently associated with decreased mortality ($p=0.0002$; odds ratio 0.49) when adjusting for demographic covariates.	Paper focuses on operative volume in the US.
Almekhlafi MA, Menon BK, Freiheit EA et al. (2013) A meta-analysis of observational intra-arterial stroke therapy studies using the Merci device, Penumbra system, and retrievable stents. American Journal of Neuroradiology 34 (1) 140-145	Meta-analysis n=16 studies	The use of the Penumbra system and retrievable stents was associated with comparable procedural time to recanalization. Available data did not allow this parameter to be determined for trials using the Merci device. Retrievable stents achieved the highest rate of successful recanalization and functional outcome and the lowest mortality	More recent RCTs are included.
Almekhlafi MA, Davalos A, Bonafe A et al. (2014) Impact of age and baseline NIHSS scores on clinical outcomes in the mechanical thrombectomy using solitaire FR in acute ischemic stroke study. American Journal of Neuroradiology 35: 1337-1340	Case series n=202	A significantly lower proportion of patients with a positive SPAN-100 (Stroke Prognostication Using Age and NIHSS Stroke Scale) achieved favourable outcome in this cohort. SPAN-100 was an independent predictor of favourable outcome after adjusting for time to treatment and the extent of preintervention tissue damage according to the Alberta Stroke Program Early CT Score.	Study focuses on the use of a new scoring system for patient selection.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Bae GS, Kwon HJ, Kang C W et al (2012) Mechanical thrombectomy using a solitaire stent in acute ischemic stroke; initial experience in 40 patients. Journal of Cerebrovascular & Endovascular Neurosurgery 14: 164-9	Case series n=40 FU=90 days	Successful revascularisation=90% Mean NIHSS score=11.6 at 24 hours after the procedure Modified Rankin scale score of ≤ 2 at 90 days=43%. New occlusion by migrated emboli was observed in 1 patient. Post-procedural intracerebral haemorrhage occurred in 1 patient, with an all-cause mortality of 2 (5%)	Larger studies are included.
Baker WL, Colby JA, Tongbram V, et al. (2011) Neurothrombectomy devices for the treatment of acute ischemic stroke: state of the evidence. Annals of Internal Medicine 154: 243–52	Review n=87 studies (25 studies included in main data synthesis)	Rates of successful recanalisation varied between 43% and 100%. Rates of symptomatic harms were reported at 0 to 11% while asymptomatic harms reported rates of 1 to 43% with intracranial haemorrhage and vessel perforation or dissection rates of 0% to 7%. Successful recanalisation was the sole predictor of good outcome.	Review, with no pooled data.
Barreto AD, Albright KC, Hallevi H, et al. (2008) Thrombus burden is associated with clinical outcome after intra-arterial therapy for acute ischemic stroke. Stroke 39: 3231–5	Case series n=135	Overall recanalisation rate=54%	Retrospective study. Mixed methods with variation in combinations of treatments used.
Belisle JG, McCollom VE, Tytle TL, et al. (2009) Intra-arterial therapy for acute ischemic strokes. Journal of Vascular & Interventional Radiology 20: 327–33	Case series n=83 FU=90 days	Modified Rankin Scale score of 2 or less at 90 days=51%. Recanalisation rate=76% symptomatic ICH=6% 90 day mortality=22%	Retrospective study. Mixed methods with variation in combinations of treatments used.
Behme D, Gondecki L, Fiethen S et al. (2014) Complications of mechanical thrombectomy for acute ischemic stroke-a retrospective single-center study of 176 consecutive cases. Neuroradiology 56: 467-476	Case series n=176	Complications occurred in 20/176 patients (11%) comprising 23 adverse events at the following rates: sICH 8/176 (5%), emboli to new vascular territories 4/176 (2%); vessel dissection 3/176 (2%); vasospasm of the access vessel 5/176 (3%); stent dislocation in 1/42 (2%); and stent occlusion in 2/42 (5%). 2 out of 20 (10%) suffered from 2 or more procedure-related complications. There was a statistically significant correlation of complications with time from groin puncture to revascularization, unfavourable revascularisation results, and unfavourable clinical outcome	Retrospective review of complications, most of which are already reported in table 2.

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Behme D, Kowoll A, Mpotsaris A et al. (2014) Multicenter clinical experience in over 125 patients with the Penumbra Separator 3D for mechanical thrombectomy in acute ischemic stroke. Journal of Neurointerventional Surgery doi:10.1136/neurintsurg-2014-011446	Case series n=129 FU=90 days	Reperfusion to mTICI 2b or 3 was successful in 96/129 (74%) target arterial lesions, with more than half of cases (51%) achieving mTICI 3. The mean time from arterial puncture to revascularisation was 65 min. At 90 days, the symptomatic intracranial haemorrhage rate was 4%, all cause mortality was 32%, and 43/99 patients (43%) achieved functional independence with an mRS score of </=2.	Small case series.
Binning MJ, Adel JG, Maxwell CR et al. (2014) Early postmarket experience after US Food and Drug Administration approval with the Trevo device for thrombectomy for acute ischemic stroke. Neurosurgery 75: 584-589	Case series n=52	Thrombolysis in Cerebral Infarction grade 2 to 3 revascularisation was achieved in 93% of group 1 (symptom onset within 8 hours) and 84% of group 2 (symptom onset beyond 8 hours) patients. In-hospital mortality and symptomatic intracranial haemorrhage rates were 4% and 12% for groups 1 and 2, respectively. 90-day mortality was 15% and 24% for groups 1 and 2, respectively. In groups 1 and 2, 48% and 42% of patients, respectively, had good outcomes (modified Rankin Scale score, 0-2). Group 2 had longer revascularisation times and required adjuvant devices more frequently.	Small case series.
Brekenfeld C, Schroth G, Mordasini P, et al. (2011) Impact of retrievable stents on acute ischemic stroke treatment. American Journal of Neuroradiology 32: 1269–73	n=40 FU=3 months	The Solitaire stent group exhibited reduced doses of IAT, shorter treatment times, and higher recanalisation rates than were seen across other treatment approaches.	Larger studies are included.
Brinjikji W, Rabinstein AA, Kallmes DF et al. (2011) Patient outcomes with endovascular embolectomy therapy for acute ischemic stroke: a study of the national inpatient sample: 2006 to 2008. Stroke 42: 1648-52	n=3864 (retrospective) FU=unclear	In-hospital mortality rate=24% (940/ 3864). Intracranial haemorrhage=16% without concomitant thrombolysis and 20% with concomitant thrombolysis (p=0.0009).	More recent RCTs are included.
Brinjikji W, Rabinstein AA, Cloft HJ (2014) Outcomes of endovascular mechanical thrombectomy and intravenous tissue plasminogen activator for the treatment of vertebrobasilar stroke. Journal of Clinical Neurology 10: 17-23	Case series n=631 (mechanical thrombectomy)	The in-hospital mortality rate for mechanical thrombectomy patients was significantly lower for those aged <50 years than for those aged 50-64 years (30% versus 47%, p<0.01) and those aged >65 years (30% versus 43%, p<0.01).	Limited outcomes are reported.

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Brinjikji W, Murad MH, Rabinstein AA et al. (2015) Conscious sedation versus general anesthesia during endovascular acute ischemic stroke treatment: A systematic review and meta-analysis. American Journal of Neuroradiology 36: 525–9	Systematic review and meta-analysis n=1956	Patients with acute ischemic stroke undergoing intra-arterial therapy may have worse outcomes with general anesthesia compared with conscious sedation. However, the difference in stroke severity at the onset may confound the comparison in the available studies; thus, a randomized trial is necessary to confirm this association.	Comparison of general anaesthesia versus conscious sedation.
Broderick JP, Palesch YY, Demchuk AM, Yeatts SD et al. (2013) Endovascular therapy after intravenous t-PA versus t-PA alone for stroke. New England Journal of Medicine 368: 893-903	RCT (IMS III) n=656 FU=90 days	Modified Rankin Scale ≤2=41% (endovascular therapy) vs 39% (IV t-PA) (p=not significant) Recurrent stroke=5% vs 6%	More recent RCTs are included. (study was included in table 2 of 2013 overview)
Broderick JP, Palesch YY, Demchuk AM et al. (2014) Evolution of practice during the Interventional Management of Stroke III Trial and implications for ongoing trials. Stroke 45: 3606-3611	Review of IMS III trial n=656	Endovascular technology and diagnostic approaches to acute stroke patients changed substantially during the IMS III Trial. Efforts to decrease the time to delivery of endovascular therapy were successful.	Review of practice changes during the course of the IMS III trial.
Broussalis E, Trinka E, Hitzl Wet al. (2013) Comparison of Stent-Retriever Devices versus the Merci Retriever for Endovascular Treatment of Acute Stroke. American Journal of Neuroradiology 34: 366-72	Case series n=122 FU=90 days	In the 90-day follow-up, 65% of patients treated by stent retrievers and 35% of those treated by the Merci had achieved a good clinical outcome (p=0.002). Patients treated by stent retrievers had a significantly shorter treatment time (72 versus 122 minutes, p<0.01) and less severe intracerebral haemorrhages (10% versus 28%, p<0.01)	More recent RCTs are included.
Broussalis E, Trinka E, Wallner A et al. (2014) Thrombectomy in patients with large cerebral artery occlusion: a single-center experience with a new stent retriever. Vascular & Endovascular Surgery 48: 144-152	Case series n=50 FU=90 days	Good clinical outcome after 90 days (mRS<2)=61%. Symptomatic intracerebral haemorrhage=12% (6/50). Overall mortality rate=14%.	Small case series.

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Castonguay AC, Zaidat OO, Novakovic R et al. (2014) Influence of age on clinical and revascularization outcomes in the North American Solitaire Stent-Retriever Acute Stroke Registry. Stroke 45: 3631-3636	Registry data n=354	Greater than 80 years of age is predictive of poor clinical outcome and increased mortality compared with younger patients in the NASA registry. However, intravenous tissue-type plasminogen activator use, lower NIHSS, and shorter revascularization time are associated with better outcomes. Further studies are needed to understand the endovascular therapy role in this cohort compared with medical therapy.	Study focuses on the influence of age on outcomes.
Chalouhi N, Ghobrial G, Tjoumakaris S et al. (2013) CT perfusion-guided versus time-guided mechanical recanalization in acute ischemic stroke patients. Clinical Neurology & Neurosurgery 115: 2471-2475	Case series n=132	CT perfusion-based patient selection was associated with lower ICH and mortality rates. Favourable outcomes, however, did not differ between the 2 groups. These results may suggest a possible benefit in terms of in-hospital mortality with CT perfusion-guided triage of AIS patients for endovascular treatment.	Study focuses on the use of CT perfusion-guided patient selection.
Chalouhi N, Tjoumakaris S, Starke RM et al. (2014) Endovascular stroke intervention in young patients with large vessel occlusions. Neurosurgical Focus 36 (1) E6-2014.	Case series n=45	Endovascular therapy provides remarkably high rates of arterial recanalization and favourable outcomes in young patients with acute ischemic stroke and large vessel occlusions. These findings support aggressive interventional strategies in these patients.	Small case series.
Cheang MY, Manning N, Churilov L et al. (2014) Recanalisation success is associated with good clinical outcome despite advanced age and stroke severity in patients treated with the Solitaire stentriever. Journal of Clinical Neuroscience 21: 401-405	Case series n=60 FU=3 months	Successful recanalisation (TICI > 2b) =73% (44/60). Of these 44 patients, 25 patients (57%) achieved mRS<2 at 3months. Multiple logistic regression showed significant association between recanalisation success and improved clinical outcome (p=0.019). Of all patients, 4 (7%) developed symptomatic intracranial haemorrhage. Overall mortality=28%.	Small case series.
Ciccone A, Valvassori L, Nichelatti M, et al. (2013) Endovascular treatment for acute ischemic stroke. New England Journal of Medicine 368: 904-13	RCT (SYNTHESIS) n=362 FU=3 months	At 3 months, 30% (55/181) of patients in the endovascular-therapy group and 35% (63/181) in the intravenous t-PA group were alive without disability (odds ratio adjusted for age, sex, stroke severity, and atrial fibrillation status at baseline, 0.71; 95% confidence interval, 0.44 to 1.14; p=0.16).	More recent RCTs are included. (study was included in table 2 of 2013 overview)

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Costalat V, Machi P, Lobotesis K et al. (2011) Rescue, combined, and stand-alone thrombectomy in the management of large vessel occlusion stroke using the solitaire device: a prospective 50-patient single-center study: timing, safety, and efficacy. Stroke 42: 1929–35	Case series n=50 FU=3 months	Modified Rankin score ≤2 or NIHSS score 0–1 at 3 months=54% 3-month mortality=12%	More recent RCTs are included. (study was included in table 2 of 2013 overview)
Daniere F, Lobotesis K, Machi P et al. (2015) Patient selection for stroke endovascular therapy--DWI-ASPECTS thresholds should vary among age groups: insights from the RECOST study. American Journal of Neuroradiology 36: 32-39	Case series n=165 FU=3 months	The elderly may benefit from thrombectomy when their ischemic core volume is low in comparison with younger patients who still benefit from acute recanalisation despite larger infarcts. Stroke volume thresholds should, therefore, be related and adjusted to the patient's age group.	More recent RCTs are included.
Dávalos A, Pereira VM, Chapot R et al. (2012) Retrospective Multicenter Study of Solitaire FR for Revascularization in the Treatment of Acute Ischemic Stroke. Stroke 43: 2699–2705	Case series n=141 FU=3 months	Modified Rankin score ≤2 at 3 months=66% (clot retrieval with IV tPA) and 42% (clot retrieval without IV tPA) Successful revascularisation=85% Symptomatic intracranial haemorrhage=3% (clot retrieval with IV tPA) and 5% (clot retrieval without IV tPA)	More recent RCTs are included. (study was included in table 2 of 2013 overview)
Day JS, Hurley MC, Chmayssani M, et al. (2011) Endovascular stroke therapy: a single-center retrospective review. Neurosurgical Focus 30(6): E10	Case series n=39 FU=1 month or more.	9 patients lost to follow up. Reported mRS ≤2 in 11/30 patients (37%). Mortality=27% (8/30) 17 patients (43%), developed ICH, 3 of these (8%) were symptomatic.	Retrospective review, some outcomes estimated.
Deshaies EM, Singla A, Villwock MR et al. (2014) Early experience with stent retrievers and comparison with previous-generation mechanical thrombectomy devices for acute ischemic stroke. Journal of Neurosurgery 121 (1) 12-17	Case series n=102	Solitaire-FR treatment resulted in significantly more patients being discharged as functionally independent in comparison with MERCI treatment (p=0.016). A multivariate model found the use of Solitaire-FR to improve the odds of good clinical outcome in comparison with prior-generation devices (OR 6.3, 95% CI 1.8-22.1, p=0.004). Additionally, the use of Solitaire-FR significantly increased the odds of successful reperfusion (OR 3.3, 95% CI 1.2 - 9.1, p=0.025)	Small retrospective case series.

