

Acute Ischemic Stroke: A Review of Imaging, Patient Selection, and Management in the Endovascular Era. Part II: Patient Selection, Endovascular Thrombectomy, and Postprocedure Management

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J Clin Interv Radiol ISVIR 2018;2:169–183

Abstract

Appropriate patient selection and expedient recanalization are the mainstay of modern management of acute ischemic stroke (AIS). Only a minority of patients (7–15%) of patients are eligible for endovascular therapy. Patient selection may be time based or perfusion based. Central to both paradigms is the selection of a patient with a small core, a significant penumbra that can be differentiated from areas of oligemia. A brief review of patient selection methods is presented. Endovascular thrombectomy techniques using stentrievers or aspiration catheters have now become the treatment of choice for AIS with large vessel occlusion. A range of devices, each with its own advantages and disadvantages, are available in the market for the neurointerventionist to choose. Techniques vary between devices and between operators, but standardization and protocolization are important within each center. Complications must be anticipated to be avoided. Once reperfusion is achieved, outcomes must be safeguarded with competent postprocedure management to prevent secondary brain injury. These aspects are reviewed in this article.

Keywords

- ▶ stroke
- ▶ mechanical thrombectomy
- ▶ aspiration thrombectomy

Introduction

Patient selection is crucial in optimizing the balance between achieving good functional outcomes and avoiding complications in patients with acute ischemic stroke (AIS). Only a minority (7–15%) of patients with AIS are eligible for mechanical thrombectomy (MT).^{1–3} In this precious population, recanalization must therefore be rapid, effective, and safe. MT⁴ may be achieved by myriad techniques and devices, and the interventional neuroradiologist must be conversant and resourceful in this high-stress situation. Once reperfusion is achieved, outcomes must be safeguarded with competent postprocedure management to prevent secondary brain injury. We review these aspects in this article.

Medical Acute Reperfusion Treatments

Intravenous thrombolysis (IVT): IVT is the mainstay of treatment for almost any AIS syndrome with a measurable deficit. Intravenous (IV) infusion of recombinant tissue-type plasminogen activator (IVrt-PA or alteplase) is approved for use within 4.5 hours of onset.⁴ Though the standard dose is 0.9 mg/kg, low-dose regimens using only 0.6 mg/kg have been found to be noninferior in Asian populations and may reduce costs of treatment.^{5,6} Tenecteplase, a drug with a similar profile, has the advantage of single bolus administration (0.4 mg/kg). Though not yet FDA (Food and Drug administration) approved for use in AIS, results of the ATTEST (Alteplase-Tenecteplase Trial Evaluation for Stroke Thrombolysis) and EXTEND-IA (Extending the time

received

May 4, 2018

accepted after revision

June 29, 2018

published online

December 6, 2018

DOI <https://doi.org/>

10.1055/s-0038-1675882

ISSN 2457-0214.

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for Thrombolysis in Emergency Neurological Deficits with Intra-Arterial therapy) trials suggest that its use may result in similar, if not better outcomes.^{7,8} Administration of thrombolytics requires intensive neurologic monitoring to document improvement and rule out symptomatic intracranial hemorrhage (sICH). Prompt delivery of the drug is essential as good outcomes decrease with increasing delays. The number-needed-to-treat (NTT) nearly doubles from five to nine at administration times within 90 minutes and 3 to 4.5 hours, respectively.⁹ American Heart Association (AHA) criteria for administration of IVrt-PA have been summarized in ►Tables 1 and 2.⁴ An extensive list of contraindications must also be ruled out, in particular the presence of coexisting coagulopathies (platelet count < 100,000/cc, international normalized ratio [INR] > 1.7, prothrombin time > 15 seconds, activated partial thromboplastin time > 40 seconds), possible sources of systemic hemorrhage, or recent trauma/surgery.⁴

The efficacy of IVT in achieving reperfusion in AIS with emergent large vessel occlusion (ELVO) is relatively suboptimal with < 30% success rates.¹⁰ This led to newer techniques of intra-arterial thrombolysis (IAT) initially and MT later.

Sonothrombolysis: Contemporaneous insonation of ultrasound using a transcranial Doppler probe augments the effect of clot-busting drugs.¹¹ This effect may be further enhanced by the use of microbubble contrast media. The CLOTBUST (Combined Lysis of Thrombus in Brain Ischemia With Transcranial Ultrasound and Systemic tPA) and NOR-SASS (Norwegian Sonothrombolysis in Acute Stroke Study) trials showed a good safety profile but conflicting results regarding efficacy with a trend toward better outcomes over IVT alone in the former.^{12,13} However, outcomes have been inferior compared with MT.¹⁴ Sonothrombolysis is not recommended by the American Heart Association (AHA).⁴ Nonetheless, in a resource-poor environment such as ours, sonothrombolysis may be a viable and economical option helping improve outcomes.¹⁵ The CLOTBUST Hands-free

trial is currently an ongoing study that uses operator-independent insonation and may change current perspectives.¹⁶

Bridging therapy (BT): BT refers to the administration of IVT as an adjunct to MT in an eligible patient. The use of IVT + MT results in better functional outcomes increased recanalization rates with few number of device passes and reduced mortality with equivalent rates of sICH.^{17,18} However, controversy remains with some reporting nonsuperiority of BT over direct MT and increased mortality.¹⁹ Nonetheless, the AHA considers it a reasonable management strategy in-transit to a cath laboratory. However, waiting for clinical improvement post-IVT before considering MT (rescue BT) in an eligible patient has fallen out of practice and is no longer recommended.⁴

Endovascular Treatment

Patient Selection and Decision Algorithm

Patient selection is a nuanced cognitive process requiring consideration of multiple factors in stages to justify aggressive

Table 1 Criteria for IV alteplase in AIS

< 3 h	<ul style="list-style-type: none"> • Age: any > 18 y
	<ul style="list-style-type: none"> • Severity <ul style="list-style-type: none"> • Disabling—any severity (severe, moderate, mild) • Nondisabling—mild (reasonable)
3–4.5 h	<ul style="list-style-type: none"> • Age: 18 to < 80 y
	<ul style="list-style-type: none"> • Risk factors <ul style="list-style-type: none"> • Not having both DM and prior stroke • Not on OAC (unless INR < 1.7)
	<ul style="list-style-type: none"> • Nonsevere stroke i.e. <ul style="list-style-type: none"> • NIHSS < 25 • < 1/3rd MCA territory
	<ul style="list-style-type: none"> • Vitals <ul style="list-style-type: none"> • BP < 180/110 mm Hg • RBS > 50 mg/dL, but < 400 mg/dL

Abbreviations: AIS, acute ischemic stroke; BP, blood pressure; DM, diabetes mellitus; INR, international normalized ratio; IV, intravenous; MCA, middle cerebral artery; NIHSS, National Institutes of Health Stroke Scale; OAC, oral anticoagulation; RBS, random blood sugar.

