Chapter 7
Mechanical Thrombectomy for Acute Ischemic Stroke

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7.1 Introduction

Mechanical thrombectomy is a tool to open the major arteries in the brain which are blocked after an ischemic stroke. One of the greatest advances in the care of stroke patients has been the definitive evidence that mechanical thrombectomy reduces the burden of disability that patients face after stroke. Patients who receive mechanical thrombectomy within 6 h of stroke syndrome onset are two times more likely to be independent 90 days after the stroke as compared to similar patients who do not receive the therapy. Despite the demonstrated clinical benefit, the selection of appropriate patients and timely administration of the therapy requires streamlined systems of care and triage of patients to comprehensive stroke centers.

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7.1.1 IV Thrombolysis and the Need for Better Treatments

Thrombolytic agents function by dissolving preexisting blood clots. The major thrombolytic agent is intravenous recombinant tissue plasminogen activator (IV-tPA). Overall, major therapeutic advancements such as IV thrombolysis have contributed to a decrease in the number of deaths from stroke by 23% between 1999 and 2009 [1]. However, the majority of patients do not qualify for IV thrombolysis, and many who survive still live with severe disabilities [2]. Fewer than 10% of patients meet the eligibility criteria for IV-PA because the standard treatment window is 4.5 h due to increased risk of intracranial hemorrhage with late administration of thrombolytic agents [3, 4]. Furthermore, as many as 20% patients who improve initially with intravenous thrombolysis experience clinical deterioration, possibly due to vessel reocclusion [5].

7.1.2 Mechanical Thrombectomy

An alternative strategy to thrombolytic agents is endovascular mechanical thrombectomy. Multiple studies have found that intravenous thrombolytic agents only yield 10–30% recanalization of large-vessel occlusions [6]. This is in contrast to mechanical recanalization with success rate of 83.6% [7].

Five recent multicenter randomized controlled trials using the mechanical thrombectomy technology known as stent retrievers have provided the necessary evidence to make this strategy the standard of care for large-vessel occlusions [8–12].

The Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands (MR CLEAN) gave the first glimpse and is the largest of the four trials with 500 patients [13]. This trial compared endovascular therapy plus usual care and usual care alone in participants with radiographically confirmed proximal arterial occlusion within 6 h of stroke onset. Of all the participants, 89% were treated with IV alteplase before randomization. Second-generation mechanical thrombectomy devices were used in 82% of the endovascular therapy group. Patients with endovascular therapy achieved lower mRS scores at 90 days (odds ratio of 1.67). Also, the rates of symptomatic intracerebral hemorrhage (SICH) (7.7% vs. 6.4%) and mortality at 30 days (18.9% vs. 18.4%) were statistically similar between the two groups.

The Endovascular Treatment for Small Core and Proximal Occlusion Ischemic Stroke (ESCAPE) trial was the next major trial to show a benefit to endovascular therapy with standard care compared to standard care alone in ischemic stroke caused by proximal artery occlusion in the anterior circulation within 12 h of stroke onset in 316 participants [14]. A total of 75% of the patients received IV alteplase in the two groups. With multiphase CT angiography utilized to reduce patient motion artifact and for the rapid determination of collateral status, the study excluded patients with large infarct cores and poor collateral circulation. After an interim analysis performed by the Data and Safety Monitoring Board (DSMB), the study was terminated early due to the significantly better performance in the group receiving endovascular therapy. Participants with endovascular therapy had improved functional status at 90 days (modified Rankin score (mRS) 0–2; 53.0% vs. 29.3%) and lower 90-day mortality (10.4% vs. 19.0%).