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Desilles JP, Rouchaud A, Labreuche J et al. (2013) Blood-brain barrier disruption is associated with increased mortality after endovascular therapy. Neurology 80: 844-851	Case series n=220	Blood-brain barrier disruption has a detrimental effect on outcome and is independently associated with mortality after endovascular therapy.	Study focuses on blood-brain barrier disruption.
Dorn F, Stehle S, Lockau H et al. (2012) Endovascular treatment of acute intracerebral artery occlusions with the solitaire stent: Single-centre experience with 108 recanalization procedures. Cerebrovascular Diseases 34: 70-7	n=104 [108 occlusions-Solitaire stent alone (25) or in conjunction with other mechanical/aspiration thrombectomy] (retrospective analysis) FU=unclear	The mean NIHSS score decreased by 7.8 points from 15.3 at baseline at discharge. Good recanalization rate was achieved in 79% (TICI scale 2b/3) and 95% (TIMI 2/3). Complications recorded were 2 cases of periprocedural intracranial haemorrhage (unrelated to stent) and 6 cases of subarachnoid haemorrhage (2 potentially related to the stent deployment). Additional complications were thrombus migration (4%) to previously unaffected territories, vasospasm (13%) of the target vessels and 1 device was inadvertently detached during retrieval (no clinical consequence).	Larger studies are included.
Dorn F, Lockau H, Stetefeld H et al. (2015) Mechanical Thrombectomy of M2-Occlusion. Journal of Stroke and Cerebrovascular Diseases 24: 1465–70	Case series n=119 FU=3 months	Endovascular treatment of M2-occlusions in severely affected patients is not associated with a higher procedural risk or postprocedural hemorrhage. Compared with M1-occlusions, there was a greater chance for a good angiographic and clinical result in our case series. Therefore, stentretriever-based thrombectomy should also be considered for patients with severe symptoms because of an acute M2-occlusion.	Small case series comparing patients with M2 occlusions against those with M1 occlusions.

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Eesa M, Burns PA, Almekhlafi MA et al. (2014) Mechanical thrombectomy with the Solitaire stent: is there a learning curve in achieving rapid recanalization times? Journal of Neurointerventional Surgery 6: 649-651	Case series n=83	Recanalisation (Thrombolyis in Cerebral Infarction score 2A) occurred in 75 (90%) patients. CT to recanalisation demonstrated significant improvement over time, which was greatest between the first 25 and the most recent 25 cases (161-94min; p<0.01). The maximal contribution to this was from improvements in first stent deployment to recanalisation time (p=0.001 between the first and third groups), with modest contributions from moving patients from CT to the angiography suite faster (p=0.02 between the first and third groups) and from groin puncture to first stent deployment (p=0.02 between the first and third groups).	Small case series.
Enomoto Y, Yoshimura S, Egashira Y et al. (2014) Long-term magnetic resonance angiography follow-up for recanalized vessels after mechanical thrombectomy. Journal of Stroke & Cerebrovascular Diseases 23: 2834-2839	Case series n=49 FU=3 months	Reocclusion or late stenosis of successfully recanalized vessels was observed in 16 of patients. Long-term MRA follow-up of recanalized vessels will be useful, in particular, for the patient with middle cerebral artery occlusion who undergoes mechanical thrombectomy.	Small case series.
Eom Y-I, Hwang Y-H, Hong JM et al. (2014) Forced arterial suction thrombectomy with the penumbra reperfusion catheter in acute basilar artery occlusion: A retrospective comparison study in 2 Korean university hospitals. American Journal of Neuroradiology 35: 2354-2359	Non-randomised comparative study n=57	Fair outcome, indicated by a modified Rankin Scale 0-3, at 3 months was achieved in 34% of patients undergoing forced arterial suction thrombectomy and 8% of patients undergoing fibrinolysis (p=0.019), and the mortality rate was significantly higher in the fibrinolysis group (25% versus 68%, p=0.001).	Small non-randomised study.
Eugene F, Gauvrit JY, Ferre JC et al. (2015) One-year MR angiographic and clinical follow-up after intracranial mechanical thrombectomy using a stent retriever device. American Journal of Neuroradiology 36: 126–32	Case series n=39 FU=19 months	MR showed intracranial artery abnormalities in 10 patients, including 5 delayed intracranial artery abnormalities in 4 patients (4 stenoses and 1 dilation), 4 cases of pre-existing intracranial artery stenosis, and 2 occlusions. All these patients remained asymptomatic during the follow-up period. A significant clinical improvement was observed at 1-year follow-up in comparison with 3-month follow-up (p<0.0001), with a good outcome achieved in 63% of patients and an acceptable quality of life restored	Small case series

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Fesl G, Holtmannspoetter M, Patzig M et al. (2014) Mechanical thrombectomy in basilar artery thrombosis: technical advances and safety in a 10-year experience. Cardiovascular & Interventional Radiology 37: 355-361	Case series n=81	High recanalisation rates have been achieved since the introduction of mechanical thrombectomy in basilar artery occlusion. However, modern stent retriever and suction devices allow for safer and more rapid recanalisation compared with previous devices.	Small case series.
Fischer U, Mono ML, Schroth G et al. (2013) Endovascular therapy in 201 patients with acute symptomatic occlusion of the internal carotid artery. European Journal of Neurology 20: 1017-1024	n=201	The outcome of acute symptomatic internal carotid artery occlusion is poor. However, recanalization is associated with better outcome, and recanalization rates with mechanical techniques were superior to merely pharmacological recanalization attempts.	More recent RCTs are included.
Fjetland L, Roy S, Kurz KD et al. (2012) Endovascular acute stroke treatment performed by vascular interventional radiologists: is it safe and efficacious? Cardiovascular & Interventional Radiology 35:1029-35	n=39 [20 treated by Pneumbra stent; 10 treated by Solitaire stent; 6 with IA thrombolysis; 6 patients with ICA stents- 4 in combination with either Pneumbra or Solitaire) FU=90 days	74% (29/39) patients with a baseline TIMI score of 0 or 1 had a TIMI score of 2 or 3 after treatment: 70% (14) in the Penumbra group and 23% (9) in the Solitaire group and 67% (4) in the IA thrombolysis group. Intracranial haemorrhage was reported in 40% (16) 24 hours after the procedure. Subarachnoid haemorrhage was reported in 1 patient who died 1 day after the procedure. Iatrogenic carotid-cavernous fistula was reported in 1 patient (timing unclear; CCF remained asymptomatic). 9 patients died during the first 90 days.	Larger studies are included.
Flint AC, Duckwiler GR, Budzik RF, et al. (2007) Mechanical thrombectomy of intracranial internal carotid occlusion: pooled results of the MERCI and Multi MERCI Part I trials. Stroke 38(4): 1274–80	n=80 FU=90 days	Recanalisation=53% (42/80) with retriever alone, and in a further 8 patients with use of both the retriever and IA thrombolytics. Modified Rankin Scale score ≤2 at 3 months=25% (20/79) Symptomatic haemorrhage, n=8 (7 patients died) 90-day mortality=30% (15/50) in patients who had recanalisation, and 73% (22/30) in the non-recanalised group.	Larger studies are included.

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Frahm D, Wunderlich S, Schubert MI et al. (2014) Mechanical Thrombectomy in Acute Occlusion of the Carotid-T: A Retrospective Single Centre Study in 51 Patients. Clinical Neuroradiology DOI: 10.1007/s00062-014-0322-6	Case series n=51 FU=90 days	Successful recanalization (TICI 2b/3) was achieved in 78% (40/51). Good clinical outcome (mRS 0-2) was observed in 24% of patients, and only in patients treated successfully (TICI 2b/3). Stent retrievers yielded higher recanalisation rates and better clinical outcomes than non-stent retriever devices. 12 patients died (29%). Clinically relevant procedure-related complications occurred in 2 patients: 1 vessel perforation and 1 symptomatic parenchymal haemorrhage after initiation of antiplatelet therapy following the inadvertent detachment of a stent retriever.	Small case series.
Friedrich B, Kertels O, Bach D et al. (2014) Fate of the penumbra after mechanical thrombectomy. American Journal of Neuroradiology 35: 972-977	Case series n=73	Mechanical thrombectomy is a potent method to rescue large areas of penumbra in acute stroke.	Small case series.
Frei D, Gerber J, Turk A et al. (2013) The SPEED study: initial clinical evaluation of the Penumbra novel 054 Reperfusion Catheter. Journal of NeuroInterventional Surgery 5: i74-i76	Case series n=86 FU=90 days	The Thrombolysis In Myocardial Infarction (TIMI) 2 or 3 revascularisation rate was 91%. 18 (21%) patients experienced an intracranial haemorrhage of which 12 (14%) were symptomatic. Good neurologic outcome (modified Rankin scores < 2) at 90-day follow-up was achieved in 35% of patients. All-cause mortality was 26%.	Small case series.
Froehler MT, Tateshima S, Duckwiler G et al. (2013) The hyperdense vessel sign on CT predicts successful recanalization with the Merci device in acute ischemic stroke. Journal of Neurointerventional Surgery 5: 289-293	Case series n=67	Successful recanalisation was achieved in 79% of patients with the hyperdense vessel sign (33/42), but in only 36% (9/25) of patients without it (p=0.001). The hyperdense vessel sign was the only significant predictor of recanalisation while accounting for age, treatment with IV-tPA, clot location, stroke aetiology, time to treatment, and number of retrieval attempts.	Small case series.
Galimanis A, Jung S, Mono ML, et al. (2012) Endovascular therapy of 623 patients with anterior circulation stroke. Stroke 43(4): 1052–7	n=623 FU=3 months	Partial or complete recanalisation achieved in 70% of patients. At 3 months, 81% of patients had survived, and 49% of patients had favourable outcome (mRS ≤2). Symptomatic ICH occurred in 6%.	Retrospective study. Mixed methods.

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Gascou G, Lobotesis K, Machi P et al. (2014) Stent retrievers in acute ischemic stroke: complications and failures during the perioperative period. American Journal of Neuroradiology 35: 734-740	Case series n=144	35% (50/144) of patients received stand-alone thrombectomy, and 65% (94/144) received combined therapy. The procedural failure rate was 14%. Embolic complications were recorded in 13% and symptomatic intracranial haemorrhage in 8%. The overall rate of failure, complications, and/or death was 40%. The perioperative mortality rate was 18% in the overall cohort but was higher in cases of failure (45%; p=0.003), embolic complications (39%; p=0.0176), symptomatic intracranial haemorrhages (46%; p=0.0236), and intracranial stenosis (50%; p=0.0176). Age was the only significant predictive factor of intracranial haemorrhage (p=0.043).	Small case series.
Georgiadis AL, Memon MZ, Shah QA et al. (2012) Intra-arterial tenecteplase for treatment of acute ischemic stroke: feasibility and comparative outcomes. Journal of Neuroimaging 22:249-54	n=114 FU=30 days	Favourable neurological outcome at 30 days was similar in patients treated with mechanical thrombectomy alone and those treated with IA thrombolytics alone. Death within 30 days due to recurrent stroke (n=3), intracranial haemorrhage (n=3) and asystole (n=2) were reported.	Small, retrospective study.
Ghobrial GM, Chalouhi N, Zohra M et al. (2014) Saving the ischemic penumbra: endovascular thrombolysis versus medical treatment. Journal of Clinical Neuroscience 21: 2092-2095	Non-randomised comparative study n=42	Endovascular thrombolysis may be more efficient than medical therapy alone in saving ischaemic penumbra. Future advances in recanalisation techniques will further improve the efficacy of endovascular therapy.	More recent RCTs are included.
Ginsberg MD, Hill MD (2015) Symptomatic intracranial hemorrhage in the ALIAS Multicenter Trial: relationship to endovascular thrombolytic therapy. International Journal of Stroke 10: 494-500	Case series n=830	Endovascular thrombolysis was the major factor predisposing to symptomatic intracranial haemorrhage, and albumin contributed to this predisposition.	The trial was focused on the use of albumin.

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Goktekin O, Tasal A, Uyarel H et al. (2014) Endovascular therapy of acute ischaemic stroke by interventional cardiologists: single-centre experience from Turkey. Eurointervention 10: 876-883	Case series n=38 FU=90 days	Successful revascularisation (Thrombolysis in Cerebral Infarction [TICI] 2b and 3) was achieved in 34 of 38 (89%) patients; a TICI 3 state was observed in 24 (63%) patients. Almost three quarters of the patients (74%) improved by >5 points on the NIHSS at discharge, and 58% showed a modified Rankin Scale (mRS) score of <2 at 90 days.	Small case series.
Goyal M, Almekhlafi MA, Fan L et al. (2014) Evaluation of interval times from onset to reperfusion in patients undergoing endovascular therapy in the Interventional Management of Stroke III trial. Circulation 130: 265-272	RCT (IMS III)	Important delays were identified before reperfusion in the IMS III trial. Delays decreased as the trial progressed. Use of CT angiography and endovascular treatment in the same center were associated with time savings.	Subanalysis of IMS III trial.
Gratz PP, Jung S, Schroth G et al. (2014) Outcome of standard and high-risk patients with acute anterior circulation stroke after stent retriever thrombectomy. Stroke 45: 152-158	Case series n=227	Patients<80 years of age, without extensive pretreatment ischaemic signs, and baseline National Institutes of Health Stroke Scale score<30 had high rates of favourable outcome and low periprocedural complication rates after Solitaire thrombectomy. Successful reperfusion was also common in patients not fulfilling standard inclusion criteria, but worse clinical outcomes warrant further research with a special focus on optimal patient selection.	More recent RCTs are included.
Guedin P, Larcher A, Decroix JP et al. (2015) Prior IV Thrombolysis Facilitates Mechanical Thrombectomy in Acute Ischemic Stroke. Journal of Stroke & Cerebrovascular Diseases 24: 952-957	Case series n=68 FU=3 months	The median duration of the endovascular procedure (from groin puncture to recanalisation) was significantly shorter in the IVT + MET group compared with that in MET alone (35 minutes [21-60] versus 60 minutes [25-91]; p=0.043). The number of passes of the thrombectomy device per patient tended to be lower in the IVT + MET group than those in the MET group (p=0.080). The IVT + MET group also had a higher rate of complete recanalisation and a better outcome at 3 months.	Small case series.