Table 2 Technique and requirement of IVT administration

<p>Dose: IV, 0.9 mg/kg, max 90 mg. 10% as bolus over 1 min, rest over 60 min (In Asians, 0.6 mg/kg was found to be noninferior)</p>
<p>Monitoring</p> <ul style="list-style-type: none"> • Requires ICU admission • Monitoring: BP and neurologic examination • q15m × 2h → q30m × 6h → q1h × 24h • Delay all tubes and catheter (NG, Foley's, arterial) insertions till completion of infusion
<p>Red flags: Discontinue infusion if</p> <ul style="list-style-type: none"> • Severe headache • Acute hypertension • Nausea, vomiting • Worsening neurologic deficits
<p>If symptomatic ICH</p> <ul style="list-style-type: none"> • Resend CBC, coag profile, cross-match • Emergent CT of head • Cryoprecipitate 10 U over 10–30 min (+10 U if fibrinogen < 200 g/dL) • Tranexamic acid (1,000 mg IV over 10 min) or E-amino caproic acid 4–5 g IV over 1 h f/b 1 g IV till bleeding controlled • Supportive therapy: BP, ICP, CPP, temperature, sugars • Neurosurgery/hematology consults
<p>If orolingual edema</p> <ul style="list-style-type: none"> • Treat as per AHA guidelines
<p>Postinfusion imaging</p> <ul style="list-style-type: none"> • Repeat CT/MRI at 24 h for hemorrhage prior to initiating antiplatelet/coagulant therapy

Abbreviations: AHA, American Heart Association; CPP, cerebral perfusion pressure; CT, computed tomography; BP, blood pressure; CBC, complete blood cell count; ICH, intracranial hemorrhage; ICU, intensive care unit; IV, intravenous; IVT, intravenous thrombolysis; MRI, magnetic resonance imaging; NG, nasogastric.

invasive management. The first stage requires consideration of the patient's age, baseline functional status, and any comorbidities (and in our country, affordability) that are primary modifiers of the decision-making paradigm.

The next stage is to gather data on the degree of damage and decide whether the residue justifies endovascular treatment (EVT). Essentially two methods of patient selection are present: time- and perfusion-based. Central to both paradigms is the selection of a patient who has a relatively small core with ELVO and a significant salvageable penumbra. The AHA criteria for EVT are summarized in ►Table 3.⁴

The management of a patient who presents ≤ 6 hours is time based and requires only establishment of a disabling stroke but with a small core (clinical-radiologic mismatch) and ELVO. Treatment must be individualized in those with large core infarcts (discussed in the section on perfusion in part 1) and those with minimal symptoms (discussed below). Beyond 6 hours, the presence of a significant core/penumbra mismatch must be identified by perfusion imaging to justify EVT. An algorithm for imaging and management is presented in ►Fig. 1.

Several prognostication scores are available that help predict outcomes of EVT (►Table 4).²⁰ Though most can predict poor outcomes, the PRE score is capable of predicting good outcomes as well.²¹ Only a few incorporate imaging characteristics suggesting that further work is required to create a more comprehensive score.²⁰

The last stage is consideration of treatment options, their individual pros and cons with respect to patient comorbidities, vascular anatomy, and occlusion characteristics. It is important to remember to be flexible in the approach to patient selection with the knowledge that outcomes are a product of bayesian probability.²²

Technique of Endovascular Thrombectomy

The procedure can be divided into three phases: preprocedure, diagnostic-access, and intervention phases.

Preprocedure Phase

Rapid transit to a cath laboratory is necessary. The ESCAPE and SWIFT-PRIME (Solitaire with the Intention for Thrombectomy as Primary Endovascular Treatment for Acute Ischemic Stroke) trials recommend a time period of < 60 minutes and < 70 minutes (maximum 90 minutes).^{23,24} Advance activation of the neurointervention team is necessary.

Patient preparation: Unlike a traditional elective neurointervention case, time is of the essence. A simple electric shaver will do for groin preparation. Foley's catheterization is an unnecessary delay. Ensure a large-bore IV line is inserted. Maintain blood pressures (BP) using nonglucose crystalloids to avoid hyperglycemia.

Anesthesia: The potential advantages of general anesthesia (GA) cannot be ignored. Patient movement whether related to pain or altered sensorium is disruptive to the procedure. Groin puncture and stentriever retrieval can cause pain. Airway aspiration is also an ever-present danger. Apart from analgesia, GA can streamline the interventional procedure, improving recanalization times and reducing fluoroscopy

times.²⁵ GA, however, does not allow neurologic examination during and immediately postprocedure. Further, it results in poorer chances of a good functional outcome, increased hospital stay post revascularization, and a higher case fatality rate.^{26,27} These differences remained despite accounting for the likelihood that patients with more severe strokes were

Table 3 AHA eligibility criteria for MT in AIS with ELVO

Age	<ul style="list-style-type: none"> • Definite indication • ≥ 18 y • Reasonable indication but uncertain benefit • ≥ 90 y—consider life expectancy, quality of life, etc.
Prestroke mRS	<ul style="list-style-type: none"> • Definite indication • 0–1 • Reasonable indication but uncertain benefit • > 1
NIHSS	<ul style="list-style-type: none"> • Definite indication • ≥ 6 and < 25 • Reasonable indication but uncertain benefit • < 6 (i.e., stroke with minimal symptoms) and ICA or M1 ELVO
ASPECTS	CT ≥ 6 (if DWI ≥ 5)
ELVO	<ul style="list-style-type: none"> • Definite indication • ICA, M1 MCA • Reasonable indication but uncertain benefit • M2/M3 MCA • ACA • VA, BA, PCA
Ictus to groin puncture time	<ul style="list-style-type: none"> • ≤ 6 h—indicated if above criteria satisfied • 6–16 h—indicated if ELVO and DAWN or DEFUSE 3 criteria satisfied <ul style="list-style-type: none"> ◦ DAWN criteria <ul style="list-style-type: none"> ▪ Age ≤ 80 y: NIHSS ≥ 10, infarct volume < 31 cc ▪ Age > 80 y: NIHSS ≥ 10, infarct volume < 21 cc ◦ DEFUSE 3 criteria <ul style="list-style-type: none"> ▪ Infarct volume < 70 cc ▪ Ischemic tissue-to-core ratio > 1.8 • 6–24 h—indicated if ELVO + DAWN eligibility criteria satisfied

Abbreviations: ACA, anterior cerebral artery; AHA, American Heart Association; AIS, acute ischemic stroke; ASPECTS, Alberta Stroke Program Early CT Score; BA, basilar artery; CT, computed tomography; DAWN, Diffusion Weighted Imaging (DWI) or Computerized Tomography Perfusion (CTP) Assessment With Clinical Mismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention; DEFUSE, Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution; DWI, diffusion-weighted imaging; ELVO, emergent large vessel occlusion; ICA, internal carotid artery; MCA, middle cerebral artery; mRS, modified Rankin scale; MT, mechanical thrombectomy; NIHSS, National Institutes of Health Stroke Scale; VA, vertebral artery.