The Extending the Time for Thrombolysis in Emergency Neurological Deficits-Intra-Arterial (EXTEND-IA) compared mechanical thrombectomy with the Solitaire FR device vs. IV alteplase in 70 patients [15]. After patients with core infarction volumes greater than 70 mL were excluded using CT perfusion imaging, the thrombectomy group reported higher rates of functional independence (mRS 0–2; 71% vs. 40%) without a difference in SICH rate (0% vs. 6%). The

DSMB also terminated the next study, the Solitaire FR With the Intention for Thrombectomy as Primary Endovascular Treatment for Acute Ischemic Stroke (SWIFT PRIME) trial [16]. This trial enrolled 196 patients, only used the Solitaire FR retrievers in the endovascular intervention group, and selected for patients with confirmed occlusion of a large artery in the anterior circulation within 6 h of symptom onset. Similar to the previous trials, significantly improved rates of functional status (mRS: 0–2; 60% vs. 37%) without statistically different rates of SICH (1% vs. 4%) or 90-day mortality (9% vs. 12%) were achieved in the mechanical thrombectomy group compared to IV tPA within 4.5 h of stroke onset.

Similar findings were replicated in Swift Prime and REVASCAT [16, 17].

7.2 Case Example

An 81-year-old man has a history of atrial fibrillation for which he takes apixaban. His apixaban was recently held for a dental procedure and restarted yesterday. He was last seen normal by his wife at 9:00 AM, and was found at 9:30 AM by his wife slumped in his chair. She noticed a right facial droop, right-sided weakness, and difficulty with speech. 911 was called and he arrived in the emergency department at 10:00 AM.

His initial evaluation revealed a blood pressure of 165/80, a pulse of 75 and a respiratory rate of 16, with oxygen saturation of 96%. On a brief neurological examination, he was

Fig. 7.1 Head CT with hyperdense left MCA sign

found to have global aphasia, left-gaze deviation, right facial droop, right arm plegia and right leg weakness. This tallied to an NIHSS of 19. Head CT demonstrated no early signs of ischemia and revealed a hyperdensity near the branch off the left middle cerebral artery (MCA) (see Fig. 7.1).

He was not a candidate for IV tPA due to his recent use of the blood thinner apixaban. After determining that he would be a good candidate for mechanical thrombectomy, the risks

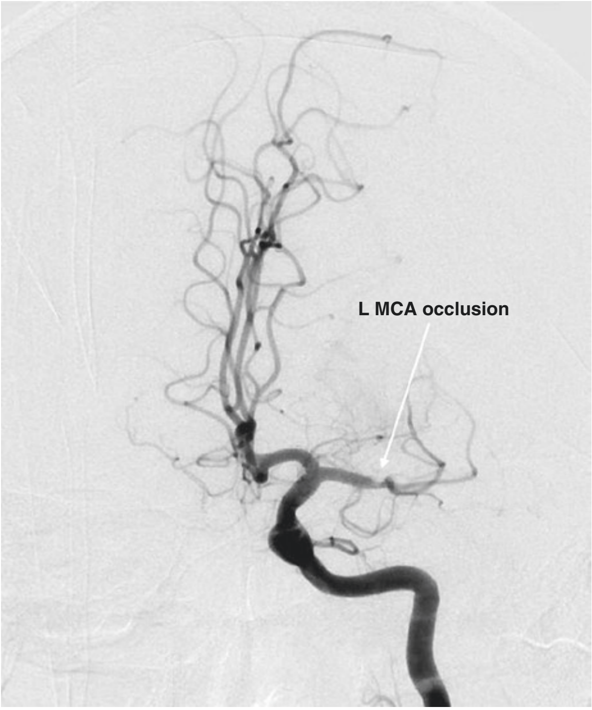

Fig. 7.2 Angiogram demonstrating left MCA thrombus

and benefits of the procedure were explained to his wife, who agreed to proceed. He was taken urgently to the interventional radiology suite. The cerebral angiogram confirmed a proximal occlusion of the left MCA (Fig. 7.2). A stent retriever was deployed and the clot was retrieved. A repeat angiogram showed near complete revascularization of the

Fig. 7.3 Angiogram with stent retriever crossing thrombus

left MCA (Figs. 7.3 and 7.4). This was graded as TICI 3 revascularization. Postprocedure, the patient's neurological exam drastically improved, with resolution of his aphasia and near-complete resolution in his right arm's weakness