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Hann S, Chalouhi N, Starke R et al. (2013) Comparison of neurologic and radiographic outcomes with Solitaire versus Merci/Penumbra systems for acute stroke intervention. BioMed Research International 2013 715170-2013.	n=51	Compared with the Merci/Penumbra group, the Solitaire group showed a statistically significant improvement in favourable outcomes (mRS<2) (69% versus 35%, p=0.03) and symptomatic ICH rate (0 versus 15%, p=0.05) with a trend towards higher recanalization rates (94% versus 75%, p=0.096) and shorter length of procedure (59 min versus 71 min, p=0.08). Radiographic comparison also showed a significantly larger area of salvage in the Solitaire group (82% versus 72%, p=0.05)	Small non-randomised comparative study.
Hassan AE, Aman MM, Chauhdry SA et al. (2013) Value of Other Endovascular Techniques Among Patients with MERCI Device Failure during the Treatment of Acute Ischemic Stroke: What to do when MERCI fails? Journal of Vascular & Interventional Neurology 5: 9-13	Case series n=40	Continued attempts using the MERCI device did not result in higher recanalisation rates when compared to alternate endovascular treatment modalities following initial MERCI failure. Both techniques produced comparable rates of recanalisation and favourable outcome.	Small case series.
Hassan AE, Chaudhry SA, Miley JT et al. (2013) Microcatheter to recanalization (procedure time) predicts outcomes in endovascular treatment in patients with acute ischemic stroke: when do we stop? American Journal of Neuroradiology 34: 354-359	Case series n=209	Complete or partial recanalisation was observed in 176 (84%) patients, while unfavourable outcome (mRS 3-6) was observed in 138 (66%) patients at discharge. In univariate analysis, patients with procedure time <30 minutes had lower rates of unfavourable outcome at discharge compared with patients with procedure time >30 minutes (52% versus 72%, p=0.0049). In logistic regression analysis, unfavourable outcome was positively associated with age (p=0.0012), admission NIHSS strata (p=0.0017), and longer procedure times (p=0.0379)	More recent RCTs are included.
Hill MD, Demchuk AM, Goyal M et al. (2014) Alberta Stroke Program early computed tomography score to select patients for endovascular treatment: Interventional Management of Stroke (IMS)-III Trial. Stroke 45: 444-449	RCT n=656	Alberta Stroke Program Early CT Score (ASPECTS) is a strong predictor of outcome and a predictor of reperfusion. ASPECTS did not identify a subpopulation of subjects that particularly benefitted from endovascular therapy immediately after routine intravenous tPA.	Subgroup analysis from IMS III trial. More recent RCTs are included.

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Htyte N, Parto P, Ragbir S et al. (2015) Predictors of outcomes following catheter-based therapy for acute stroke. Catheterization and Cardiovascular Interventions 85: 1043-1050	Case series n=124 FU=90 days	Successful revascularization with catheter-based therapy leads to a good neurologic outcome in selected stroke patients. Medical co-morbidities and increased age >65 years contributed to poor outcomes.	Small case series.
Huded V, Nair RR, de Souza R et al. (2014) Endovascular treatment of acute ischemic stroke: an Indian experience from a tertiary care center. Neurology India 62: 276-279	Case series n=45 FU=3 months	The median pre-procedure Thrombolysis In Myocardial Infarction (TIMI) score was 0 and the median post-procedure TIMI score was 3. Nine patients underwent decompressive craniectomy. On follow-up at 3 months, the median Modified Rankin Scale (mRS) was 0. Eight patients died during 3 months following stroke.	Small case series.
Humphries W, Hoit D, Doss V et al. (2015) Distal aspiration with retrievable stent assisted thrombectomy for the treatment of acute ischemic stroke. Journal of Neurointerventional Surgery 7: 90-94	Case series n=105	Successful recanalization (Thrombolysis in Cerebral Infarction score 2B) was achieved in 92 (88%) of these patients. 44% of patients had favourable (mRS score 0-2) outcomes at 90 days. There were 5 (5%) symptomatic intracerebral haemorrhages and 3 procedure related deaths (3%)	Retrospective case series.
Inoue M, Olivot JM, Labreuche J et al. (2014) Impact of diffusion-weighted imaging Alberta stroke program early computed tomography score on the success of endovascular reperfusion therapy. Stroke 45: 1992-1998	Case series n=210	DWI-ASPECTS>5 seems to be the optimal threshold to predict favourable outcomes among patients undergoing endovascular reperfusion within 6 hours. Selected patients with a DWI-ASPECTS of <5 may still benefit when a complete reperfusion is achieved.	Study focuses on impact of diffusion-weighted imaging Alberta stroke program early CT score.
Jang MU, Hong JH, Kang J et al. (2014) Current status of recanalization therapy in acute ischemic stroke with symptomatic intracranial arterial occlusion in Korea. Journal of Stroke & Cerebrovascular Diseases 23: e339-e346	Prospective register n=642 FU=3 months	Early neurologic improvement (ENI), 3-month modified Rankin scale (mRS) score of 2 or less, and symptomatic haemorrhagic transformation (SHT) were observed in 43%, 39%, and 9% of the patients in the intravenous thrombolysis only group; 52%, 27%, and 12% of the patients in the intra-arterial thrombolysis only group; and 54%, 39%, and 12% of the patients in the combined thrombolysis group, respectively.	More recent RCTs are included.

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Jankowitz B, Aghaebrahim A, Zirra A et al. (2012) Manual aspiration thrombectomy: adjunctive endovascular recanalization technique in acute stroke interventions. Stroke 43 (5): 1408-11	n=191 FU=90 days	Parenchymal hematoma=14%. Favourable outcome (90-day modified Rankin Scale ≤2)=54%. Mortality at 90 days=25%	Larger studies are included.
Jansen O, Macho JM, Killer-Oberpfalzer M et al. (2013) Neurothrombectomy for the treatment of acute ischemic stroke: results from the TREVO study. Cerebrovascular Diseases 36: 218-225	Case series n=60 FU=90 days	The overall recanalisation rate (>TICI 2a) was 92% and TICI 2b and 3 was achieved in 78%. At 90 days, 55% of the patients had a favourable neurological outcome (mRS 0-2) and 20% had died. Patients with successful recanalisation (TICI 2a,b/3) had a good 90-day neurological outcome (mRS 0-2) in 60%, whereas no patient without recanalisation had a mRS 90 <3. The overall rate of symptomatic intracerebral haemorrhage according to the SITS-MOST criteria was 5% (3/60).	Small case series.
Jayaraman MV, Hussain MS, Abruzzo T et al. (2015) Embolectomy for stroke with emergent large vessel occlusion (ELVO): Report of the Standards and Guidelines Committee of the Society of NeuroInterventional Surgery. Journal of NeuroInterventional Surgery 7: 316-321	Review	There are now multiple randomised multicentre prospective trials providing Level1, Class A evidence that, in patients with anterior circulation stroke and an emergent large vessel occlusion, the addition of embolectomy to best medical therapy is superior to best medical therapy alone. Future directions should focus on optimising systems of care to maximise patient access to rapid embolectomy, as well as further research refining the techniques of embolectomy and patient selection.	Review without a meta-analysis.
Jeong HS, Song HJ, Kim SB et al. (2013) A comparison of stent-assisted mechanical thrombectomy and conventional intra-arterial thrombolysis for acute cerebral infarction. Journal of Clinical Neurology 9: 91-96	Non-randomised comparative study n=72	The outcomes and clinical parameters were better for stent-assisted thrombectomy during thrombolytic procedures for acute intracranial artery occlusions than for aggressive mechanical clot disruption for up to 6 months. However, some device-related complications occurred during stent interventions.	Small, retrospective study.

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Jeromel M, Milosevic ZV, Kocijancic IJ et al. (2013) Mechanical revascularization for acute ischemic stroke: a single-center, retrospective analysis. Cardiovascular & Interventional Radiology 36 (2) 338-345	n=57 FU=30 days	Significant neurological improvement (≥4 NIHSS point reduction)=63% A clinically significant procedure-related adverse events (vessel disruption, peri/post-procedural intracranial bleeding) defined with decline in NIHSS of≥4 or death occurred in 3 (5%) patients.	Small case series.
Josephson SA, Saver JL, Smith WS, et al. (2009) Comparison of mechanical embolectomy and intraarterial thrombolysis in acute ischaemic stroke within the MCA: Merci and multi-Merci compared to PROACT II. Neurocritical Care 10(1): 43–9	n=149 FU=90 days	In both unadjusted and adjusted analyses, mortality rates did not significantly differ between embolectomy patients and PROACT II control patients. Compared with the PROACT II treatment group, embolectomy groups showed similar rates of good outcome and mortality.	More recent RCTs are included.
Kabbasch C, Mpotsaris A, Liebig T et al. (2014) First-In-Man Procedural Experience with the Novel EmboTrap(R) Revascularization Device for the Treatment of Ischemic Stroke-A European Multicenter Series. Clinical Neuroradiology 2014 DOI: 10.1007/s00062-014-0352-0	Case series n=40	Procedural complications were encountered in 5% of patients; both patients exhibited internal carotid artery dissection that was treated conservatively without clinical sequelae. There were no device-related complications. Of 23 available patients, 8 (35%) had a good outcome after 90 days.	Small case series.
Kang DH, Kim YW, Hwang YH et al. (2013) Switching strategy for mechanical thrombectomy of acute large vessel occlusion in the anterior circulation. Stroke 44: 3577-3579	Case series n=135	A switching strategy using 2 mechanical thrombectomy techniques (forced arterial suction thrombectomy to Solitaire) may harbour better angiographic outcomes than a 1 technique only strategy (forced arterial suction thrombectomy).	Small case series.
Kang DH, Kim YW, Hwang YH et al. (2014) Instant reocclusion following mechanical thrombectomy of in situ thromboocclusion and the role of low-dose intra-arterial tirofiban. Cerebrovascular Diseases 37: 350-355	Case series n=168	In situ thromboocclusion was characterized by a significantly higher chance of instant reocclusion during mechanical clot retrieval. In such cases, low-dose intra-arterial tirofiban administration may be effective and safe. However, future confirmation by prospective multicentre trials seems necessary.	Study focuses on the use of intra-arterial tirofiban.
Kappelhof M, Marquering HA, Berkhemer OA et al. (2015) Intra-arterial treatment of patients with acute ischemic stroke and internal carotid artery occlusion: a literature review. Journal of Neurointerventional Surgery 7: 8-15	Review n=1107	This review shows that, for patients with AIS due to an extracranial and/or intracranial ICA occlusion, stenting and mechanical thrombectomy are associated with higher recanalization rates and improved functional outcomes compared with IA thrombolysis.	More recent RCTs are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Kass-Hout O, Sun C-H, Kass-Hout T et al. (2015) Clinical, angiographic and radiographic outcome differences among mechanical thrombectomy devices: Initial experience of a large-volume center. Journal of NeuroInterventional Surgery 7: 176-181	Case series n=287	Although initial data confirm the superiority of stent retriever technology over the Merci device, there was no significant difference in near complete/complete reperfusion, final infarct volumes or clinical outcomes between stent retrievers and Penumbra thromboaspiration.	Retrospective study comparing different devices.
Kidwell CS, Jahan R, Gornbein J I. (2013) A trial of imaging selection and endovascular treatment for ischemic stroke. New England Journal of Medicine 368: 914-23	RCT (MR RESCUE) n=127 FU=90 days	Among all patients, mean scores on the modified Rankin scale did not differ between embolectomy and standard care (3.9 vs. 3.9, p=0.99). Embolectomy was not superior to standard care in patients with either a favourable penumbral pattern (mean score, 3.9 vs. 3.4; p=0.23) or a nonpenumbral pattern (mean score, 4.0 vs. 4.4; p=0.32).	More recent RCTs are included. (study was included in table 2 of 2013 overview)
Kim ST, Jin SC, Jeong HW et al. (2014) Unexpected Detachment of Solitaire Stents during Mechanical Thrombectomy. Journal of Korean Neurosurgical Society 56: 463-468	Case series n=232	Solitaire stents unexpectedly detached in 9 cases (4%) during the retrieval of Solitaire stents.	
Koh JS, Lee SJ, Ryu CW et al. (2012) Safety and efficacy of mechanical thrombectomy with solitaire stent retrieval for acute ischemic stroke: a systematic review. Neurointervention 7: 1–9	Systematic review n=262 FU=3 months	Successful recanalisation=90% (235/262) NIHSS improvement of ≥10 points=52% (102/196) mRS≤2=51% (133/262) Mortality=11% (29/262) Symptomatic haemorrhagic complication=7% (16/236) Procedure induced complications=3% (9/262)	More recent RCTs are included. (study was included in table 2 of 2013 overview)
Kuntze Soderqvist A, Kaijser M, Soderman M et al. (2014) Mechanical thrombectomy in acute ischemic stroke-experience from 6 years of practice. Neuroradiology 56: 477-486	Case series n=240	Good functional outcome (mRS 0-2) was achieved in 50% (120/240) of all patients. For patients with no neurological deficit prior to stroke onset, the proportion with good functional outcome was 54%. Symptomatic haemorrhages occurred in 5% of the cases (6% in the anterior circulation).	More recent RCTs are included.

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Kurre W, Perez MA, Horvath D. et al (2012) Does Mechanical Thrombectomy in Acute Embolic Stroke Have Long-term Side Effects on Intracranial Vessels? An Angiographic Follow-up Study. Cardiovascular Interventional Radiology DOI 10.1007/s00270-012-0496-8	n=261 FU= median 107 days	Vasospasm=26% Dissection, n=1 Intraprocedural haemorrhage, n=2 (either wire or device induced) Post-treatment vasospasm was more frequent in patients with de novo stenosis and occlusion (p=0.038).	Safety outcomes are already reported in table 2.
Kurre W, Vorlaender K, Aguilar-Perez M et al. (2013) Frequency and relevance of anterior cerebral artery embolism caused by mechanical thrombectomy of middle cerebral artery occlusion. American Journal of Neuroradiology 34: 1606-1611	Case series n=105	New anterior cerebral artery (ACA) emboli occurred in 12 of 105 (11%) M1 recanalisation procedures and were caused by a stent-retriever in 11 instances. Attempts to recanalise the ACA were made in 6 patients and were deemed technically successful in 5 with no adverse events. There were 6 (6%) new infarcts on follow-up imaging.	Small case series.
Kurre W, Aguilar-Perez M, Niehaus L et al. (2013) Predictors of outcome after mechanical thrombectomy for anterior circulation large vessel occlusion in patients aged >80 years. Cerebrovascular Diseases 36: 430-436	Case series n=109	ASPECTS and NIHSS were independent predictors of a favourable outcome in patients aged >80 years after mechanical thrombectomy for anterior circulation large vessel occlusion and may support decision making with regard to the treatment modality. Since the chances of gaining functional independence are limited, careful consideration of each individual case is mandatory.	Small case series.
Kurre W, Aguilar-Perez M, Schmid E et al. (2014) Clinical experience with the pREset stent retriever for the treatment of acute ischemic stroke--a review of 271 consecutive cases. Neuroradiology 56: 397-403	Case series n=271	Successful recanalisation was achieved in 76%. Device-related complications occurred in 9% of which 2% were clinically significant. PH I, PH II, focal SAH, and diffuse SAH was observed in 5, 5, 12, and 2%, respectively. A total of 40% of patients had favourable clinical outcome.	More recent RCTs are included.
Lazzaro MA, Zaidat OO, Saver JL et al. (2014) Predictors and Outcomes Associated with Rescue Therapy in SWIFT. Interventional Neurology 2: 178-182	Case series n=144	Merci treatment group and age were predictors of rescue therapy, while a trend toward an increased need of rescue therapy was observed with hypertension and proximal clot location. Rescue therapy was associated with fewer good outcomes.	Small case series.