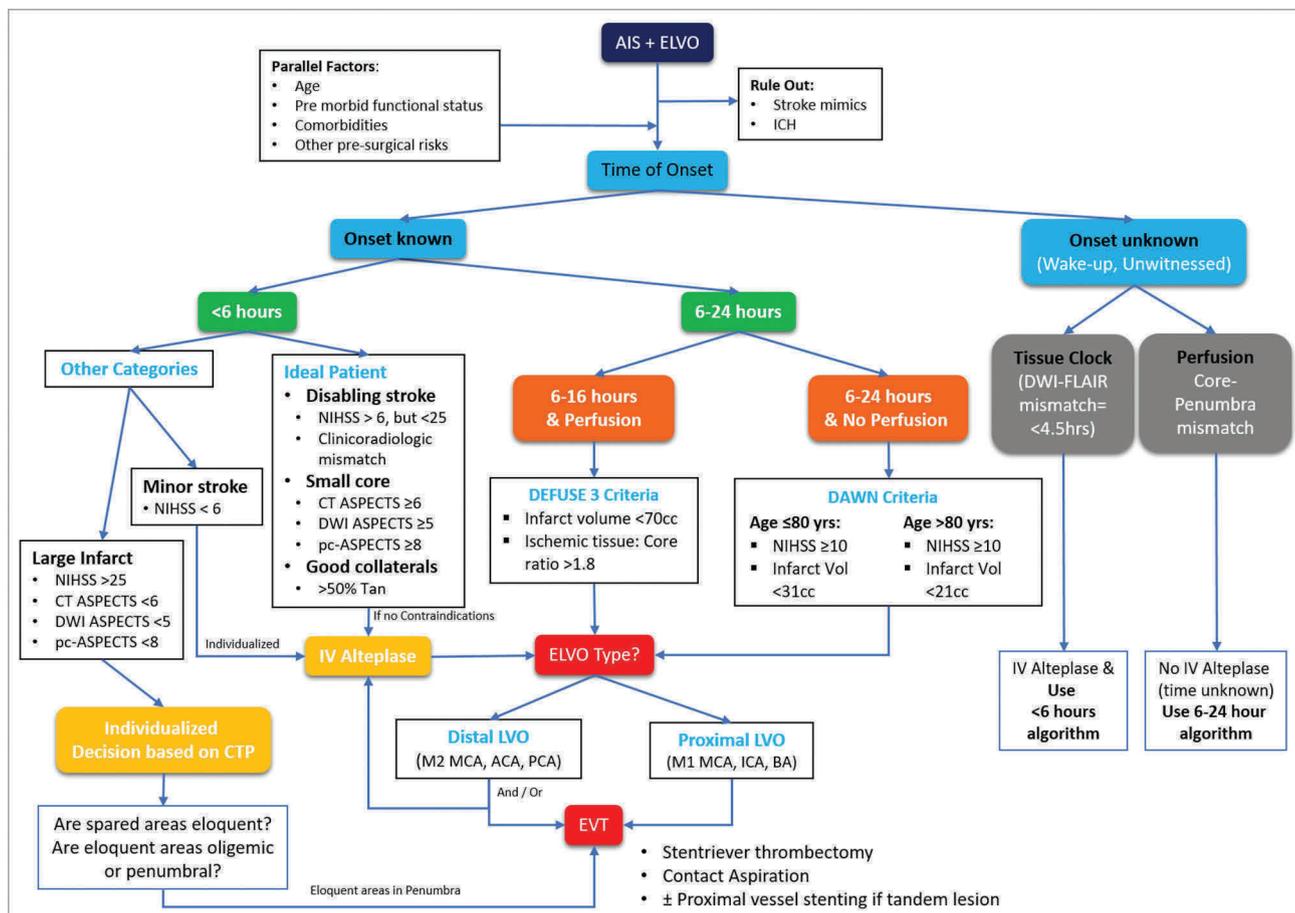


Fig. 1 Suggested algorithm for imaging and patient management in acute ischemic stroke (AIS). ACA, anterior cerebral artery; ASPECTS, Alberta Stroke Program Early CT Score; CT, computed tomography; DWI, diffusion-weighted imaging; ELVO, emergent large vessel occlusion; FLAIR, fluid-attenuated inversion recovery; ICH, intracranial hemorrhage; IV, intravenous; MCA, middle cerebral artery; NIHSS, National Institutes of Health Stroke Scale; PCA, posterior cerebral artery; pc-ASPECTS, posterior circulation ASPECTS.

more likely to be intubated. One likely cause is transient patient hypotension during induction that can compromise already failing cerebral circulation.²⁸ Delays during induction may be another reason.²⁸ However, an experienced anesthesiologist, rapid induction techniques, and strict maintenance of normotension and normocarbia can produce equivalent outcomes as was shown in the SIESTA (Sedation vs. Intubation for Endovascular Stroke Treatment) trial.^{29,30} At present time, conscious sedation is the standard of care, and GA is preferred in neurologically or hemodynamically unstable patients, excessively uncooperative patients, or those with compromised airway protective reflexes.

Diagnostic-Access Phase

Diagnostic angiography: Obtain femoral arterial access and secure a 5 to 7F short sheath initially, which will need to be switched to an 8F sheath later on. Heparin may be given as for any intervention, usually 3,000 to 5,000 IU.³¹ Use a diagnostic catheter (vertebral, right coronary or Simmons) to navigate into the ipsilateral internal carotid artery (ICA) and obtain a diagnostic cerebral angiogram. Angiograms of the contralateral ICA or vertebral artery (VA) are unnecessary and may be obtained only if neck vessel occlusion is present. Assess level

of occlusion using bony landmarks and degree of collaterals visually. It is important to formally assign a baseline modified thrombolysis in cerebral infarction (TICI) score (►Table 5) and grade collateral status using the Higashida scheme post-procedure (►Table 6).

Access phase: Use an exchange length 0.035 in Terumo Glidewire (Terumo Interventional Systems) or an extrastiff Amplatz wire (Boston Scientific, Cook Medical) to exchange a guide catheter into the cervical vessels. Choice of a guide catheter is dependent on the MT technique and is discussed as follows. Consider using a long sheath or Neuron Max (Penumbra Inc.) if significant vascular tortuosity.

Intervention Phase

Intra-arterial thrombolysis: IAT is now considered obsolete. The ProACT (Procalcitonin Antibiotic Consensus Trial) trials did show a significantly higher rate of good functional outcome (40% vs. 25%) in patients achieving recanalization (66% vs. 18%) with IA pro-urokinase and heparin than IVT alone but with a much higher rate of sICH (10% vs. 2%).³² A confirmatory trial was never performed, and FDA approval was never given. This technique was thus superseded by other more effective techniques (►Table 7).