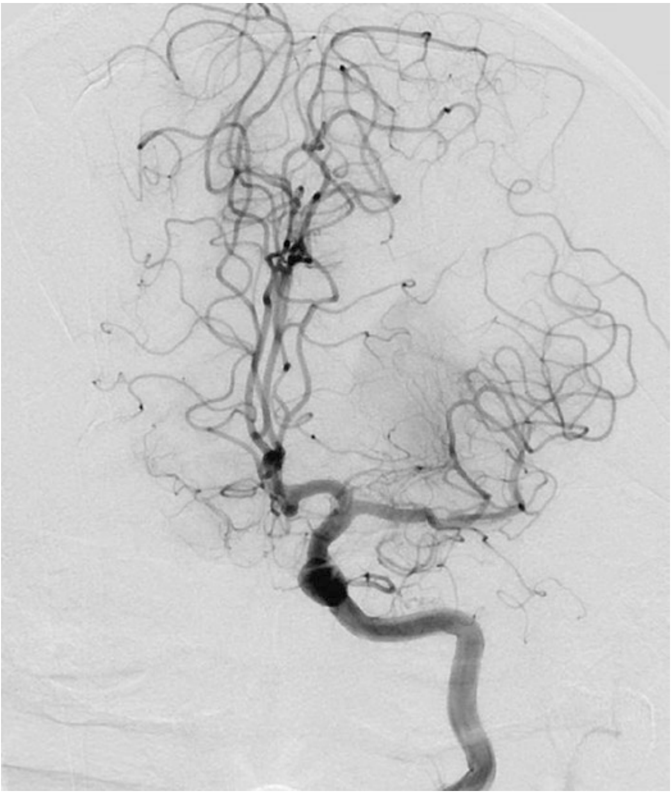

Fig. 7.4 Angiogram demonstrating restoration of flow in the left MCA

(NIHSS 4). He was admitted to the neurology service for further surveillance. MRI the following day demonstrated an ischemic stroke in the left basal ganglia, which was much smaller than the territory originally at risk at the time of presentation (Fig. 7.5).