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Lee HG, Rhim JK, Kim YH, et al. (2011) The comparison of outcome between thromboaspiration and aggressive mechanical clot disruption in treating hyperacute stroke patients. Journal of Korean Neurosurgical Society: 50(4): 311–6	n=36 FU=Not reported	After using thromboaspiration, better recanalisation rates, mRS and reperfusion injury compared with aggressive mechanical clot disruption were found, with a recanalisation rate of 81%, mRS of 2.85, and <1% haemorrhagic formation.	Mixed methods, few outcome or efficacy data reported.
Lee SY, Youn SW, Kim HK et al. (2015) Inadvertent Detachment of a Retrievable Intracranial Stent: Review of Manufacturer and User Facility Device Experience. Neuroradiology Journal 28: 172–6	Case series n=80	16% (13/80) of patients with stent detachment died after the procedure. Morbidity data were available in 62 patients, among whom 11 (18%) had suffered a procedure-related injury. A rescue manoeuvre was reported in 20 (25%) of the 80 patients in whom the adverse event was attributable to detachment of the device, resulting in flow reestablishment in 13 (65%).	Case series of inadvertent stent detachment – this complication is already reported in table 2.
Lefevre PH, Lainay C, Thouant P et al. (2014) Solitaire FR as a first-line device in acute intracerebral occlusion: a single-centre retrospective analysis. Journal of Neuroradiology Journal: 80-86	Case series n=62 FU=3 months	Stand-alone thrombectomy was used in 47 patients (76%). Recanalisation was successful (TICI score 2b or 3) in 89% (23/26) of patients with posterior circulation occlusion and in 64% (23/36) of patients with anterior circulation occlusion. NIHSS improved by more than 10 points for 15 of 59 patients with initial NIHSS over 10. MRS was 0-2 in 40%. Overall mortality=37% (23/62). No complications related to the Solitaire device occurred.	Small case series.
Leiva-Salinas C, Aghaebrahim A, Zhu G et al. (2013) Tissue at risk in acute stroke patients treated beyond 8 h after symptom onset. Neuroradiology 55: 807-812	Case series n=75	There is potentially salvageable ischaemic tissue at risk in acute stroke patients treated beyond 8 h after symptom onset.	Small case series.
Liebeskind DS, Jahan R, Nogueira RG et al. (2015) Early arrival at the emergency department is associated with better collaterals, smaller established infarcts and better clinical outcomes with endovascular stroke therapy: SWIFT study. Journal of Neurointerventional Surgery 2015 doi: 10.1136/neurintsurg-2015-011758.	RCT (SWIFT) n=137	Time was a critical factor in successful clinical outcomes for neurothrombectomy in the SWIFT trial. Shorter times to presentation were associated with better collaterals, smaller established infarcts, and better clinical outcome after revascularisation.	The main outcomes from the SWIFT trial are included in table 2.

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Liebeskind DS, Jahan R, Nogueira RG et al. (2014) Impact of collaterals on successful revascularization in Solitaire FR with the intention for thrombectomy. Stroke 45: 2036-2040	RCT (SWIFT) n=119	Better collaterals were associated with lower glucose, lower blood pressure, smaller baseline infarcts in SWIFT, and greater likelihood of successful revascularisation without haemorrhage and good clinical outcomes.	The main outcomes from the SWIFT trial are included in table 2.
Liebeskind DS, Jahan R, Nogueira RG et al. (2014) Serial Alberta Stroke Program early CT score from baseline to 24 hours in Solitaire Flow Restoration with the Intention for Thrombectomy study: a novel surrogate end point for revascularization in acute stroke. Stroke 45: 723-727	Case series n=139 FU=90 days	24-hour Alberta Stroke Program Early CT Score (ASPECTS) provides better prognostic information compared with baseline ASPECTS. Predictors of dramatic infarct progression on ASPECTS are hyperglycaemia, hypertension, and nonreperfusion. Serial ASPECTS change from baseline to 24 hours predicts clinical outcome, providing an early surrogate end point for thrombectomy trials.	Small case series.
Li F, Deshaies EM, Singla A et al. (2014) Impact of anesthesia on mortality during endovascular clot removal for acute ischemic stroke. Journal of Neurosurgical Anesthesiology 26: 286-290	Non-randomised comparative study n=109	Patients needing intubation upon admission for airway protection were more likely to receive GA ($p<0.001$). The duration of the procedure and the time-to-revascularization from symptom onset were significantly longer in the GA group. Mortality was higher in the GA group compared with the CS group (40% vs. 22%, $p=0.045$). Multivariate analysis, controlled for confounding variables, identified GA and elevated postprocedure glucose level to be significant predictors of mortality.	Non-randomised study comparing general anaesthesia against conscious sedation.
Lin R, Vora N, Zaidi S, et al. (2009) Mechanical approaches combined with intra-arterial pharmacological therapy are associated with higher recanalization rates than either intervention alone in revascularization of acute carotid terminus occlusion. Stroke 40: 2092–7	n=75 FU=3 months	Recanalisation rates for the combined treatment group (mechanical plus pharmacological therapies) were significantly greater than for the mechanical only group and the IA pharmacological only group, with respective rates of 86% (18/21), 46% (6/13) and 18% (3/17). No significant differences in rates of mortality or symptomatic haemorrhage were found between treatment groups.	Small number of patients in each subgroup. Retrospective data analysis. Treatment approaches not evaluated concurrently.

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Linfante I, Starosciak AK, Walker GR et al. (2015) Predictors of poor outcome despite recanalization: a multiple regression analysis of the NASA registry. Journal of Neurointerventional Surgery 2015 doi: 10.1136/neurintsurg-2014-011525.	Case series (registry data) n=354 FU=90 days	Age, occlusion site, high NIHSS, diabetes, no IV t-PA, >/=3 passes, and use of rescue therapy are associated with poor 90-day outcome despite successful recanalisation.	More recent RCTs are included.
Lockau H, Liebig T, Henning T et al. (2015) Mechanical thrombectomy in tandem occlusion: procedural considerations and clinical results. Neuroradiology 57: 589-598	Case series n=37 FU=3 months	Acute stenting of the cervical ICA in combination with intracranial thrombectomy was technically feasible and safe in our series. Thrombectomy prior to proximal stenting was associated with shorter reperfusion times and a tendency towards better clinical outcome leading to a good outcome in about 50% of the patients.	Small case series.
Loh Y, Towfighi A, Liebeskind DS, et al. (2010) Basal ganglionic infarction before mechanical thrombectomy predicts poor outcome. Stroke 40(10): 3315–20	n=50 FU=not reported	The M1a group had worse pre-mechanical clot retrieval NIHSS, worse discharge NIHSS, longer hospital stay, and higher rates of discharge mRS ≥3 (OR 8.4, 95% CI 2.1 to 44.7) despite equivalent recanalisation rates when compared with the M1b group. The M1a group had a higher rate of parenchymal haematoma. Patients with such haematomal HT had higher rates of death or dependency discharge.	Retrospective review.
Loh Y, Kim D, Shi ZS, et al. (2010) Higher rates of mortality but not morbidity follow intracranial mechanical thrombectomy in the elderly. American Journal of Neuroradiology 31(7): 1181–5	n=106 FU=not reported	Elderly patients were more likely to die from their stroke than those younger than 80 years of age, regardless of recanalisation success. Among survivors, there was no difference in the probability of having a good functional outcome by discharge. Haemorrhagic transformation did not vary between age groups.	Retrospective review.
Loh Y, Jahan R, McArthur DL, et al. (2010) Recanalization rates decrease with increasing thrombectomy attempts. American Journal of Neuroradiology 31: 935–9	n=97 FU=not reported	Recanalisation (following 3 attempts) in 65% of patients. Subarachnoid haemorrhage=17% Air embolism=3% Dissections=2% Intraventricular haemorrhage=2% Perforation=1% There were 4 reports of device fracture.	Clinical outcomes not a measure of the study.

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Lummel N, Schulte-Altedorneburg G, Bernau C et al. (2014) Hyperattenuated intracerebral lesions after mechanical recanalization in acute stroke. American Journal of Neuroradiology 35: 345-351	Case series n=101	The extent of postinterventional hyperattenuated intracerebral lesions underestimates the volume of final infarction. Although hyperattenuated lesions indicate a higher risk of secondary haemorrhagic transformation, their presence seems not to be of any prognostic value regarding clinical outcome.	Study focuses on prognostic value of hyperattenuated lesions.
Lutsep HL, Hill MD (2012) Effects of sex on mechanical embolectomy outcome. Journal of Stroke and Cerebrovascular Diseases 21(3): 240–2	n=305 FU=not reported	Revascularisation was significantly associated with favourable outcomes in both women and men, and rates of favourable outcome, mortality, and symptomatic ICH did not differ between women and men when the vessel was revascularised.	Review
Ma Q-F, Chu C-B, Song H-Q. (2015) Intravenous versus intra-arterial thrombolysis in ischemic stroke: A systematic review and meta-analysis. PLoS ONE 10: DOI: 10.1371/journal.pone.0116120	Systematic review and meta-analysis	IAT conferred a significantly greater probability of achieving a favourable outcome compared with IVT. There was also a significant difference in mortality rates between IAT and IVT. The studies included in this analysis were small and heterogeneous; therefore, larger randomised prospective clinical studies are necessary to further investigate this issue.	Search date of review: October 2013
Machi P, Costalat V, Lobotesis K et al. (2012) Solitaire FR thrombectomy system: immediate results in 56 consecutive acute ischemic stroke patients Journal of NeuroInterventional Surgery. 4: 62–6	n=56 FU=not reported	Successful recanalisation=89% procedure related complications: 2 asymptomatic SAH, 2 thromboembolic events and 1 symptomatic ICH (PH2). Thirty patients (54%) demonstrated at discharge a NIHSS of ≤1 or an improvement of at least 10 points from baseline, and 26 patients (46%) had a mRS ≤2.	Small case series.
Maingard J, Paul A, Churilov L et al. (2014) Recanalisation success is independent of ASPECTS in predicting outcomes after intra-arterial therapy for acute ischaemic stroke. Journal of Clinical Neuroscience 21: 1344-1348	Case series n=44 FU=90 days	Recanalisation success was strongly associated with good clinical outcome, unaffected by known predictive factors, which included age and stroke severity.	Small case series.

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Man S, Aoki J, Hussain MS et al. (2015) Predictors of infarct growth after endovascular therapy for acute ischemic stroke. Journal of Stroke & Cerebrovascular Diseases 24: 401-407	Case series n=76	Diffusion-weighted imaging reversal or no growth translated to a favourable outcome. Small initial ischaemic core, good collateral support, and better recanalisation grades predict the smaller infarct growth and favourable outcome after endovascular thrombectomy.	Small case series.
Man S, Hussain MS, Wisco D et al. (2015) The location of pretreatment hyperdense middle cerebral artery sign predicts the outcome of intraarterial thrombectomy for acute stroke. Journal of Neuroimaging 25: 263-268	Case series n=126 FU=30 days	For acute ischemic stroke due to large vessel occlusion, the lack of hyperdense middle cerebral artery sign (HMCAS) on non-enhanced CT does not predict favourable outcome after intra-arterial therapy. Among those with HMCAS, proximal and longer HMCAS predicts unfavourable outcome.	Small case series.
Mangiafico S, Pracucci G, Saia V et al. (2015) The Italian Registry of Endovascular Treatment in Acute Stroke: rationale, design and baseline features of patients. Neurological Sciences 36: 985-93	Case series (registry data) n=960	The most frequent occlusion site was middle cerebral artery (47%). Intra-arterial thrombolytics were used in 165 (18%) patients, in 531 (58%) thrombectomy was used, and 228 (25%) patients received both treatments.	The study only reports baseline features.
Mathews MS, Sharma J, Snyder KV, et al. (2009) Safety, effectiveness, and practicality of endovascular therapy within the first 3 hours of acute ischaemic stroke onset. Neurosurgery 65(5): 860–5	n=94 FU=10.6 months mean	Mortality rate=27%. 16 patients (17%) were discharged home, 49 (52%) to rehabilitation, and 4 (4%) to long-term care facilities. Overall, 37% had mRS ≤2 at discharge. The mean NIHSS score at discharge was 6.5, representing an overall 8-point improvement.	Small case series; retrospective chart review.
Mazighi et al, (2009) Comparison of intravenous alteplase with a combined intravenous-endovascular approach in patients with stroke and confirmed arterial occlusion (RECANALISE study): a prospective cohort study. Lancet Neurology: 8(9):802-9	n=53 IV-endovascular group and 108 IV group FU=90 days	87% of patients treated with the IV-endovascular approach achieved recanalisation versus 52% in the IV group (adjusted relative risk [RR] 1.49, 95% CI 1.21-1.84; p=0.0002). Early neurological improvement (NIHSS score of 0 or 1 or an improvement of 4 points or more at 24 h)=60% vs 39% (adjusted RR 1.36, 0.97-1.91; p=0.07). Favourable outcome (mRS of 0-2 at 90 days)= 57% vs 44% (adjusted RR 1.16, 0.85-1.58; p=0.35). Mortality at 90 days=17% in both groups. Symptomatic intracranial haemorrhage=9% vs 11%.	Larger studies are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
McDonald JS, Brinjikji W, Rabinstein AA et al. (2014) Conscious sedation versus general anaesthesia during mechanical thrombectomy for stroke: a propensity score analysis. Journal of Neurointerventional Surgery doi: 10.1136/neurintsurg-2014-011373.	n=2512	Thrombectomy patients receiving conscious sedation have decreased in-hospital mortality, decreased rates of pneumonia, and lower hospital costs and lengths of stay when compared with patients who received general anaesthesia.	Comparison of general anaesthesia against conscious sedation.
Menon BK, Almekhlafi MA, Pereira VM et al. (2014) Optimal workflow and process-based performance measures for endovascular therapy in acute ischemic stroke: analysis of the Solitaire FR thrombectomy for acute revascularization study. Stroke 45: 2024-2029	Case series n=202 FU=90 days	For each 1-hour increase in stroke onset to final digital subtraction angiography (or TICI 2b/3) time, odds of good clinical outcome decreased by 38%.	More recent RCTs are included.
Meyne JK, Zimmermann PR, Rohr A et al. (2015) Thrombectomy vs. Systemic Thrombolysis in Acute Embolic Stroke with High Clot Burden: A Retrospective Analysis. Rofo 187: 555-560	Non-randomised comparative study n=82 FU=90 days	Thrombectomy in acute stroke with high clot burden using the Trevo(R) device has a low risk and improved clinical outcome compared to intravenous thrombolysis alone. Treatment selection by a clot length of >/= 8 mm might be a powerful approach to improve the outcome of mechanical thrombectomy.	More recent RCTs are included.
Mokin M, Kass-Hout T, Kass-Hout O et al. (2012) Intravenous thrombolysis and endovascular therapy for acute ischemic stroke with internal carotid artery occlusion: a systematic review of clinical outcomes. Stroke 43:2362–8	Systematic review n=969	Favourable outcome=34% (endovascular therapy) vs 25% (IV thrombolysis only), p=0.004 Mortality=32% vs 27%, p=0.12 Symptomatic intracranial haemorrhage=11% vs 5%, p=0.001	More recent RCTs are included. (study was included in table 2 of 2013 overview)
Mokin M, Dumont TM, Veznedaroglu E et al. (2013) Solitaire Flow Restoration thrombectomy for acute ischemic stroke: retrospective multicenter analysis of early postmarket experience after FDA approval. Neurosurgery 73: 19-25	Case series n=101 FU=30 days	Intravenous thrombolysis was used in 39% of patients; other endovascular techniques were used in conjunction with the Solitaire FR in 52%. Successful recanalisation (Thrombolysis in Myocardial Infarction 2/3) was achieved in 88%. The rate of symptomatic intracranial haemorrhage within the first 24 hours was 15%. In-hospital mortality was 26%. At 30 days, 38% of patients had favourable functional outcome (modified Rankin scale score <2).	Small case series.