Stentriever MT: Stentriever are the current standard of care. *Thrombectomy devices* underwent three generations of evolution:

- The *first-generation devices* were the Merci retriever devices (Concentric Medical/Stryker, Inc.). These consisted of a

Table 4 Prognostic scores for EVT

PRE Pittsburgh Response to Endovascular therapy	Age + 2 (NIHSS-10) × ASPECTS	-25 to +49 = High likelihood of benefit ≥ 50 = Not likely to benefit
SPAN Stroke Prognostication using Age and NIHSS	Age + NIHSS	≥100 poor outcomes, high risk
THRIVE Total Health Risks in Vascular Events	NIHSS + age + comorbidities (max 9) • NIHSS (≤ 10, 11-20, ≥ 21 = 0, 2, 4 points) • Age (≤ 59, 60-79, ≥ 80y = 0, 1, 2) • Comorbidities (HTN, DM, Afib = +1 each)	6-9 = poor outcome
HIAT Houston Intra-Arterial Therapy	Age + NIHSS + glucose (max 3) • Age > 75 y = 1 • NIHSS > 18 • Glucose > 150 mg/dL = 1	≥ 2 = poor outcomes
HIAT 2 Houston Intra-Arterial Therapy 2	Age + NIHSS + glucose (max 8) • Age (≤ 59, 60-79, ≥ 80 y = 0, 2, 4) • Glucose (< 150, ≥150 mg/dL = 0, 1) • NIHSS (≤10, > 10 = 0, 1)	≥ 5 = poor outcome
SAD Stanford Age and Diffusion-weighted imaging	Age + DWI volume • Age (≤55, 56-69, 70-79, ≥ 80 y = 0, 1, 2, 3) • DWI volume (≤15 mL, > 15 mL = 0, 1)	
MRPREDICTS Multivariable Personalized Intra-arterial treatment Clinical Decision tool for ischemic Stroke	http://mrpredicts.shinyapps.io/RRRR/	
ISCORE Ischemic Stroke predictive Risk	http://www.sorcan.ca/iscore/	

Abbreviations: ASPECTS, Alberta Stroke Program Early CT Score; DM, diabetes mellitus; HTN, hypertension; DWI, diffusion-weighted imaging; EVT, endovascular treatment; NIHSS, National Institutes of Health Stroke Scale.

nitinol based coil that was delivered through a microcatheter into the clot. There were three iterations of the devices themselves: the X series (with a corkscrew appearance of coil), L series (nontapering coil bent at 90 degrees with arcading filaments), and the V series (a hybrid version with nontapering coil and arcading filaments provided in soft and firm versions).³³ The MERCI (Mechanical Embolus Removal in Cerebral Ischemia) and Multi-MERCI trials showed a higher rate of recanalization and good outcomes but with higher mortality rates compared with historical controls. These had a high rate of nontarget embolization (NTE).^{34,35} Nonetheless, they paved the way for future trials and devices.

- The *second-generation device* was the Penumbra aspiration system (Penumbra, Inc.) consisting of a reperfusion catheter with a separator. These were available in four sizes (with internal diameters [IDs] of 0.054-0.026 in) with a corresponding sized separator for occlusions from the ICA to the M2 middle cerebral artery (MCA). The aim was to size the catheter to the artery without causing wedging so as to efficiently aspirate the thrombus. A proprietary aspiration pump was used to generate a continuous negative suction of up to 20 mm Hg with the separator moved back and forth to clear the ingested clot.³⁶ The Penumbra Pivotal trial was a nonrandomized trial to establish the efficacy and safety of the devices. Despite high recanalization rates (82%), good clinical outcomes remained poor (only 25%) with high complication rates of 12.8%.³⁷
- The *third-generation devices* were the stentriever (► **Table 8**, ► **Fig. 2**) consisting of a retrievable stent. They were initially used to only act as a temporary bypass across the thrombus to allow IAT. Only later were

Table 5 mTICI score

Grade	Antegrade flow	Tissue reperfusion	Original TICI grade
0	Nil	Nil	Same
1	Present	Nil	Same
2A	Present	Partial < 50%	Partial < 66%
2B	Present	Partial 50-99%	Partial 66-99%
3	Present	Complete 100%	Complete 100%

Abbreviations: mTICI, Modified thrombolysis in cerebral Infarction.

Table 6 ASITN/SIR collateral vessel grading system (by Higashida et al)

Grade	Ischemic site filling	Speed of retrograde flow	Perfusion deficit
1	No	-	Whole territory
2	Till periphery	Slow	Partial
3	Till periphery	Rapid	Partial
4	Complete	Slow	Nil
5	Complete	Rapid	Nil

Abbreviations: ASITN, American Society of Interventional and Therapeutic Neuroradiology; SIR, Society of Interventional Radiology.

they used directly for MT. The first of these were the Solitaire-AB (ev3/Medtronic) and Trevo (Stryker, Inc.) devices whose safety and efficacy were first established by the SWIFT and TREVO 2 trials. These devices were the reason for the success of the six recent landmark

trials being used in more than 80% of patients.^{23,24,38–41} MT with third-generation stentriever is the recommended treatment for ELVO achieving reperfusion (TICI 2b/3) in 59 to 88% of cases.⁴²

The *technique* of stentriever delivery first requires blindly crossing the occlusion with a microwire-microcatheter combination. A microcatheter angiogram is necessary to ensure correct intraluminal position and evaluation of distal flow patterns.⁴³ The microwire is exchanged for the stentriever that is then deployed across the thrombus by pulling back the microcatheter like a sleeve (unsheathing technique). For closed cell devices such as Trevo, pushing in the stentriever into the clot during deployment (the push and fluff technique) causes foreshortening and increases radial force resulting in better clot integration.⁴⁴ Longer stentriever result in better outcomes.⁴⁵ The stentriever are deployed for a few minutes (usually 5 minutes) for integration of the clot into the struts (→ Fig. 3). An increased dwell time (~8 minutes) allows for superior clot embedment and higher rates of recanalization with a single pass.⁴⁶ This is likely related to the shape memory effect of nitinol.⁴⁷ During clot retrieval, the microcatheter is minimally advanced onto the detachment zone of the stentriever, and the entire stentriever-microcatheter assembly is pulled back as a unit. Aspiration needs to be applied to the guide catheter throughout this retrieval process, to prevent NTE. Though there is no agreed-upon limit for the maximum number of passes, five passes may be reasonable before considering the procedure a failure.⁴⁸ The aim is to achieve

Table 7 EVT techniques

EVT technique	Remarks
Mechanical thrombectomy	Stentriever-based enmeshment of clot (previously Merci)
Distal Aspiration thrombectomy	FAST (manual aspiration using older Penumbra system) ADAPT (newer direct large-bore catheter aspiration without BGC)
Solumbra	Combination of retrieval device (Solitaire) and aspiration catheter (Penumbra)
PROTECT	PROTECT aspiration during stent retriever thrombectomy—combination of BGC, aspiration catheter, and stentriever
Distal embolization protection	Lazarus effect cover for stentriever thrombectomy

Abbreviations: ADAPT, A Direct Aspiration first Pass Thrombectomy; BGC, Balloon guide catheter; EVT, endovascular treatment; FAST, Forced Aspiration Suction Thrombectomy; PROTECT, Proximal balloon Occlusion Tether with direct Thrombus.