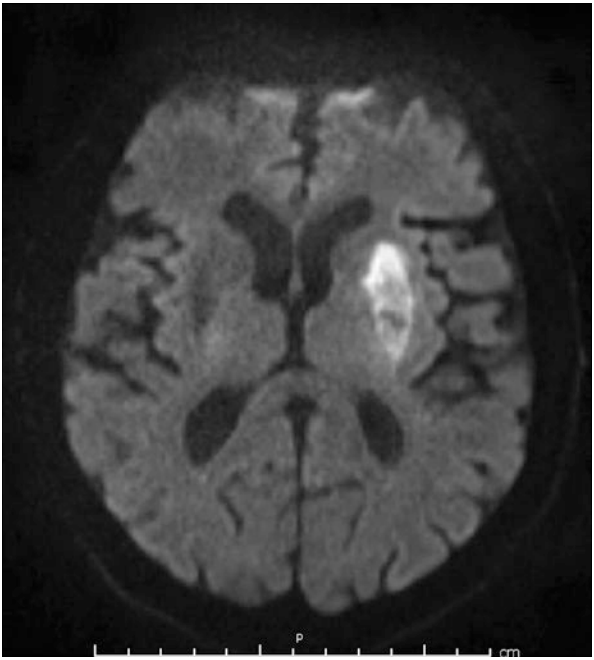

Fig. 7.5 MRI with resultant ischemic stroke

7.2.1 *Stroke Systems of Care*

Mechanical thrombectomy has demonstrated benefits in carefully selected patients; however most patients with acute ischemic stroke do not receive this therapy. The primary reason for this is delayed arrival to the hospital. As with IV-tPA, mechanical thrombectomy is a time-sensitive procedure with the greatest benefit if pursued early. Therefore, patient recognition of the signs and symptoms of a stroke and calling 911 is the first step to ensure acute stroke care is delivered. The second challenge is the prompt triage of patients with acute ischemic stroke to a center that can offer mechanical thrombectomy [18]. In the US, certain hospitals are designated as Primary Stroke Centers, or Comprehensive Stroke Centers (CSC) by the Joint Commission. Primary stroke centers should have the capability to diagnose and treat stroke patients, including thrombolytics, but they may not have an ability to perform mechanical thrombectomy. Therefore, it is essential that prompt recognition of large-vessel occlusion occurs in hospitals that do not have the capability to administer such therapy, so that urgent transfer can occur to a CSC. At present, because of geographic distances and the difficulty of identifying a large-vessel occlusion in the field, patients with acute stroke may not be preferentially transferred to a CSC by emergency medical services. Patients may instead be brought to the closest hospital which is often a primary stroke center. Often times, the delay in transport to a CSC can cause the patient to be ineligible for thrombectomy, either because they arrive >6 h after symptoms onset, or sufficient time has passed to allow the infarct to fully develop. Future efforts in improving stroke systems of care need also focus on protocols for urgent transfer of patients to appropriate stroke centers where they can receive the full spectrum of care.

7.3 Initial Evaluation

The initial evaluation of a patient with acute ischemic stroke is summarized elsewhere (see Chap. 6 on Acute Ischemic Stroke). Here, we emphasize the aspects of clinical management specifically related to mechanical thrombectomy. During the teams' initial evaluation, a judgment is made as to whether the patient is likely to have a large-vessel occlusion. A large-vessel occlusion is defined as acute thrombosis in the proximal segment of the anterior, middle, or posterior cerebral artery, the basilar artery, or the internal carotid artery. The presence of a large-vessel occlusion will determine if the patient can proceed to mechanical thrombectomy.

The determination of a large vessel occlusion can be made in several ways. In some centers, a neurologic examination suspicious for a "large-territory" infarction that would include a proximal vascular territory is enough evidence to warrant consideration for mechanical thrombectomy. A conventional cerebral angiogram to confirm a large-vessel occlusion is the first step in mechanical thrombectomy. Because of this, some centers have adopted a protocol to rely on the neurologic examination prior to transfer of the patient to the angiogram suite. However, all of the large-scale clinical trials that demonstrated a benefit of mechanical thrombectomy on functional outcome included at minimum a head CT and vascular imaging.

Other centers have created protocols which incorporate vessel imaging, or other advanced imaging techniques to examine the ischemic penumbra to confirm a large-vessel occlusion prior to recommending mechanical thrombectomy. These protocols are often the result of an ability to quickly obtain advanced imaging, and reflect the selection used in the published trials that confirmed the benefit of mechanical thrombectomy [13, 14, 16]. Options for advanced imaging include a CT or MR angiogram, a CT or MR perfusion study.

7.3.1 Patient Selection for Mechanical Thrombectomy Using Imaging

There are several methods supported by the literature to select patients that may benefit from mechanical thrombectomy. The most commonly used methods include the CT-based scoring system of the ASPECTs score and CT and MR perfusion. The purpose of patient selection is to offer mechanical thrombectomy to patients that are most likely to benefit from revascularization. Examples of patients that are unlikely to benefit include those with a minimal ischemic penumbra, suggesting that there is no “tissue to save” or patients with a large stroke who are more likely to experience hemorrhagic transformation of the stroke if revascularization is achieved. The key principles, no matter what advanced imaging technique is used, is to select patients with a small ischemic core infarct, and large ischemic penumbra. The ratio of the penumbra to core would be large in patients who are most likely to benefit from reperfusion.