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Mokin M, Kan P, Sivakanthan S et al. (2015) Endovascular therapy of wake-up strokes in the modern era of stent retriever thrombectomy. Journal of Neurointerventional Surgery doi: 10.1136/neurintsurg-2014-011586	Case series n=51 FU=3 months	Successful recanalisation (Thrombolysis in Cerebral Infarction (TICI) 2b/3) was achieved in 36 (69%) patients. Favourable clinical outcome at 3 months, defined as a modified Rankin Scale score of 0-2, was achieved in 25 (48%) patients. Duration of intervention <30 min and its success, defined as TICI 2b/3 recanalization, were strong predictors of favourable clinical outcome at 90 days ($p<0.001$ and $p<0.0001$, respectively).	Small case series.
Mokin M, Morr S, Natarajan SK et al. (2015) Thrombus density predicts successful recanalization with Solitaire stent retriever thrombectomy in acute ischemic stroke. Journal of Neurointerventional Surgery 7: 104-107	Case series n=41	In acute stroke treated with Solitaire stent retriever thrombectomy, higher thrombus Hounsfield Unit values are predictive of successful recanalisation.	Small case series.
Mosimann PJ, Sirimarco G, Meseguer E et al. (2013) Is intracerebral hemorrhage a time-dependent phenomenon after successful combined intravenous and intra-arterial therapy? Stroke 44: 806-808	Prospective registry data n=157	Onset-to-reperfusion time influences the rate but not the volume of ICH and appears to be a critical predictor of symptomatic haemorrhage after successful combined intravenous and intra-arterial therapy. To minimize the risk of bleeding, revascularisation should be achieved within 4.5 hours of stroke onset.	More recent RCTs are included.
Mourand I, Brunel H, Costalat V, et al. (2011) Mechanical thrombectomy in acute ischaemic stroke: catch device. American Journal of Neuroradiology 32(8): 1381–5	n=40 FU=90 days	Successful recanalisation achieved in 65% (26/40) with procedural complications occurring in 6 patients (15%).	Small case series.
Mpotsaris A, Bussmeyer M, Buchner H et al. (2013) Clinical outcome of neurointerventional emergency treatment of extra- or intracranial tandem occlusions in acute major stroke: antegrade approach with wallstent and solitaire stent retriever. Clinical Neuroradiology 23 (3) 207-215	n=50	Acute extracranial stenting with the Wallstent combined with intracranial Solitaire-based thrombectomy is safe and may lead to an improvement in neurological outcome in patients with an otherwise poor prognosis under intravenous thrombolysis alone.	Small case series.

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Mpotsaris A, Kowoll A, Weber W et al. (2015) Endovascular stroke therapy at nighttime and on weekends-as fast and effective as during normal business hours? Journal of Vascular & Interventional Neurology 8 (1) 39-45	Case series n=98	There was a statistically significant prolongation of door-to-reperfusion timings for patients admitted during nighttime and weekends; it went along neither with a lower rate of successful revascularisations nor with a lower rate of favourable outcome in our series.	Small case series focusing on time of admission.
Nagel S, Kellert L, Mohlenbruch M et al. (2013) Improved clinical outcome after acute basilar artery occlusion since the introduction of endovascular thrombectomy devices. Cerebrovascular Diseases 36: 394-400	Case series n=147	Outcomes were improved for patients treated after July 2009. The treatment approach in this group was an independent predictor of both good outcome and mortality. Especially in patients with basilar artery occlusion - where endovascular treatment strategies are common clinical practice - bridging protocols with rtPA and modern thrombectomy devices should be used more frequently.	Case series focusing on basilar artery occlusion.
Nelles M, Greschus S, Mohlenbruch M et al. (2014) Patient selection for mechanical thrombectomy. Clinical Neuroradiology 24: 239-244	Case series n=65 (mechanical thrombectomy)	The size of the infarct core and the ratio relative to the tissue at risk are more relevant parameters for clinical outcome after mechanical thrombectomy than time related factors.	Small case series.
Nikoubashman O, Reich A, Pjontek R et al. (2014) Postinterventional subarachnoid haemorrhage after endovascular stroke treatment with stent retrievers. Neuroradiology 56:1087-1096	Case series n=113	Subarachnoid haemorrhages after endovascular mechanical thrombectomy in acute ischemic stroke are likely to occur in complicated cases in which more than one revascularisation attempt is performed. They do not appear to be associated with an impaired clinical outcome or an elevated risk for consecutive haemorrhage.	Small case series.
Nguyen TN, Malisch T, Castonguay AC et al. (2014) Balloon guide catheter improves revascularization and clinical outcomes with the solitaire device: Analysis of the north american solitaire acute stroke registry. Stroke 45: 141-145	Registry n=354	Use of a balloon guide catheter with the Solitaire Flow Restoration device resulted in superior revascularisation results, faster procedure times, decreased need for adjunctive therapy, and improved clinical outcome.	Study focuses on the role of the balloon guide catheter.

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Nogueira RG, Liebeskind DS, Sung G, et al. (2009) Predictors of good clinical outcomes, mortality, and successful revascularization in patients with acute ischaemic stroke undergoing thrombectomy: pooled analysis of the Mechanical Embolus Removal in Cerebral Ischaemia (Merci) and multi-Merci Trials. Stroke 40(12): 3777–83	n=305 FU=90 days	In the univariate analysis, final revascularisation, baseline NIHSS, age, and systolic blood pressure were associated with both good outcomes and mortality at 90 days. In the multivariate analysis, final revascularisation, baseline NIHSS, and age were independent predictors of good outcome. Final revascularisation, baseline NIHSS, age, and internal carotid artery occlusion were the strongest predictors of mortality. Systolic blood pressure and M2 occlusion were independent predictors of revascularisation.	Pooled analysis of data from Merci and Multi-Merci trials. More recent RCTs are included.
Nogueira RG, Smith WS, Sung G, et al. (2011) Effect of time to reperfusion on clinical outcome of anterior circulation strokes treated with thrombectomy: pooled analysis of the Merci and multi-Merci trials. Stroke 42(11): 3144–9	n=175 FU=90 days	Baseline NIHSS and age were independent predictors of independent outcome and mortality. High glucose demonstrated a strong trend toward worse outcomes. After adjustment for age, baseline NIHSS, and glucose, there was a strong trend toward fewer independent outcomes with later reperfusion times. Notably, 40% of the patients re-perfused at ≥6.9 hours achieved independent functional outcomes.	Pooled analysis of data from Merci and Multi-Merci trials. More recent RCTs are included.
Nogueira RG, Lutsep HL, Gupta R et al. (2012) Trevo versus Merci retrievers for thrombectomy revascularisation of large vessel occlusions in acute ischaemic stroke (TREVO 2): a randomised trial. Lancet 380: 1231–40	RCT (stent retriever versus coil retriever) n=178 FU=90 days	76 (86%) patients in the Trevo group and 54 (60%) in the Merci group met the primary endpoint after the assigned device was used (odds ratio 4·22, 95% CI 1·92-9·69; p(superiority)<0·0001). Incidence of the primary safety endpoint did not differ between groups (13 [15%] patients in the Trevo group vs 21 [23%] in the Merci group; p=0·1826).	More recent RCTs are included. (study was included in table 2 of 2013 overview)
Nogueira RG, Gupta R, Jovin TG et al. (2015) Predictors and clinical relevance of hemorrhagic transformation after endovascular therapy for anterior circulation large vessel occlusion strokes: a multicenter retrospective analysis of 1122 patients. Journal of Neurointerventional Surgery 7: 16-21	Case series n=1122	Overall rate of intracranial haemorrhage=32% Independent predictors for haemorrhagic infarction: diabetes mellitus, preprocedure IV tissue plasminogen activator, Merci thrombectomy, and longer time to puncture. The presence of haemorrhagic infarction and parenchymal haematomas were associated with poor functional outcomes.	Study focuses on haemorrhagic transformation.

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Osanai T, Pasupuleti V, Deshpande A et al. (2015) Acute endovascular reperfusion therapy in ischemic stroke: a systematic review and meta-analysis of randomized controlled trials. PLoS ONE [Electronic Resource] 10 (4) e0122806	Systematic review and meta-analysis n=1612 (10 studies)	Intra-arterial therapy did not show significant increase in good outcomes and no changes in either mortality or sICH in patients with acute ischemic stroke. We need further RCTs with better design and quality to evaluate the true efficacy of endovascular therapy.	Review does not include the recent RCTs that are described in table 2.
Pagola J, Rubiera M, Flores A et al. (2013) Selecting endovascular treatment strategy according to the location of intracranial occlusion in acute stroke. Cerebrovascular Diseases 35: 502-506	Non-randomised comparative study n=180	Among acute stroke patients undergoing endovascular therapies, the benefits of mechanical thrombectomy by retrievers over intra-arterial therapy are greater in internal carotid artery occlusions. Retrievers may be considered as the first therapeutic option in these patients.	More recent RCTs are included.
Pereira VM, Gralla J, Davalos A et al. (2013) Prospective, multicenter, single-arm study of mechanical thrombectomy using Solitaire Flow Restoration in acute ischemic stroke. Stroke 44: 2802-2807	Case series n=202 FU=90 days	Successful revascularisation was achieved in 79% of patients. Device and procedure-related severe adverse events were found in 7%. Favourable neurological outcome was found in 58%. The mortality rate was 7%. Any intracranial haemorrhagic transformation was found in 19% of patients, 1.5% were symptomatic.	More recent RCTs are included.
Penumbra Pivotal Stroke Trial Investigators (2009) The penumbra pivotal stroke trial: safety and effectiveness of a new generation of mechanical devices for clot removal in intracranial large vessel occlusive disease. Stroke 40: 2761–8	Case series n=125 FU=90 days	Modified Rankin score ≤2 at 90 days=25% 90 day mortality=33% Symptomatic intracranial haemorrhage=11%	More recent RCTs are included. (study was included in table 2 of 2013 overview)
Pfefferkorn T, Holtmannspotter M, Patzig M, et al. (2012) Preceding intravenous thrombolysis facilitates endovascular mechanical recanalization in large intracranial artery occlusion. International Journal of Stroke 7(1): 14–8	n=65 FU=3 months	Successful recanalisation in 49/65 patients, 2 patients developed arterial perforation and consecutive SAH. Mortality at 3 months 27% (13/49) of successfully treated patients.	Small, retrospective study.
Pi Y, Zhang L, Yang Q et al. (2012) Neurothrombectomy for the treatment of acute ischemic stroke in 1530 patients. Journal of Clinical Neuroscience.19 (10) 1363-8	Meta-analysis n=1530 [46 studies] FU=3 months	Mortality (at 3 months) was 26% in recanalised patients compared to 52% in non-recanalised patients, Odds ratio 0.37 (85% CI 0.24, 0.57); I^2=10%.	More recent RCTs are included.

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Prabhakaran S, Chen M, Choi JH et al. (2008) Major neurologic improvement following endovascular recanalization therapy for acute ischemic stroke. Cerebrovascular Diseases 25 (5): 401-7	n=68 (multimodal therapy [37%]; mechanical only [35%]; pharmacologic only [28%])	TIMI 2 or 3 recanalisation was achieved in 65% (mechanical only 46%, pharmacologic only 63% and multimodal 84%). Symptomatic intracerebral haemorrhage (12%) was also reported.	Small case series.
Prabhakaran S, Ruff I, Bernstein RA (2015) Acute stroke intervention: a systematic review. JAMA 313 (14) 1451-1462	Systematic review n=108,082 (68 articles)	Intravenous rtPA remains the standard of care for patients with moderate to severe neurological deficits who present within 4.5 hours of symptom onset. Outcomes for some patients with acute ischemic stroke and moderate to severe neurological deficits due to proximal artery occlusion are improved with endovascular reperfusion therapy. Efforts to hasten reperfusion therapy, regardless of the mode, should be undertaken within organized stroke systems of care	No meta-analysis for mechanical clot retrieval.
Prabhakaran S, Jovin TG, Tayal AH et al. (2014) Posttreatment variables improve outcome prediction after intra-arterial therapy for acute ischemic stroke. Cerebrovascular Diseases 37: 356-363	Case series (registry data) n=734	Among patients with acute ischaemic stroke treated with endovascular reperfusion therapy, pretreatment scores such as the Totaled Health Risks in Vascular Events (THRIVE) score provide only fair prognostic information. Inclusion of posttreatment variables such as reperfusion and symptomatic haemorrhage greatly influences outcome and results in improved outcome prediction.	Study focuses on the development of a simple outcome prediction score.
Prothmann S, Lockau H, Dorn F et al. (2012) The PHenox clot retriever as part of a multimodal mechanical thrombectomy approach in acute ischemic stroke: single center experience in 56 patients The Scientific Work Journal doi:10.1100/2012/190763	n=56 (Clot retriever alone or in combination with other devices)	Overall TICI 2b/3 reperfusion rates of 62% was achieved. Symptomatic intracranial haemorrhage was reported in 3 patients. There were no device-related adverse events.	Small case series.
Psychogios M-N, Kreusch A, Wasser K et al. (2012) Recanalization of large intracranial vessels using the penumbra system: A single-center experience. American Journal of Neuroradiology 33: 1488-93	n=91 FU=unclear	At follow-up, 36% of the patients showed an NIHSS improvement of ≥10%, and 34% of the patients with an anterior circulation occlusion had an mRS score of ≤2, whereas only 7% of the patients with a posterior occlusion had a favourable outcome at follow-up. In total, 20 patients died during hospitalisation; none of these deaths were device-related.	Small case series.