Table 8 Types of stentriever

Stentriever	Company	Remarks
Solitaire FR, AB, 2	Medtronic	Overlapping stent design Detachable electrolytic (AB), nondetachable (FR, 2)
Mindframe Capture LP	Medtronic	Low profile, delivery through 0.017-in microcatheter, for distal occlusions
Trevo ProVue, XP Provue, Baby Trevo	Stryker	Fully visible struts, Baby Trevo for use in distal occlusions
pREset, pREset Lite	Phenox	Helical slit design allows increase radial force Proximal ring design allows complete opening even in curves Small profile—0.021 in (standard) and 0.0165 in (Lite) microcatheter compatible
3D revascularization device	Penumbra	Unique design minimizes vessel contact Meant for use with ADAPT
Eric	Microvention	ERIC Series of interlinked adjustable nitinol cages with high metal coverage—allows for faster thrombus capture, integration, and withdrawal
ReVive SE	Codman	Closed end basket reduced NTE
Aperio	Acandis	Hybrid cell design: Smaller cells for apposition; larger cells allow integration of clot, small profile—0.021 in microcatheter compatible
Catch Plus (Standard, Mini, Maxi, Mega)	Balt	Wide range of device sizes; can be delivered through 0.017 in microcatheter (mini) to 0.040 in (mega)
Tigertriever	Rapid Medical	Adjustable diameter with handle
Neuravi EmboTrap II revascularization device	Neuravi	Dual-stent design—inner stent mesh has high radial force that creates consistent central revascularization channel; outer stent mesh has lower radial force that allows clot embedment
Golden retriever	Amnis Therapeutics	Thinnest stentriever; passes through clot like a wire when collapsed; consists of 5 crown elements that can be opened up for retrieval

Abbreviations: ADAPT, A Direct Aspiration first Pass Thrombectomy; ERIC, Embolus Retrieval with Interlinked Cages; NTE, nontarget embolization.

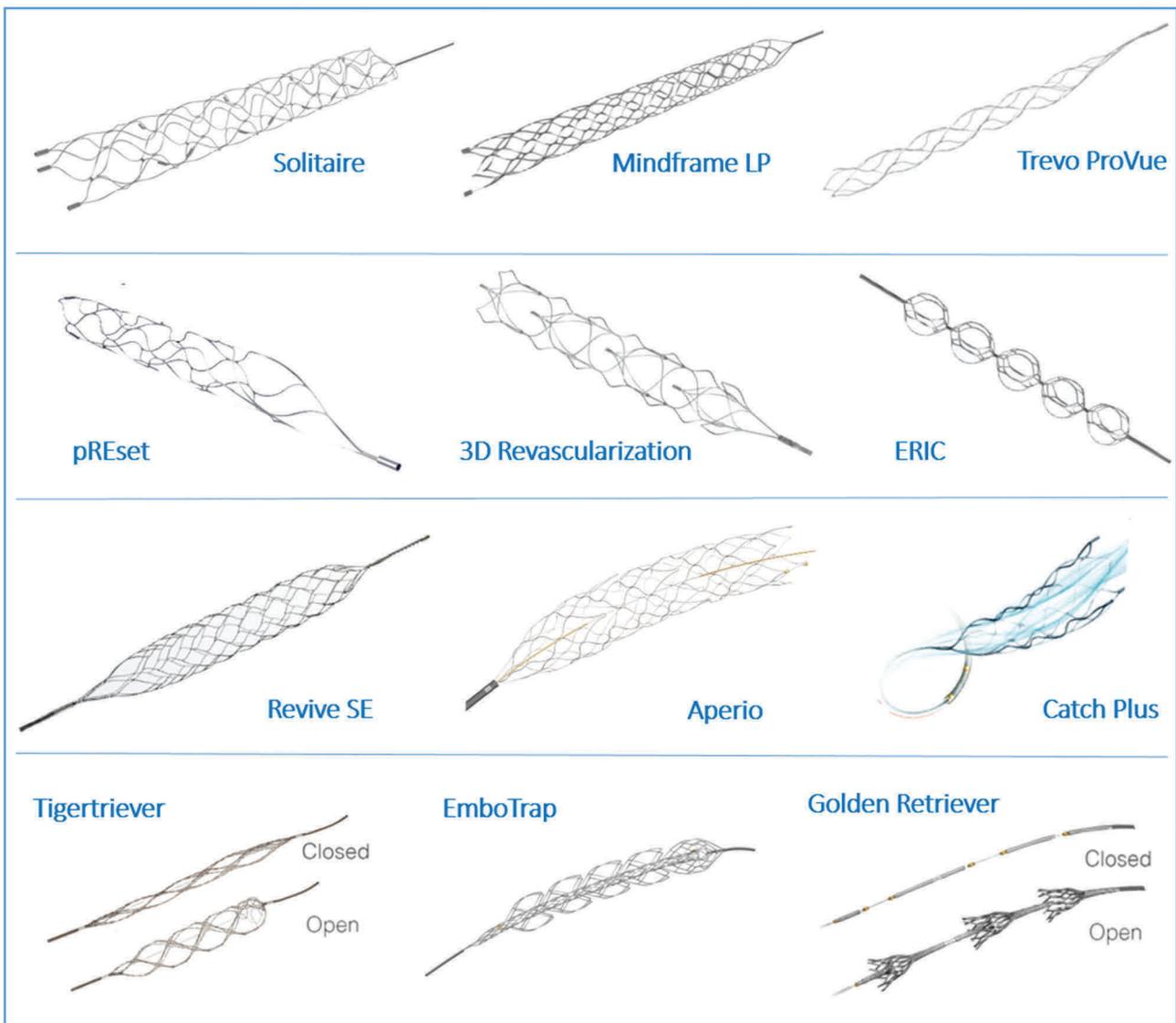


Fig. 2 Different designs of stentriever.

recanalization within 60 minutes in at least 70% of patients with the caveat that the complication rate increases with the number of passes.⁴⁹

The *guide catheter system*, usually large bore (8–9F), can have an impact on the safety and efficiency of aspiration. Three options exist: conventional (CGC), and balloon guide catheters (BGCs), and distal access catheters (DAC).⁵⁰ The advantage of BGCs over CGC is that they allow flow arrest permitting more efficient aspiration and reduced rates of NTE (10–12% vs. 53% with BGC).⁵¹ An exchange method or coaxial advancement technique is used to place the GC. The tip is usually parked at the ICA bulb or V1/V2 segments.⁵⁰ CGCs such as Neuron or Envoy are more practical in the posterior circulation. DACs require a triaxial system and are of use in more distal occlusions or tortuous vasculature. They are parked as close to the occlusion as possible to reduce the retrieval corridor and thrombus dispersion. The efficiency of aspiration is, however, reduced due to their narrower lumens.⁵²

Aspiration thrombectomy (AT): Also known as the contact aspiration technique, AT was originally used with the

Penumbra aspiration pump system (PS) in combination with a separator to break up the clot. Concurrent with the rise of stentriever, refinements in AT continued. The forced aspiration thrombectomy (FAST) technique was the first of these and was used as a bailout procedure when revascularization failed with the PS separator.⁵³ Manual aspiration with a 20/50 cc syringe was done through the reperfusion catheter without the separator. This resulted in an improved rate of recanalizations over the original PS technique.⁵³

A direct aspiration first-pass technique (ADAPT) completely did away with the use of a separator and depended solely on the aspiration force of a pump to remove the clot. The technique uses the newer-generation, more flexible, atraumatic large-bore, coil-reinforced catheters (►Table 9, ►Fig. 4) whose larger lumens allow a larger surface area of contact with the clot and increase aspiration capacity.⁵⁴ Two modes of clot retrieval are possible: if the clot is disrupted, blood flows into the pump canister (disrupted clot type), whereas lack of flow into the canister means that the intact clot is wedged at the tip (whole clot type).⁵³ Because crossing the occlusion is