One method of image selection incorporates the CT-based ASPECTs score. The ASPECTS score was developed in 2000 as an attempt to quantify the size of the ischemic infarct on a CT scan in order to predict outcome after mechanical thrombectomy [19]. The benefit of this scoring system is that all centers that administer tPA have the ability to quickly obtain a CT scan. The ASPECTS scoring system is qualitative and ranges from 0 to 10, with higher numbers indicating less ischemia. In this scoring system, a point is subtracted for each of ten territories where there is evidence of ischemia. For information and training on this scoring system, see http://www.aspectsinstroke.com. Two large randomized controlled trials demonstrated benefit to mechanical thrombectomy in patients with an ASPECTS score > 6 or >7 [14, 17]. These trials help establish a cutoff from which treatment may be beneficial to select patients for mechanical thrombectomy.

The benefit of CT perfusion as compared with an ASPECTS-based scoring system is that the ischemic penumbra can be visualized along and the core infarct area can be estimated. Three of the recently completed trials that demonstrated a benefit for mechanical thrombectomy utilized CT perfusion for some of the participants [14–16]. CT perfusion displays the physiologic function of the brain in the form of perfusion maps. A perfusion map is a view of the brain where each pixel measures blood flow to that area, with different colors assigned to represent a measurement over time. For example, one type of perfusion map is called the mean transit time (MTT). This map measures the mean amount of time it takes for the contrast to get to each pixel and can provide an estimate of the size of the ischemic penumbra. Other types of perfusion maps include the cerebral blood flow (CBF) and cerebral blood volume (CBV) maps [20]. Regions of the brain with reduced CBV and CBF can represent the area of core ischemic damage. There are several vendor software packages and institutional methods that are used to determine thresholds, or cutoffs to distinguish the ischemic core from the penumbra. These thresholds are based on a relatively few number of studies, and each institution that interprets CT perfusion should establish its own standards for decision-making.

In institutions where MRI scanning is readily and quickly available, MR perfusion techniques are often used to select patients for mechanical thrombectomy. The benefit of MRI over CT is that a more accurate determination can be made of the ischemic core. This is because of the higher sensitivity and specificity of MRI in detecting hyperacute ischemia [21]. Ischemic core can be accurately estimated using the diffusion-weighted imaging (DWI) sequence in the MRI protocol. MR perfusion begins with administration of gadolinium which allows for the generation of maps similar to those created during CT perfusion. The ischemic penumbra can be defined by MTT or time-to-maximum (T_{max}) maps which highlight areas of hemodynamic compromise. The ratio of the ischemic penumbra to the core infarction measured on DWI can be used to augment decision-making. As with CT perfusion, several different thresholds exist to measure the ischemic penumbra and several vendor software packages are available to assist in the measurement of the volumes. In MRI, the amount of poorly perfused tissue that is still at risk of infarction is often called the diffusion–perfusion mismatch. It is this number which can accurately predict whether there is a substantial amount of “brain to save” through revascularization.

In summary, selecting patients for mechanical thrombectomy requires advanced decision-making, knowledge of advanced imaging, and the experience of multiple practitioners, including stroke neurologists, interventionalists, and radiologists. The decision on what imaging modality to use will depend on resource availability at each hospital.

7.4 Interventions and Management

7.4.1 Current Guidelines

The established benefit of mechanical thrombectomy in acute ischemic stroke has led to the revision of established guidelines in recent years [22]. The American Heart Association advises that patients presenting with acute ischemic stroke should continue to receive intravenous tPA if eligible and that intra-arterial treatment should be considered for all patients meeting the following parameters:

- Prestroke modified Rankin score of 0–1
- The causative occlusion is in the internal carotid artery or proximal middle cerebral artery
- Age ≥18 years
- NIHSS ≥6
- ASPECTS score of ≥6

Beyond these parameters, thrombectomy can be considered for patients presenting with other large-vessel occlusions,

Table 7.1 Thrombolysis in Cerebral Infarction (TICI) categories

Grade	Appearance on final angiographic image
0	No perfusion
1	Penetration with minimal perfusion
2	Partial perfusion
2a	Only partial filling (<2/3) of the entire vascular territory is visualized
2b	Complete filling of the vascular territory, but filling is slower than normal
3	Complete perfusion

Adapted from Higashida [26]

including basilar artery, vertebral artery, and M2 branches of the middle cerebral artery. In all cases, the goal of thrombectomy is to restore flow through the occluded vessel. The extent of revascularization is categorized using the Thrombolysis in Cerebral Infarction (TICI) Perfusion Categories (Table 7.1).