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Qureshi AI, Miley JT, Chaudhry SA et al. (2013) Safety and effectiveness of endovascular treatment after 6 hours of symptom onset in patients with anterior circulation ischemic stroke: a matched case control study. Journal of Stroke & Cerebrovascular Diseases 22: 1076-1081	Non-randomised comparative study n=104 FU=7 days	In an analysis limited to only those patients who underwent CT perfusion imaging or MRI before receiving endovascular treatment, the rate of favourable outcome at 7 days or discharge was similar between patients who underwent endovascular treatment and control patients (36% versus 32%; p=0.77)	More recent RCTs are included.
Rai A, Carpenter JS, Raghuram K et al. (2012) Endovascular therapy yields significantly superior outcomes for large vessel occlusions compared with intravenous thrombolysis: is it time to randomize? Journal of NeuroInterventional Surgery 0: 1–5	Case series n=223 FU=90 days	Endovascular therapy compared with IV thrombolysis was significantly associated with a favourable outcome: OR 3.9 (95% CI 1.8 to 9); p=0.0004	More recent RCTs are included. (study was included in table 2 of 2013 overview)
Rai AT, Jhadhav Y, Domico J et al. (2012) Procedural predictors of outcome in patients undergoing endovascular therapy for acute ischemic stroke. Cardiovascular & Interventional Radiology 35: 1332-1339	Case series n=89 FU=3–6 months	Favourable outcome was seen in 49% of patients and mortality in 26% of patients. Younger age (p=0.006), lower baseline NIHSS score (p=0.001), successful recanalisation (p<0.0001), collateral support (p=0.0008), distal occlusion (p=0.001), and shorter procedure duration (p=0.01) were associated with a favourable outcome.	Small case series.
Rai AT, Raghuram K, Domico J et al. (2013) Pre-intervention triage incorporating perfusion imaging improves outcomes in patients undergoing endovascular stroke therapy: a comparison with the device trials. Journal of Neurointerventional Surgery 5: 121-127	Case series n=99	Despite similar or lower recanalisation rates, there was a significantly higher rate of good outcomes in the recanalised population and thus a significantly lower rate of futile recanalisation in this study versus the device trials, suggesting a role for pre-intervention perfusion imaging for patient selection.	Small case series.
Rangaraju S, Liggins JT, Aghaebrahim A et al. (2014) Pittsburgh outcomes after stroke thrombectomy score predicts outcomes after endovascular therapy for anterior circulation large vessel occlusions. Stroke 45: 2298-2304	Case series n=247	Pittsburgh Outcomes After Stroke Thrombectomy (POST) score is a validated predictor of outcome in patients with anterior circulation large vessel occlusions after endovascular therapy.	Study focuses on development of a prognostication tool.
Raoult H, Eugene F, Ferre JC et al. (2013) Prognostic factors for outcomes after mechanical thrombectomy with solitaire stent. Journal of Neuroradiology Journal: 252-259	Case series n=45 FU=3 months	Two main prognostic factors for predicting a good clinical outcome after thrombectomy at 3 months were short time from symptom onset to recanalisation and patient age.	Small case series.

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Rentzos A, Lundqvist C, Karlsson JE et al. (2014) Mechanical embolectomy for acute ischemic stroke in the anterior cerebral circulation: the Gothenburg experience during 2000-2011. American Journal of Neuroradiology 35: 1936-1941	Case series n=156 FU=90 days	A high recanalisation rate was obtained with the Amplatz GooseNeck snare without any device-related complications. Favourable outcome, mortality, and symptomatic intracerebral hemorrhage are comparable with results of newer embolectomy devices.	More recent RCTs are included.
Rha JH and Saver JL (2007) The impact of recanalization on ischaemic stroke outcome: a meta-analysis. Stroke 38(3): 967–73	n=2066 FU=3 months	Recanalisation rates for mechanical intervention were 84%. Clinical outcome data categorised by success or failure in achieving recanalisation were available from 33 articles encompassing 998 patients. Good functional outcomes at 3 months were more frequent in recanalised versus non-recanalised patients with an odds ratio of 4.43. 3-month mortality was reduced in recanalised patients. Rates of symptomatic haemorrhagic transformation did not differ between the 2 groups.	Review. Mixed methods, most not mechanical clot retrieval.
Ribo M, Molina CA, Jankowitz B et al. (2014) Stentrievers versus other endovascular treatment methods for acute stroke: comparison of procedural results and their relationship to outcomes. Journal of Neurointerventional Surgery 6: 265-269	Non-randomised comparative study n=315	In acute endovascular treatment of stroke, the use of stent retrievers may increase recanalisation and reduce time to flow restoration leading to improved outcomes.	More recent RCTs are included.
Roth C, Reith W, Walter S et al. (2013) Mechanical recanalization with flow restoration in acute ischemic stroke: the ReFlow (mechanical recanalization with flow restoration in acute ischemic stroke) study. Jacc: Cardiovascular Interventions 6: 386-391	Case series n=40 FU=90 days	24 patients (60%) showed a good clinical outcome (mRS<2) at 90 days. One symptomatic haemorrhage was detected on follow-up CT. The death rate was 12.5% (5/40). Successful recanalisation (Thrombolysis In Cerebral Infarction score>2b) of the target vessel was achieved in 95% of the patients.	Small case series.
Rouchaud A, Mazighi M, Labreuche J et al. (2011) Outcomes of mechanical endovascular therapy for acute ischemic stroke: a clinical registry study and systematic review. Stroke 42: 1289–94.	Register and meta-analysis n=1113	Partial or complete recanalisation=79% Mortality=28% Haemorrhagic complication=27% Symptomatic ICH=8%	More recent RCTs are included. (study was included in table 2 of 2013 overview)

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Rozeman AD, Wermer MJ, Lycklama A et al. (2014) Intra-arterial treatment of acute ischemic stroke: Better outcome with stent retrievers? Interventional Neurology 2:144-152	Non-randomised comparative study n=84	There was a trend towards poorer outcome in the thrombolysis only (ND) group (adjusted RR 1.18; 95% CI 0.74-1.88) and the MERCI group (adjusted RR 1.17; 95% CI 0.79-1.74) compared with the stent retriever (SR) group. Furthermore, failed recanalisation occurred more often in the ND group (adjusted RR 2.59; 95% CI 1.50-4.49) and MERCI group (adjusted RR 2.32; 95% CI 1.33-4.05) compared with the SR group.	Small, non-randomised comparative study.
Ruberia M, Cava L, Tsivgoulis G, et al. (2010) Diagnostic criteria and yield of real-time transcranial Doppler monitoring of intra-arterial reperfusion procedures. Stroke 41: 695–9	n=51 FU=3 months	TIMI 2 or 3 achieved in 75% (38/51) At 3 months 35% (18/51) had mRS ≤2. At 12–24 hours, 27%(14/51) of patients had ICH; 6% (3/51) were symptomatic, and 10% (5/51) had parenchymal haemorrhage without neurological worsening.	A combination of methods with 55% receiving more than one. Adverse events and outcomes not clearly reported and unclear which events linked to clot retrievers.
Saad A, Adil MM, Patel V et al. (2014) Clinical outcomes after thrombectomy for acute ischemic stroke on weekends versus weekdays. Journal of Stroke and Cerebrovascular Diseases 23: 2708-2713	Case series n=12,055	Acute ischaemic stroke patients undergoing thrombectomy who were admitted to nonteaching hospitals on weekends were more likely to be discharged with moderate-to-severe disability than those admitted on weekdays. No weekend effect on discharge clinical outcome was seen in teaching hospitals.	Study focuses on time of admission.
Saeed F, Adil MM, Piracha BH et al. (2014) Outcomes of endovascular versus intravenous thrombolytic treatment for acute ischemic stroke in dialysis patients. International Journal of Artificial Organs 37: 727-733	Non-randomised comparative study n=2313 (915 endovascular treatment)	The in-hospital mortality rate and moderate-to-severe disability were lower in dialysis patients receiving endovascular treatment (8% versus 15% p=0.04) and (30% versus 52% p=<0.0001), respectively. After adjusting for age, gender, and potential confounders, endovascular treatment was associated with lower in-hospital mortality (OR 0.5, 95% CI 0.2-0.9) and moderate-to-severe disability (OR 0.3, 95% CI 0.2-0.5).	Endovascular treatment was intra-arterial tPA with or without mechanical thrombectomy.

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Sanak D, Kocher M, Veverka T et al. (2013) Acute combined revascularization in acute ischemic stroke with intracranial arterial occlusion: self-expanding solitaire stent during intravenous thrombolysis. Journal of Vascular & Interventional Radiology 24: 1273-1279	Case series n=50 FU=3 months	Recanalisation=94% Complete recanalisation (ie, TICI 3 flow)=72% Mean time from stroke onset to maximal recanalisation=244 minutes, with a median of 233 minutes. Symptomatic intracerebral haemorrhage=6% Median mRS score at 90 days=1 60% of patients had a good outcome (ie, mRS score 0-2). The overall 3-month mortality rate was 14%	Small case series.
San Roman L, Obach V, Blasco J et al. (2012) Single-center experience of cerebral artery thrombectomy using the TREVO device in 60 patients with acute ischemic stroke. Stroke 43:1657-9	n=60 FU=90 days	Mortality rate was 28%,12% of patients presented a symptomatic intracranial haemorrhage and 12% had serious bleedings. There was 1 carotid dissection and 1 symptomatic distal embolisation (resolved). No other major complications were detected.	Larger studies are included.
Schwaiger BJ, Kober F, Gersing AS et al. (2014) The pREset Stent Retriever for Endovascular Treatment of Stroke Caused by MCA Occlusion: Safety and Clinical Outcome. Clinical Neuroradiology DOI: 10.1007/s00062-014-0329-z	Case series n=48	Successful recanalisation (TICI 2b/3)=81% (39/48). There were 4 subarachnoid haemorrhages and 4 parenchymal hematomas, none of which was associated with clinical deterioration. Middle cerebral artery curvature significantly influenced recanalization success ($p<0.005$). Successful recanalisation correlated significantly with lower NIHSS scores and favourable clinical outcome (mRS score 0-2) at discharge ($p<0.05$). Mortality within 90 days was significantly lower in patients with TICI 2b/3 ($p<0.005$).	Small case series.
Schwaiger BJ, Gersing AS, Zimmer C et al. (2015) The Curved MCA: Influence of Vessel Anatomy on Recanalization Results of Mechanical Thrombectomy after Acute Ischemic Stroke. American Journal of Neuroradiology 36: 971-976	Case series n=159	This retrospective analysis showed that mechanical thrombectomy in the anterior circulation was significantly less often successful in patients with large vessel angles. Therefore, vessel curvature significantly influences the results of mechanical thrombectomy with stent retrievers for treatment of acute ischemic stroke.	Retrospective study focusing on the influence of vessel anatomy on results of mechanical clot retrieval.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Shah VA, Martin CO, Hawkins AM et al. (2015) Groin complications in endovascular mechanical thrombectomy for acute ischemic stroke: a 10-year single center experience. Journal of Neurointerventional Surgery doi:10.1136/neurintsurg-2015-011763	Case series n=472	There was a very low rate of clinically significant groin complications (0.4-0.8%) associated with the use of large-bore sheaths.	Study focuses on rate of groin complications, which are already reported in table 2.
Shi ZS, Loh Y, Walker G, et al. (2010) Endovascular thrombectomy for acute ischaemic stroke in failed intravenous tissue plasminogen activator versus non-intravenous tissue plasminogen activator patients: revascularization and outcomes stratified by the site of arterial occlusions. Stroke 41(6): 1185–92	n=305 FU=90 days	Non-responders to IV tPA trended toward a higher revascularisation rate, lower mortality and similar rates of symptomatic haemorrhage and procedural complications. Favourable 90-day outcomes were similar in failed and non–IV tPA patients with no difference according to occlusion site. Among patients failing IV tPA, good outcomes were more frequently seen in revascularised patients although this was attributable to middle cerebral artery occlusions, with no difference in mortality. Among IV tPA–ineligible patients, revascularisation correlated with good outcome and less mortality.	Pooled analysis of data from Merci and Multi-Merci trials. More recent RCTs are included.
Shi Z-S, Duckwiler GR (2010) Clinical outcomes in middle cerebral artery trunk occlusions versus secondary division occlusions after mechanical thrombectomy: Pooled analysis of the MERCI and Multi MERCI trials. Stroke 41: 953–60	n=178 FU=90 days	Patients with isolated M2 occlusions were revascularised at a higher rate, required a lower mean number of passes, and were associated with a trend towards shorter mean procedure time than patients with M1 occlusions. No statistically significant differences were found between M2 and M1 groups for symptomatic haemorrhage, clinically significant procedural adverse events, favourable 90-day outcome, or 90-day mortality, although in all instances, the M2 outcomes were numerically better than those in M1 subjects. In multivariate analysis, final revascularisation was the strongest independent predictor of good outcome at 90 days.	Pooled analysis of data from Merci and Multi-Merci trials. More recent RCTs are included.