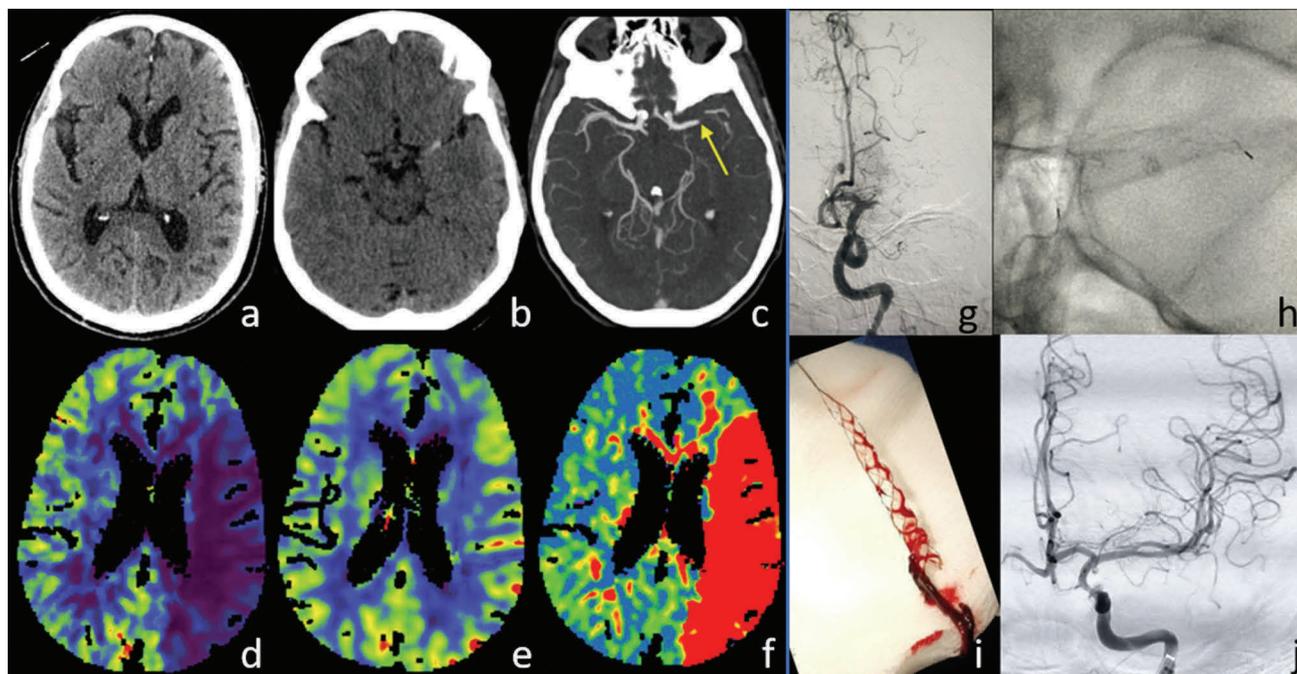


Fig. 3 Illustrative case: A 56-year-old man presented with AIS features localizing to the left cerebral hemisphere (NIHSS 19) within 2 hours of ictus. Plain CT showed no definite early ischemic changes (a) but a dense MCA sign (b). A CT perfusion was performed. (d) MTT, (e) CBV, and (f) CBF maps showed no significant core with a large penumbra. (c, arrow) CTA confirmed an occlusion of the left M1 MCA and > 50% collaterals. (g) Initial DSA showed cutoff of the left MCA. (h) A Solitaire stentriever was deployed across the occlusion with retrieval of clot in first attempt (i). (j) Check angiogram showed TIC1 grade 3 recanalization.

no longer necessary, rates of NTE and hemorrhage associated with superselective angiography are reduced.⁵⁵ This also reduces recanalization times (sometimes just 4.5 minutes from puncture).⁵⁶ Indeed, early recanalization (< 35 minutes) results in more complete revascularization and better clinical outcomes.⁵⁷ Further, the procedure is versatile, allowing easy bailout with stentriever techniques (usually after three failed attempts). With comparable rates of successful reperfusion (78% in the ADAPT-FAST trial, improving to 95% with stentriever bailout), AT has challenged the monopoly of stentriever techniques.⁵⁵ The ASTER (Contact Aspiration Versus Stent Retriever for Successful Revascularization) trial, however, showed mixed results with poorer 90-day clinical outcomes (45.3% in AT vs. 50% in MT) despite better rates of recanalization (85.4% vs. 83.1% respectively).⁵⁸ Stentriever techniques thus are the preferred option in the AHA guidelines, although use of the ADAPT technique remains reasonable.⁴

Switching/bailout technique: For switching from *stentriever thrombectomy* to *aspiration*, two possible options are available. The first option involves removal of the microcatheter-stentriever combination completely and then introducing the aspiration catheter as usual similar to primary ADAPT. The second option is to remove only the stentriever leaving the microcatheter in place. The next step is to pass the microwire with a docking wire and use this to exchange the aspiration system directly into place. This latter option is particularly useful if navigation was difficult. For switching from *aspiration* to *stentriever thrombectomy*, an additional microcatheter wire is navigated through the indwelling aspiration catheter for subsequent delivery of the stentriever.

Table 9 Types of aspiration catheters

Aspiration catheter	Company	Remarks
Ace 3, 4, 5 Max	Penumbra	2nd-generation aspiration catheters 3, 4 Max still useful for distal occlusion of M2 MCAs or for co-axial delivery of larger aspiration catheters
Ace 60, 64, 68	Penumbra	Latest 3rd-generation aspiration catheters, more flexible, better support, high-flow aspiration—to replace Ace 5 Max. Sizing to fit OD into vessel diameter, number represents ID. Ace 60 for distal M1, Ace 64, 68 for proximal M1 and ICA
Sofia, Sofia Plus Distal Access Catheter	Microvention	Soft torqueable catheter, optimized for intracranial access, distal IDs of 0.068 and 0.70 (plus)
Arc, Arc Mini Intracranial Support catheter	Medtronic	Distal ID of 0.061 in
Catalyst (Cat 6)	Stryker	Distal ID of 0.060 in, claims 3x more trackability than Ace 64.
Revive IC	Cordis	Distal ID of 0.056 in

Abbreviations: ACA, anterior cerebral artery; ID, inner diameter; MCA, middle cerebral artery; OD, outer diameter.