Clinical benefit is more clearly established for treatment within 6 h of symptom onset; however, continued advances are being made toward understanding the relationship between ischemic changes on neuroimaging (including MRI, CT, CT perfusion) and the potential benefits of delayed revascularization for salvaging the penumbra. The decision to pursue mechanical thrombectomy beyond 6 h of symptom onset requires a multidisciplinary approach best achieved at experienced stroke centers.

7.4.2 Postprocedure Care of Patients

The ICU care of patients receiving mechanical thrombectomy often mirrors that of patients after they receive tPA, and in fact many of these patients will have also received tPA. The primary reason for ICU triage is for neurologic monitoring for any deterioration. Patients are at high risk of reperfusion hemorrhage or complications of the procedure, such as arterial dissection and progressive ischemia. Additionally, patients need to be monitored for the potential complications of a large ischemic stroke, like malignant cerebral edema. In most ICUs, nursing protocols include neurological exams and NIHSS scoring every hour for the first 24 h after tPA administration. Changes in neurologic examination often prompt notification of the advanced practitioner or physician, who must make a decision as to the cause of the neurologic decline.

Careful monitoring of blood pressure is essential after mechanical thrombectomy, especially if reperfusion has been obtained. There is no prospective randomized data which supports a recommended goal blood pressure after mechanical thrombectomy [23]. Therefore, the blood pressure goals must be decided on a per-patient basis or as per institutional policy. Patients who received tPA should have a goal blood pressure of at least <180 systolic and <105 diastolic. Many institutions recommend implementing a blood pressure goal of <140 systolic and <100 diastolic if revascularization was obtained, or allowing permissive hypertension if the large-vessel occlusion remains [24].

Reperfusion injury and hemorrhagic transformation is the feared complication of mechanical thrombectomy. Predictors of reperfusion hemorrhage include a large ischemic core infarct or delayed reperfusion. The key to treatment of reperfusion hemorrhage is early identification and prevention of hematoma expansion. If tPA has been given, its reversal is essential. Strict blood pressure control is a key component of prevention of hemorrhage expansion. Decompressive hemicraniectomy after reperfusion hemorrhage has not been studied specifically after mechanical thrombectomy and may represent a life-saving option for some patients [23].

Management of cerebral edema with hypertonic therapy or surgical decompression is reviewed in Chap 8. on Malignant Ischemic Stroke. The groin access site must also be monitored postprocedure for evidence of hematoma formation.

Summary Points

- Mechanical thrombectomy for large-vessel occlusion is now part of standard care [25].
- Currently the accepted time frame is last seen normal within 6 h from presentation.
- Patient selection for mechanical thrombectomy is a complex process utilizing clinician judgment and advanced imaging techniques.
- Postprocedure care revolves around close neurologic monitoring and early detection of neurologic decline.

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References

1. Go A, Mozaffarian D, Roger V, et al. Heart disease and stroke statistics--2013 update: a report from the American Heart Association. Circulation. 2013;127(1):e6–e245.
2. Kasner S. Editorial comment—more than one way to lyse a clot. Stroke; J Cereb Circulation. 2004;35(4):911–2.