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Shi ZS, Liebeskind DS, Loh Y, et al. (2010) Predictors of subarachnoid hemorrhage in acute ischaemic stroke with endovascular therapy. Stroke 41: 2775–81	n=159 FU=not reported	20 patients experienced SAH, 8 with pure SAH and 12 with coexisting parenchymal haemorrhages. SAH was more frequent with primary thrombectomy than in the intra-arterial thrombolysis groups. Patients with extensive SAH or coexisting parenchymal haematomas tended to have more neurologic deterioration at 3 hours, to be less independent at discharge and to experience higher mortality during hospitalisation.	Retrospective review including patients enrolled onto other trials.
Shi ZS, Duckwiler GR, Loh Y et al. (2012) Impact of Merci device fracture on clinical outcome of acute ischemic stroke after mechanical thrombectomy. CNS Neuroscience & Therapeutics 18: 841-846	Case series n=136	Of 136 patients treated by thrombectomy, 6 (4%) experienced intraprocedural Merci device fracture. Internal carotid artery occlusion was associated with device fracture. Patients with fractured devices had similar rates of successful revascularisation with those without. Patients with fractured devices tended to be more dependent (modified Rankin Scale>3) at discharge, but had similar rates of in-hospital mortality.	Study focuses on device fracture of coil device: technical device problems are included in table 2.
Shi ZS, Liebeskind DS, Xiang B et al. (2014) Predictors of functional dependence despite successful revascularization in large-vessel occlusion strokes. Stroke 45: 1977-1984	Case series n=228	The rates of functional dependence with endovascular success were 49% for Trevo thrombectomy and 58% for Merci thrombectomy. Age, National Institutes of Health Stroke Scale score, and symptom onset to endovascular treatment time were predictors of functional dependence despite successful revascularisation. Symptom onset to reperfusion time beyond 5 hours was associated with functional dependence. All subjects with symptomatic intracranial haemorrhage had functional dependence.	Pooled data from MERCI, TREVO, and TREVO 2 trials.
Shi ZS, Duckwiler GR, Jahan R, et al. (2015) Mechanical thrombectomy for acute ischemic stroke with cerebral microbleeds. Journal of Neurointerventional Surgery doi:10.1136/neurintsurg-2015-011765	Case series n=206	Patients with cerebral microbleeds are not at increased risk for haemorrhagic transformation and mortality following mechanical thrombectomy for acute stroke. Excluding such patients from mechanical thrombectomy is unwarranted.	Study focuses on patients with cerebral microbleeds.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Singer OC, Berkefeld J, Nolte CH et al. (2015) Mechanical recanalization in basilar artery occlusion: the ENDOSTROKE study. Annals of Neurology 77: 415-424	Registry data n=148 FU=median 120 days	Beside initial stroke severity, the collateral status predicts clinical outcome and recanalisation in BA occlusion. The data suggest that the use of a stent retriever is associated with high recanalisation rates, but recanalisation on its own does not predict outcome.	More recent RCTs are included.
Singer OC, Haring HP, Trenkler J et al. (2013) Periprocedural aspects in mechanical recanalization for acute stroke: data from the ENDOSTROKE registry. Neuroradiology 55: 1143-1151	Registry data n=734	Overall thrombolysis in myocardial infarction grade 2/3 recanalisation rate was 85%. Stent retrievers were used in 75%, being associated with higher recanalisation rates than non-stent retrievers. Haemorrhagic complications (symptomatic and asymptomatic) occurred in 12%.	More recent RCTs are included.
Skagen K, Skjelland M, Russell D et al. (2015) Large-Vessel Occlusion Stroke: Effect of Recanalization on Outcome Depends on the National Institutes of Health Stroke Scale Score. Journal of Stroke and Cerebrovascular Diseases 24: 1532–9	Case series n=152	In this study of acute large-vessel occlusion stroke, clinical outcome following early recanalisation was dependent on the patient's pretreatment NIHSS score. A non-negligible proportion of patients with milder strokes did well despite persistent large-vessel occlusion.	Case series focusing on the effect of the NIHSS score.
Smith WS, Sung G, Saver J et al. (2008) Mechanical thrombectomy for acute ischemic stroke: final results of the Multi MERCI trial. Stroke 39: 1205–12	Case series n=177 FU=90 days	Modified Rankin score ≤2=36% 90 day mortality=34% Symptomatic intracranial haemorrhage=10%	More recent RCTs are included. (study was included in table 2 of 2013 overview)
Smith WS (2006) Safety of mechanical thrombectomy and intravenous tissue plasminogen activator in acute ischemic stroke. Results of the multi Mechanical Embolus Removal in Cerebral Ischemia (MERCI) trial, part I. American Journal of Neuroradiology 27(6): 1177–82	n=111 patients FU=90 days	Treatment with the retriever alone resulted in successful recanalisation in 54% (60/111 treatable vessels and in 69% (77/ 111) after adjunctive therapy. Symptomatic intracranial haemorrhage occurred in 10 of 111 (9%). Clinically significant procedural complications occurred in 5 of 111 (5%) patients. The symptomatic ICH rate was 2 of 30 (7%) in patients pre-treated with IV tPA and 8 of 81 (10%) in those without.	More recent RCTs are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Smith WS, Sung G, Starkman S et al. (2005) Safety and efficacy of mechanical embolectomy in acute ischemic stroke: results of the MERCI trial. Stroke 36: 1432–8	Case series n=151	Modified Rankin score ≤2 at 90 days=28% 90 day mortality=44% Symptomatic intracranial haemorrhage=8%	More recent RCTs are included. (study was included in table 2 of 2013 overview)
Soize S, Kadziolka K, Estrade L et al. (2013) Mechanical Thrombectomy in Acute Stroke: Prospective Pilot Trial of the Solitaire FR Device while Under Conscious Sedation. American Journal of Neuroradiology 34 (2) 360-5	n=36 FU=90 days	Successful revascularisation was achieved in 28/36 patients (78%). After 3 months, 22 patients (61%) showed good functional outcome (mRS ≤2) and the median NIHSS score was 8.5. Overall mortality rate at 3 months was 22% (8/36)	Small case series.
Soize S, Barbe C, Kadziolka K et al. (2013) Predictive factors of outcome and hemorrhage after acute ischemic stroke treated by mechanical thrombectomy with a stent-retriever. Neuroradiology 55: 977-987	Case series n=59 FU=3 months	A higher baseline Alberta Stroke Program Early CT (ASPECT) score (p=0.04; OR 0.79 per point; 95% CI 0.63-0.99) and successful recanalisation (p=0.02; OR 0.07; 95% CI 0.01-0.72) were independent predictors of good functional outcome. Baseline ASPECT score (p<0.01; OR 0.65; 95% CI 0.54-0.78) independently predicted symptomatic intracranial haemorrhage at day 1.	Small case series.
Soize S, Kadziolka K, Estrade L et al. (2014) Outcome after mechanical thrombectomy using a stent retriever under conscious sedation: comparison between tandem and single occlusion of the anterior circulation. Journal of Neuroradiology Journal: 136-142	Case series n=42 FU=3 months	Tandem occlusions had poor clinical outcomes after mechanical thrombectomy compared with single occlusions. The retrograde approach (treatment of distal occlusion first) used in patients under conscious sedation may have contributed to these poor outcomes.	Small case series.
Soize S, Batista AL, Rodriguez Regent C et al. (2015) Susceptibility vessel sign on T2* magnetic resonance imaging and recanalization results of mechanical thrombectomy with stent retrievers: a multicentre cohort study. European Journal of Neurology 22: 967-972	Case series n=153	The susceptibility vessel sign was present in 113 (74%) patients. The success of recanalization in acute stroke patients treated with stent retrievers was related to thrombus length but not to the presence of the susceptibility vessel sign.	Study focuses on susceptibility vessel sign.
Song D, Kim BM, Kim DJ et al. (2014) Comparison of stent retriever and intra-arterial fibrinolysis in patients with acute ischaemic stroke. European Journal of Neurology 21: 779-784	n=105 FU=3 months	Stent retriever was as safe as and more effective than intra-arterial fibrinolysis (IAF). Our findings suggest that SR may be considered as an initial modality rather than IAF in acute stroke patients who undergo endovascular treatment.	Small non-randomised comparative study.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Spiotta AM, Vargas J, Hawk H et al. (2014) Impact of the ASPECT scores and distribution on outcome among patients undergoing thrombectomy for acute ischemic stroke. Journal of Neurointerventional Surgery 7:551-558	Case series n=149	Patients with non-perfect ASPECT scores on pretreatment imaging were more likely to have a haemorrhagic conversion (p=0.04) evident on post-procedure CT. However, functional outcomes were the same. Patients with both cortical and basal ganglia non-perfect ASPECT scores were more likely to be in a persistent vegetative state or expire. No differences were identified in outcome among patients with left- versus right-sided infarcts affecting the basal ganglia or cortical regions.	Study focuses on the use of the ASPECT scores for patient selection.
Spiotta AM, Vargas J, Turner R et al. (2014) The golden hour of stroke intervention: effect of thrombectomy procedural time in acute ischemic stroke on outcome. Journal of Neurointerventional Surgery 6: 511-516	Case series n=159	On logistic regression analysis, time to recanalisation from groin puncture, baseline NIHSS, revascularisation, diabetes, and haemorrhages were found to significantly impact on outcome at 90 days, as measured by the modified Rankin Scale. The findings suggest that extending mechanical thrombectomy procedure times beyond 60 min increases complications and device cost rates while worsening outcomes.	Larger studies are included.
Stead LG, Gilmore RM, Bellolio MF et al. (2008) Percutaneous clot removal devices in acute ischemic stroke: a systematic review and meta-analysis. Archives of Neurology 65: 1024–30	Meta-analysis n=147 FU=90 days minimum	Clinical success was related to device type (p=0.02). Patients in whom a snare device was used were significantly more likely to be independent (mRS≤2) at 90 days compared with patients in whom other devices were used.	More recent RCTs are included. (study was included in table 2 of 2013 overview)
Strbian D, Mustanoja S, Pekkola J (2012) et al. Intravenous alteplase versus rescue endovascular procedure in patients with proximal middle cerebral artery occlusion. International Journal of Stroke.. doi: 10.1111/j.1747-4949.2012.00918.x	n=41 Endovascular-ly treated patients propensity matched with 82 IV thrombolysis FU=3 months	Endovascular group patients had a recanalisation rate of 90%, and more often reached 3-month modified Rankin Scale 0-2 (37% vs 18%, p=0.03). Mortality was equally common (20%) in both groups, and frequency of symptomatic intracerebral haemorrhage was 10% vs 15% (p=0.45).	Larger studies are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Sugg RM, Jackson AS, Holloway W, Martin CO, Akhtar N, Rymer M (2010) Is mechanical embolectomy performed in non-anesthetized patients effective? American Journal of Neuroradiology 31 (8) (pp 1533-1535), 2010 Date of Publication: September 2010 (8): 1533–5	n=66 FU=90 days	Revascularisation rates were 77% for general anaesthesia patients and 70% for non-anaesthetised patients. The non-anesthetised group had better outcomes, but these were not controlled for other factors. Complications were much more frequent in the general anaesthesia patients (22%) than in the non-anaesthetised patients (3.5%).	Data taken from Merci study. Focuses on anaesthesia.
Sztajzel RF, Muller H, Sekoranja L et al. (2015) Strokes in the anterior circulation: comparison between bridging and intravenous thrombolysis. Acta Neurologica Scandinavica 131: 329-335	Non-randomised comparative study n=226 FU=3 months	Patients treated with a bridging approach were more likely to have minimal or no deficit at all at 3 months as compared to the intravenous thrombolysis alone treated group.	More recent RCTs are included.
Tarr R, Hsu D, Kulcsar Zet al. (2010) The POST trial: initial post-market experience of the Penumbra system: revascularization of large vessel occlusion in acute ischemic stroke in the United States and Europe Journal of Neurointerventional Surgery. 2(4):341-4	n=156 (retrospective) FU=90 days	6% (9/157) procedural serious adverse events were reported. All-cause mortality=20% (32/157), and 41% had a mRS of ≤2 at 90-day follow-up as compared with only 25% in the Pivotal trial. Patients who were successfully revascularised by the Penumbra system had significantly better outcomes than those who were not.: Initial post-market experience of the Penumbra system revealed that the revascularization rate and safety profile of the device are comparable to those reported in the Pivotal trial. However, the proportion of patients who had good functional outcome was higher than expected.	More recent RCTs are included.
Taschner CA, Treier M, Schumacher M, et al. (2011) Mechanical thrombectomy with the Penumbra recanalization device in acute ischaemic stroke. Journal of Neuroradiology 1: 47–52	n=40 FU=90 days	Recanalisation=78% of target vessels. On discharge 2/20 patients had a NIHSS score of 0 or 1 or an improvement ≥10 points. All-cause mortality was 3/20. 15% (3/20) of patients had mRS ≤2 at 90 days. 2 patients had symptomatic ICH: 1 died.	Small case series.
Tomsick TA, Yeatts SD, Liebeskind DS et al. (2014) Endovascular revascularization results in IMS III: intracranial ICA and M1 occlusions. Journal of Neurointerventional Surgery doi: 10.1136/neurintsurg-2014-011318.	n=200	No significant differences in efficacy or safety among revascularization methods were demonstrated after adjustment. Lack of high-quality reperfusion, adverse events, and prolonged time to treatment contributed to lower-than-expected mRS 0-2 outcomes and study futility compared with IV rt-PA.	Subanalysis of IMS III trial.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Tsivgoulis G, Alleman J, Katsanos AH et al. (2014) Comparative efficacy of different acute reperfusion therapies for acute ischemic stroke: a comprehensive benefit-risk analysis of clinical trials. Brain and Behavior 4: 789-797	Review n=18 studies	IV therapy with tenecteplase (TNK) was found to have the highest benefit-to-risk ratios (BRRs) (BRR1 [mRS score 0–1]=5.76 and BRR2 [mRS score 0–2]=6.82 for low-dose TNK; BRR= 5.80 and BRR2=6.87 for high-dose TNK), followed by sonothrombolysis (BRR1=2.75 and BRR2=3.38), while endovascular thrombectomy with MERCI retriever was found to have the lowest BRRs (BRR1 range, 0.31-0.65; BRR2 range, 0.52-1.18).	The review does not include the most recent RCTs that are described in table 2.
Turk AS, Nyberg EM, Chaudry MI et al. (2013) Utilization of CT perfusion patient selection for mechanical thrombectomy irrespective of time: a comparison of functional outcomes and complications. Journal of Neurointerventional Surgery 5: 518-522	Case series n=140 FU=90 days	No difference was found in the rates of good functional outcome between patients treated <7 h and those treated >7 h from symptom onset. These data suggest that imaging-based patient selection is a safe and viable methodology.	More recent RCTs are included.
Turk AS, Frei D, Fiorella D (2014) ADAPT FAST study: a direct aspiration first pass technique for acute stroke thrombectomy. Journal of Neurointerventional Surgery 6 (4) 260-264	Case series n=98 FU=90 days	Patients presented with an admitting median National Institutes of Health Stroke Scale (NIHSS) score of 17.0 (12.0-21.0) and improved to a median NIHSS score at discharge of 7.3 (1.0-11.0). Ninety day functional outcomes were 40% (modified Rankin Scale (mRS) 0-2) and 20% (mRS 6). There were two procedural complications and no symptomatic intracerebral haemorrhages.	Small case series.
Turk AS III, Campbell JM, Spiotta A et al. (2014) An investigation of the cost and benefit of mechanical thrombectomy for endovascular treatment of acute ischemic stroke. Journal of Neurointerventional Surgery 6 (1) 77-80	Case series	For the treatment of acute stroke patients, the use of aspiration appears to be the most cost effective method to achieve acceptable recanalisation rates and low complication rates. Stent retriever with local aspiration, despite higher costs and complication rates, yielded better overall outcome.	Retrospective chart review