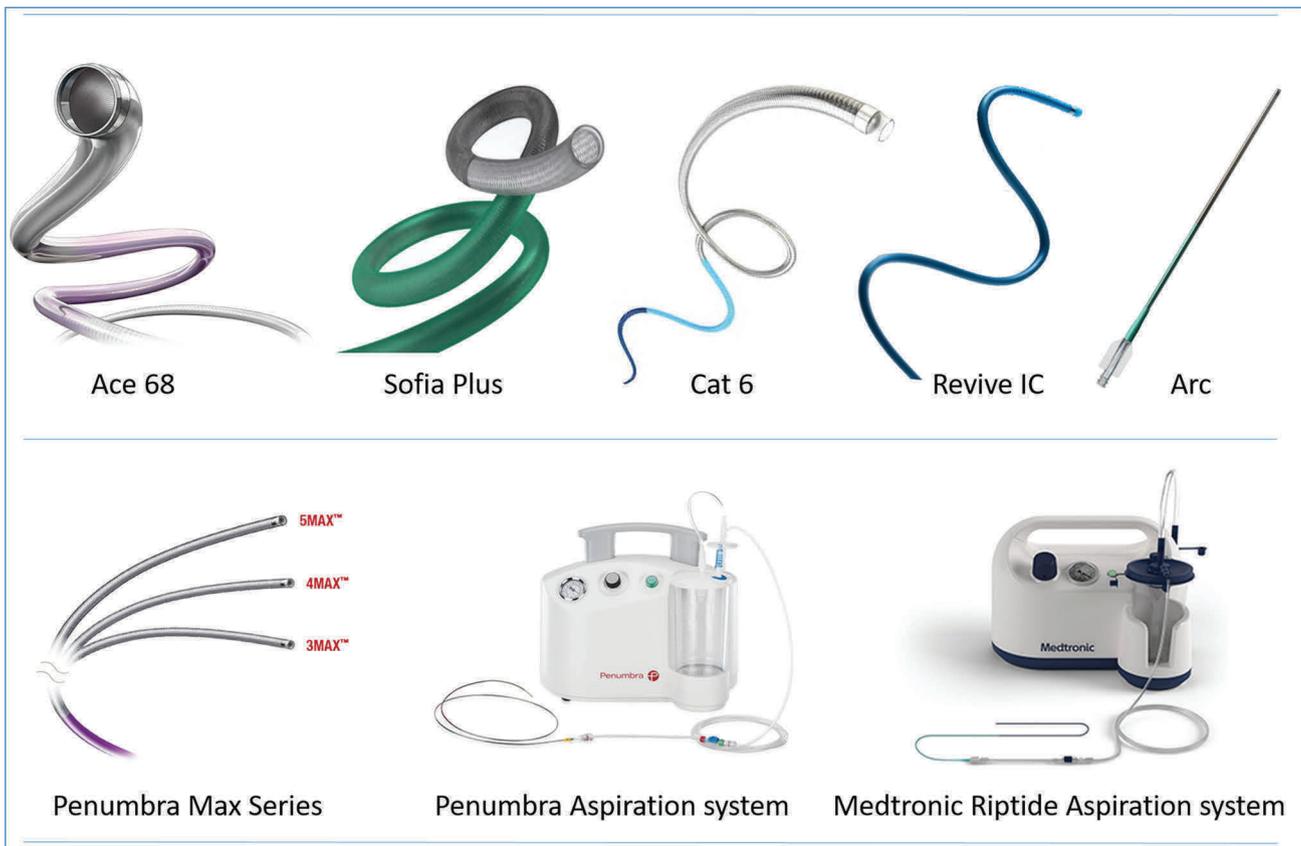


Fig. 4 Different types of aspiration catheters and pumps.

Solumbra technique: The awareness that the bailout use of stentriever with AT improved recanalization rates, a technique of primary combined use of both techniques together was devised.^{58,59} The procedure used a triaxial system consisting of a GC, a Penumbra catheter, and a Solitaire stentriever, and was aptly named the Solumbra technique. Improved support for stentriever retrieval with aspiration achieved good recanalization rates of 88%.⁵⁹ However, its efficacy remains controversial as it performed inferior to the ADAPT technique in a comparative case series.⁶⁰

PROTECT technique: PROximal balloon Occlusion TogEther with direCt Thrombus aspiration during stent retriever thrombectomy (PROTECT) is an advancement of the Solumbra technique that uses a BGC.⁶¹ The addition of a BGC has two advantages: it causes complete flow arrest preventing NTE and simultaneously improves efficacy of distal aspiration. As a result, PROTECT resulted in improved procedure times (29 vs. 40 minutes in Solumbra) and a higher rate of reperfusion (70 vs. 39% respectively) in a comparative case series.⁶² This technique is known by multiple other acronyms leading to confusion in literature.⁶³

Lazarus effect cover-assisted MT: This is a distal embolization protection device for stentriever thrombectomy. It consists of a funnel-shaped nitinol mesh designed to surround the stentriever and the enmeshed thrombus during retrieval.⁶⁴ Following stentriever deployment, the Lazarus device is positioned at its proximal end. Retraction of the stentriever against the device causes it to invert and roll over

the outside of the stentriever. This protective sheath prevents clot fragmentation and distal embolization. It has also been used with distal aspiration techniques.⁶⁵

Assessing revascularization: Recanalization should be achieved as rapidly as possible, preferably within the therapeutic window.⁴ Histopathologic and microbiological examination of the retrieved thrombi may aid in the etiologic workup and help retrospectively correlate any procedural difficulties with the type of thrombus.^{66,67} Some studies have suggested a possible correlation between stroke etiology, thrombus composition, and angiographic outcomes.^{68–70} However, a recent systematic review found no significant association between stroke etiology and clot composition.⁷¹ Regardless of etiology, however, a higher rate of recanalization was found for red blood cell (RBC)-rich thrombi as opposed to white blood cell (WBC)-rich thrombi.⁷¹ The hyperdense artery sign, an imaging marker of such RBC-rich thrombi, thus simultaneously predicts poor response to IVT and better outcomes post-EVT.^{71,72} More studies are required in this field.

Multiple reperfusion scales such as the Qureshi scale, Mori reperfusion scale, and the Arterial Lesion Occlusion score exist. However, the modified TICI score is most commonly used to assess the degree of recanalization and reperfusion (►Table 5).^{73–76} A good revascularization outcome is classified as TICI 2b or 3; however, differences remain even between these two grades. TICI 3 patients are more likely to reach a good functional outcome (71.7% vs. 50.5%) and lower

rates of ICH (23% vs. 45%) when compared with TICI 2b.⁷⁷ The brain is thus an unforgiving territory, and excellent outcomes must be aimed for. A further refinement of the mTICI score introduced 2c with 90 to 100% recanalization, but this is as yet to be validated.⁴⁹

Special Situations

Intracranial atherosclerosis-related occlusions (ICAS-O): Most revascularization therapies have been directed predominantly toward embolic occlusions (EMB-O). However, Asian populations have a higher prevalence of ICAS although the incidence of ICAS-O remains unknown. AIS may result from either hemodynamic compromise in flow-limiting lesions or vessel occlusion secondary to plaque rupture and thrombosis. ICAS-O is more frequent in males, slightly younger populations, and in the posterior circulation. Clot burden tends to be lower and with often better collaterals due to the chronic nature of the stenosis. The EVT technique remains the same. A residual stenosis may remain, which should not be confused for vasospasm or focal dissection. Vasospasm can be differentiated by a 10- to 20-minute interval angiogram.⁷⁸ Unlike EMB-O that shows progressive improvement in the caliber of the occluded segment, ICAS-O shows persistent stenosis or even reocclusion at CT/MRA 5 to 7 days after EVT.⁷⁹ Presently, residual stenosis is best managed medically in light of the negative results of the SAMMPRIS (Stenting and Aggressive Medical Management for Preventing Recurrent stroke in Intracranial Stenosis) trial.⁸⁰ Immediate initiation of glycoprotein IIb/IIIa inhibitors may prevent reocclusion.⁸¹ However, emergent stenting with or without angioplasty may play a role in residual critical stenoses.⁸²