3. Tissue plasminogen activator for acute ischemic stroke. The National Institute of Neurological Disorders and Stroke rt-PA stroke study group. N Engl J Med. 1995;333(24):1581–7.
4. de Los Ríos la Rosa F, Khoury J, Kissela B, et al. Eligibility for intravenous recombinant tissue-type plasminogen activator within a population: the effect of the European cooperative acute stroke study (ECASS) III trial. Stroke; J Cereb Circulation. 2012;43(6): 1591–5.
5. Alexandrov AV, Grotta JC. Arterial reocclusion in stroke patients treated with intravenous tissue plasminogen activator. Neurology. 2002;59(6):862–7.
6. Bhatia R, Hill MD, Shobha N, et al. Low rates of acute recanalization with intravenous recombinant tissue plasminogen activator in ischemic stroke: real-world experience and a call for action. Stroke. 2010;41(10): 2254–8.
7. Rha J-H, Saver J. The impact of recanalization on ischemic stroke outcome: a meta-analysis. Stroke; J Cereb Circulation. 2007;38(3): 967–73.
8. Gobin Y, Starkman S, Duckwiler G, et al. MERCI 1: a phase 1 study of mechanical embolus removal in cerebral ischemia. Stroke; J Cereb Circulation. 2004;35(12):2848–54.
9. Smith W, Sung G, Saver J, et al. Mechanical thrombectomy for acute ischemic stroke: final results of the multi MERCI trial. Stroke; J Cereb Circulation. 2008;39(4):1205–12.
10. Smith W, Sung G, Starkman S, et al. Safety and efficacy of mechanical embolectomy in acute ischemic stroke: results of the MERCI trial. Stroke; J Cereb Circulation. 2005;36(7):1432–8.
11. Penumbra Pivotal Stroke Trial I. 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; J Cereb Circulation. 2009;40(8):2761–8.
12. Tarr R, Hsu D, Kulcsar Z, et al. 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. J Neurointerv Surg. 2010;2(4):341–4.
13. Berkhemer OA, Fransen PSS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med. 2014;372(1):11–20.

14. Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med. 2015;372:1019–30.
15. Campbell BC, Mitchell PJ, Kleinig TJ, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. N Engl J Med. 2015;372:1009–18.
16. Saver JL, Goyal M, Bonafe A, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. N Engl J Med. 2015;372(24):2285–95.
17. Jovin TG, Chamorro A, Cobo E, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. N Engl J Med. 2015; 372(24):2296–306.
18. English JD, Yavagal DR, Gupta R, et al. Mechanical Thrombectomy-ready comprehensive stroke center requirements and endovascular stroke Systems of Care: recommendations from the endovascular stroke standards Committee of the Society of vascular and interventional neurology (SVIN). Interv Neuroradiol. 2016;4(3–4):138–50.
19. Barber PA, Demchuk AM, Zhang J, Buchan AM. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. ASPECTS study group. Alberta stroke Programme early CT score. Lancet. 2000; 355(9216):1670–4.
20. Heit JJ, Wintermark M. Perfusion computed tomography for the evaluation of acute ischemic stroke. Stroke. 2016;47(4):1153.
21. Nael K, Kubal W. Magnetic resonance imaging of acute stroke. Magn Reson Imaging Clin N Am. 2016;24(2):293–304.
22. Powers WJ, Derdeyn CP, Biller J, et al. 2015 AHA/ASA focused update of the 2013 guidelines for the early Management of Patients with Acute Ischemic Stroke Regarding Endovascular Treatment. Stroke. 2015;46:3020–35.
23. Al-Mufti F, Dancour E, Amuluru K, et al. Neurocritical care of emergent large-vessel occlusion: the Era of a new standard of care. J Intensive Care Med. 2016. PMID: 27435906.
24. Patel VN, Gupta R, Horn CM, Thomas TT, Nogueira RG. The Neurocritical Care Management of the Endovascular Stroke Patient. Curr Treat Options Neurol. 2013;15(2):113–24.
25. Jayaraman MV, Hussain MS, Abruzzo T, et al. Embolectomy for stroke with emergent large vessel occlusion (ELVO): report of the standards

and guidelines Committee of the Society of NeuroInterventional surgery. J Neurointerv Surg. 2015;7(5):316–21.
26. Higashida RT. Trial design and reporting standards for intra-arterial cerebral thrombolysis for acute ischemic stroke. Stroke (1970). 2003;34(8):e109–37.