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Turk AS, Turner R, Spiotta A et al. (2014) Comparison of endovascular treatment approaches for acute ischemic stroke: cost effectiveness, technical success, and clinical outcomes. Journal of Neurointerventional Surgery doi: 10.1136/neurintsurg-2014-011282	Case series	Successful revascularisation was defined as Thrombolysis In Cerebral Infarction (TICI) 2b/3 flow, which was achieved in 79% of cases with Penumbra system, 83% of cases with stent retriever with local aspiration, and 95% of cases with A Direct Aspiration first Pass Technique (ADAPT).	Retrospective review.
Valvassori L, Ciccone A, Piano M et al. (2011) The times to recanalization of endovascular treatment for ischemic stroke. Experience of SYNTHESIS Expansion trial. Interventional Neuroradiology 17: 53-54	RCT (SYNTHESIS) n=260 FU=3months	The organisation for endovascular treatment delays treatment initiation of about 1h as compared to intravenous rt-PA. In analogy with angioplasty for myocardial infarction, the delay of endovascular treatment might be compensated by less time spent to obtain recanalisation.	More recent RCTs are included.
Vanacker P, Lambrou D, Eskandari A et al. (2014) Improving prediction of recanalization in acute large-vessel occlusive stroke. Journal of Thrombosis and Haemostasis 12: 814-821	Case series n=439	Acute endovascular treatment is the single most important factor promoting recanalisation in acute ischemic stroke. The presence of extracranial vessel stenosis or occlusion decreases recanalisation rates. In patients with intracranial occlusions, higher NIHSS score and ASPECTS and normal vigilance facilitate recanalisation. Clinical use of these predictors could influence recanalisation strategies in individual patients.	More recent RCTs are included.
Vanicek J, Bulik M, Brichta J et al. (2014) Utility of a rescue endovascular therapy for the treatment of major strokes refractory to full-dose intravenous thrombolysis. British Journal of Radiology 87 (1036) 20130545	Case series n=87	Endovascular mechanical recanalisation by the Solitaire device is a safe and beneficial method for the rescue treatment of patients with major stroke whose neurological status does not improve and who fail to recanalise the large artery occlusion after a 1-h full dose of intravenous thrombolysis.	Small case series.
Villwock MR, Padalino DJ, Deshaies EM (2015) Trends in mortality following mechanical thrombectomy for the treatment of acute ischemic stroke in the USA. Journal of Neurointerventional Surgery doi:10.1136/neurintsurg-2015-011674	Case series n=16,307	Utilisation of mechanical thrombectomy represents a small percentage of stroke cases, although the trend is increasing. Mortality following mechanical thrombectomy has been showing a steady decline over the past 5 years. This may be a result of a learning curve, improved patient selection, and/or device improvements.	Study reports limited data from the USA National Inpatient Sample.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Yilmaz U, Roth C, Reith W et al. (2013) Thrombus attenuation does not predict angiographic results of mechanical thrombectomy with stent retrievers. American Journal of Neuroradiology 34: 2184-2186	Case series n=70	There were no significant differences in the thrombus attenuations of occlusions that were successfully recanalised (modified Thrombolysis in Cerebral Infarction >2b) and those that were not.	Small case series.
Yilmaz U, Walter S, Korner H et al. (2015) Peri-interventional Subarachnoid Hemorrhage During Mechanical Thrombectomy with stent retrievers in Acute Stroke: A Retrospective Case-Control Study. Clinical Neuroradiology 25: 173–6	Case series n=217	This small retrospective case-control study did not reveal a significant influence of peri-interventional subarachnoid haemorrhage due to angiographically occult perforations on neurologic outcome of patients treated with stent retrievers.	More recent RCTs are included.
Yoo AJ, Zaidat OO, Chaudhry ZA et al. (2014) Impact of pretreatment noncontrast CT Alberta Stroke Program Early CT Score on clinical outcome after intra-arterial stroke therapy. Stroke 45: 746-751	Case series n=249	Noncontrast CT seems useful for excluding patients with the greatest burden of ischemic damage from futile intra-arterial treatment, which is unlikely to result in patient functional independence and increases the risk of haemorrhage.	Study focuses on the use of pretreatment noncontrast CT for patient selection.
Yoon W, Jung MY, Jung SH et al. (2013) Subarachnoid hemorrhage in a multimodal approach heavily weighted toward mechanical thrombectomy with solitaire stent in acute stroke. Stroke 44: 414-419	Case series n=74 FU=3 months	Subarachnoid haemorrhage on post-therapeutic CT scans were not uncommon after primary mechanical thrombectomy with a Solitaire stent, but they seemed to be benign. Rescue angioplasty and unidentified, small vessel ruptures due to mechanical stretch during stent retrieval might give rise to these lesions.	Small case series.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Zacharatos H, Hassan AE, Vazquez G, et al. (2012) Comparison of acute non-thrombolytic and thrombolytic treatments in ischaemic stroke patients 80 years or older. American Journal of Emergency Medicine 30 (1): 158–164	n=44 FU=not reported	A prominently higher rate of neurologic improvement and favourable clinical outcome was observed among acute ischaemic stroke patients 80 years or older treated with IV rtPA or endovascular intervention when compared with non-thrombolytic medical treatment.	Retrospective study. Mixed methods.
Zaidat OO, Castonguay AC, Gupta R et al. (2014) North American Solitaire Stent Retriever Acute Stroke registry: Post-marketing revascularization and clinical outcome results. Journal of NeuroInterventional Surgery 6: 584-588	Case series (registry data) n=354 FU=90 days	The NASA registry demonstrated that the Solitaire FR device performance in clinical practice is comparable with the SWIFT and TREVO 2 trial results.	More recent RCTs are included.
Zhu L, Liebeskind DS, Jahan R, et al. (2012) Thrombus branching and vessel curvature are important determinants of middle cerebral artery trunk recanalization with Merci thrombectomy devices. Stroke 43(3): 787–92	n=64 FU=not reported	Substantial recanalisation (TICI 2b or 3) was achieved in 40% of cases. Major device related complications occurred in 5/65 (7%). Extension of thrombus into middle cerebral artery division branches and curving shape of the middle cerebral artery stem, but not thrombus length, decreased technical and clinical success.	Retrospective cohort studying outcome depending on thrombus branching and vessel curvature.

Appendix B: Related NICE guidance for mechanical clot retrieval for treating acute ischaemic stroke

Guidance	Recommendations
Interventional procedures	**Mechanical clot retrieval for treating acute ischaemic stroke. NICE interventional procedure guidance 458 (2013) (current guidance)** 1 Guidance The current evidence on mechanical clot retrieval for treating acute ischaemic stroke shows that efficacy is unproven. With regard to safety, there are risks of serious complications. The following recommendations balance these considerations against the poor prognosis of many patients with stroke. Suitability for thrombolysis can be guided by criteria used in the Pragmatic Ischaemic Stroke Thrombectomy Evaluation (PISTE) trial. 1.1 Patients with acute ischaemic stroke for whom thrombolysis is unsuitable or has failed: The procedure should only be used with special arrangements for clinical governance, consent and audit or research. Clinicians wishing to use mechanical clot retrieval for treating acute ischaemic stroke in these patients should take the following actions: • Inform the clinical governance leads in their Trusts. • Ensure that patients (and when appropriate their relatives or carers) understand the uncertainty about the procedure's safety and efficacy and provide them with clear written information. In addition, the use of NICE's information for the public is recommended. • Submit details of all patients to the Safe Implementation of Treatments in Stroke Thrombectomy (SITS-TBY) register. • NICE encourages prospective studies of mechanical clot retrieval in these patients, including comparison of outcomes against those of patients who do not have the procedure. These studies should report details of patient selection, timing of the intervention after onset of symptoms, the devices and techniques used, and functional outcomes. 1.2 Patients with acute ischaemic stroke for whom thrombolysis is suitable: The procedure should only be used in the context of research: • Research should include randomised studies comparing mechanical clot retrieval against thrombolysis or other current methods of management and should report details of patient selection, timing of the intervention after onset of symptoms, the devices and techniques used, complications and functional outcomes. • NICE encourages clinicians to enter patients into randomised trials such as the PISTE trial. In addition, details of all patients should be entered into the SITS-TBY register.

	1.3 Selection of patients for mechanical clot removal should be done by clinicians experienced in the use of thrombolysis for stroke. The procedure should be carried out in specialist centres by experienced interventional neuroradiologists with appropriate facilities and support.
Technology appraisals	**Alteplase for treating acute ischaemic stroke (review of technology appraisal guidance 122). NICE technology appraisal 264 (2012).** 1 Guidance 1.1 Alteplase is recommended within its marketing authorisation for treating acute ischaemic stroke in adults if: • treatment is started as early as possible within 4.5 hours of onset of stroke symptoms, and • intracranial haemorrhage has been excluded by appropriate imaging techniques.
NICE guidelines	**Stroke: Diagnosis and initial management of acute stroke and transient ischaemic attack (TIA). NICE clinical guideline 68 (2008).** *1.3 Specialist care for people with acute stroke* This section provides recommendations about the optimum care for people with acute stroke: where they should be cared for and how soon they should undergo brain imaging. *1.3.1 Specialist stroke units* 1.3.1.1 All people with suspected stroke should be admitted directly to a specialist acute stroke unit following initial assessment, either from the community or from the A&E department. *1.3.2 Brain imaging for the early assessment of people with acute stroke* 1.3.2.1 Brain imaging should be performed immediately for people with acute stroke if any of the following apply: • indications for thrombolysis or early anticoagulation treatment • on anticoagulant treatment • a known bleeding tendency • a depressed level of consciousness (Glasgow Coma Score below 13) • unexplained progressive or fluctuating symptoms • papilloedema, neck stiffness or fever • severe headache at onset of stroke symptoms. 1.3.2.2 For all people with acute stroke without indications for immediate brain imaging, scanning should be performed as soon as possible. *1.4 Pharmacological treatments for people with acute stroke* Urgent treatment has been shown to improve outcome in stroke. This section contains recommendations about urgent pharmacological

	treatment in people with acute stroke. *1.4.1 Thrombolysis with alteplase* 1.4.1.1 Alteplase is recommended for the treatment of acute ischaemic stroke when used by physicians trained and experienced in the management of acute stroke. It should only be administered in centres with facilities that enable it to be used in full accordance with its marketing authorisation. 1.4.1.2 Alteplase should be administered only within a well organised stroke service with: • staff trained in delivering thrombolysis and in monitoring for any complications associated with thrombolysis • level 1 and level 2 nursing care staff trained in acute stroke and thrombolysis • immediate access to imaging and re-imaging, and staff trained to interpret the images. 1.4.1.3 Staff in A&E departments, if appropriately trained and supported, can administer alteplase for the treatment of acute ischaemic stroke provided that patients can be managed within an acute stroke service with appropriate neuroradiological and stroke physician support. 1.4.1.4 Protocols should be in place for the delivery and management of thrombolysis, including post-thrombolysis complications. *1.4.2 Aspirin and anticoagulant treatment* **People with acute ischaemic stroke** 1.4.2.1 All people presenting with acute stroke who have had a diagnosis of primary intracerebral haemorrhage excluded by brain imaging should, as soon as possible but certainly within 24 hours, be given: • aspirin 300 mg orally if they are not dysphagic or • aspirin 300 mg rectally or by enteral tube if they are dysphagic. Thereafter, aspirin 300 mg should be continued until 2 weeks after the onset of stroke symptoms, at which time definitive long-term antithrombotic treatment should be initiated. People being discharged before 2 weeks can be started on long-term treatment earlier. 1.4.2.2 Any person with acute ischaemic stroke for whom previous dyspepsia associated with aspirin is reported should be given a proton pump inhibitor in addition to aspirin. 1.4.2.3 Any person with acute ischaemic stroke who is allergic to or genuinely intolerant of aspirin should be given an alternative antiplatelet agent. 1.4.2.4 Anticoagulation treatment should not be used routinely for the treatment of acute stroke.

	People with acute ischaemic stroke associated with antiphospholipid syndrome 1.4.2.7 People with antiphospholipid syndrome who have an acute ischaemic stroke should be managed in same way as people with acute ischaemic stroke without antiphospholipid syndrome[23]. *1.4.3 Anticoagulation treatment for other comorbidities* 1.4.3.1 People with disabling ischaemic stroke who are in atrial fibrillation should be treated with aspirin 300 mg for the first 2 weeks before considering anticoagulation treatment. 1.4.3.2 In people with prosthetic valves who have disabling cerebral infarction and who are at significant risk of haemorrhagic transformation, anticoagulation treatment should be stopped for 1 week and aspirin 300 mg substituted. 1.4.3.3 People with ischaemic stroke and symptomatic proximal deep vein thrombosis or pulmonary embolism should receive anticoagulation treatment in preference to treatment with aspirin unless there are other contraindications to anticoagulation.

Appendix C: Literature search for mechanical clot retrieval for treating acute ischaemic stroke

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	28/05/2015	Issue 5 of 12, May 2015
HTA database (Cochrane Library)	28/05/2015	Issue 2 of 4, April 2015
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	28/05/2015	Issue 4 of 12, April 2015
MEDLINE (Ovid)	28/05/2015	1946 to May Week 4 2015
MEDLINE In-Process (Ovid)	28/05/2015	May 27, 2015
EMBASE (Ovid)	28/05/2015	1974 to 2015 Week 21
PubMed	28/05/2015	n/a
BLIC	28/05/2015	n/a

Trial sources searched on 29/05/2015

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched on 29/05/2015

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- EuroScan
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	Infarction, Middle Cerebral Artery/
2	Middle Cerebral Artery/
3	Cerebral Infarction/
4	Brain Ischemia/
5	((brain or cerebral) adj4 (ischemi* or ischaemi* or infarction* or arter*)).tw.

6	(arter* adj4 occlusion*).tw.
7	((cerebrovascular* or vascular*) adj4 accident*).tw.
8	CVA.tw.
9	Stroke/
10	stroke.tw.
11	or/1-10
12	Mechanical thrombolysis/
13	(mechanical adj4 (thrombectom* or thromboembolectom* or thrombo-embolectom* or thrombolys* or remov* or disrupt* or clot* or embolectom* or recanalis* or recanaliz* or retriev*)).tw.
14	(mechanic* adj4 (embolus* or thrombus*)).tw.
15	Embolectomy/
16	Thrombectomy/
17	(endovasc* adj4 (thrombect* or embolect* or intervention* or recanl*)).tw.
18	neurothrombectom*.tw.
19	merci.tw.
20	penumbra system.tw.
21	solitaire.tw.
22	or/12-21
23	11 and 22
24	animals/ not humans/
25	23 not 24
26	limit 25 to ed=20130301-20150531