Distal occlusions: For occlusions of the M2 segments, contact aspiration may result in higher rate of successful recanalization and a lower risk of distal embolism.⁸³ However, delivery of these larger-bore aspiration catheters may be impeded by proximal vessel tortuosity. Thrombus location at the M1–M2 junction or at an acute angle may result in sub-optimal contact and poor aspiration. Further, the efficacy of aspiration drops rapidly with increase in number of attempts. In such cases, primary stentriever thrombectomy or early switching may be considered.⁸³ For a thrombus extending from the M1 or basilar bifurcation, a dual-stentriever technique with deployment in a double-barrel Y-configuration is useful for simultaneous thrombectomy.⁸⁴

Large DWI lesions: Patients with large DWI lesions > 60 or 70 mL are not necessarily exempt from EVT. Although the frequency remains low, EVT may result in a significantly higher probability of achieving modified Rankin scale (mRS) 0–3.⁸⁵ EVT may be of benefit more in patients with isolated M1 MCA occlusions or lesions restricted to the superficial MCA territory than in those with carotid occlusions or deep MCA territory involvement.⁸⁶ Perfusion studies are necessary to exclude oligemic tissue. Judicious patient selection is necessary.

Stroke with minimal symptoms: Minor stroke is defined by an NIHSS (National Institutes of Health Stroke Scale) score of ≤ 5 . The lack of major neurological deficit is

due to presumably a relatively small penumbra and a large area of benign oligemia. The question arises, therefore, as to the necessity of treatment in such patients. However, the presence of an underlying large vessel occlusion is the main predictor of deterioration in such patients, resulting in poor outcomes in up to one-third.^{87,88} Further, slow-flowing collaterals, as assessed by either triple-phase computed tomographic angiography (CTA) or computed tomographic perfusion (CTP) source images, are associated with thrombus extension and increasing core.⁸⁹ MT is thus a viable option in such patients and results in a favorable shift of NIHSS and higher rates of independence at discharge as well as at long-term follow-up.⁹⁰

Tandem occlusions: Concurrent carotid stenting and embolectomy remain reasonable as per the AHA guidelines. However, controversies remain regarding the optimal approach. The antegrade/distal-to-proximal method reduces time to recanalization of the intracranial vessel, thus decreasing the duration of ischemia and reliance on collaterals. Alternatively, a retrograde/proximal-to-distal approach addresses the offending thromboembolic cervical plaque first, improving collateralization and theoretically reducing distal embolization while intracranial recanalization is being performed.⁹¹ A recent meta-analysis suggests no difference between either approach or between angioplasty and stenting of the extracranial lesion.⁹²

Surgical embolectomy: In cases still within the time window, a minimally invasive and rapid surgical embolectomy (MIRSE) technique via a superciliary or supraorbital keyhole provides rapid access to the target artery.⁹³ The role of extracranial-intracranial (EC-IC) bypass has been largely relegated to the prevention of recurrent stroke.⁹⁴

Complications

Mechanical thrombectomy is associated with a major complication rate of up to approximately 15%.^{95,96} Major complications can adversely affect functional outcomes, resulting in prolonged hospital stay, long-term disability, and even mortality. These are classified in **Table 10**. The neurointerventionist must be cognizant of the potential complication for each step of the MT procedure. The risk of complications increases with prolongation of the procedure highlighting the importance of rapid recanalization.

The most common complication encountered is that of sICH. Though IVT is associated with a risk of systemic and intraparenchymal hemorrhage, EVT is associated with a higher risk of *subarachnoid hemorrhage* (SAH). Assessment and management of sICH is described in the next section. *Arterial perforations* (AP) occur at a frequency between 0.6 and 4.9% in the six recent RCTs.^{23,24,38–41} The risk of AP is increased during two critical times of the procedure: during “blind maneuvering” across the thrombus and while retrieving the stentriever.⁹⁵ It is usually seen as extravasation. Management is as for any perforation—resisting the urge to withdraw the perforating device, reversal of heparin, inducing mild systemic hypotension, and tamponading with an intracranial balloon. Minor degrees of resultant SAH need not necessarily affect outcomes.⁹⁶ Perforation of the cavernous ICA may

Table 10 Complications of EVT in AIS

Hemorrhagic complications	• sICH
	• PH 1/2 or
	• HI 1/2
	• SAH
	• IVH
Device/procedure-related complications	• Stent detachment/fracture
	• Arterial dissection
	• Carotid-cavernous fistula
	• Arterial perforation
Distal NTE	• Distal territory (NTE-D)
	• New territory (NTE-N)
Others	• Vessel vasospasm
	• Reocclusion/incomplete recanalization
	• Access site complications
	• Anesthesia related
	• Hypersensitivity—device (Nickel) and contrast media
	• Radiation-related risks

Abbreviations: AIS, acute ischemic stroke; EVT, endovascular treatment; HI, hemorrhagic infarction; IVH, intraventricular hemorrhage; NTE, nontarget embolization; PH, parenchymal hematoma; SAH, subarachnoid hemorrhage; sICH, spontaneous intracerebral hemorrhage.

result in carotid-cavernous fistula as well.⁹⁷ Irritation of the vessel may lead to *vasospasm* that occurred between 3.9 and 23% in the six RCTs.^{23,24,38–41} Although usually asymptomatic, it must be treated when severe to prevent potential reocclusion.⁹⁸ Off-label use of nimodipine, avoiding systemic hypotension, is reasonable.⁹⁵ *Arterial dissection* can occur both intra- and extracranially during microcatheter or guide catheter navigation. Early recognition is necessary to modify the MT procedure and prevent extension or worsening. Management options included anticoagulant or dual-antiplatelet therapy when non-flow limiting or plasty or stenting when flow limiting.⁹⁹ Unexpected *stent detachment* is associated with a higher risk of ICH, poor outcomes, and increased mortality.^{100,101} The probability increases with the number of passes and the manufacturer's instructions for use must be adhered to.^{95,102} Treatment options include leaving the stent in place if the vessel has opened, angioplasty if only partial vessel opening, using a second device for retrieval, and only if necessary surgical extraction.⁹⁵ Other complications are managed as for any interventional procedure.

Posttreatment Management

Admission of the patient to a designated neurointensive care unit is preferred as protocolized and specialized care results in improved rates of good outcomes and better monitoring for complications.¹⁰³

Failed or incomplete recanalization: Failure to achieve TICI 2b/3 recanalizations results in persistence of the ischemic penumbra. Leptomeningeal collaterals require at least

24 hours to reach adequate capacity and measures need to be taken during this time to sustain them.¹⁰⁴ Therapeutic hypertension improves both cerebral perfusion pressure and mean flow velocities and is a reasonable approach to augmenting collateral flow. Target to increase mean arterial pressure (MAP) by 10 to 20% above baseline or a maximum systolic blood pressure (SBP) of 185 mm Hg if IV alteplase has already been given. Patients with ICH, congestive cardiac failure, or SBP > 200 mm Hg should be excluded. Targets may be reached by withholding antihypertensives, the use of vasopressor therapy (phenylephrine or norepinephrine is preferred), fluid expansion (bolus of 0.5–1 L followed by maintenance), and supine positioning (unless risk of aspiration, then maintain 30 degrees).¹⁰⁵ Success of augmentation must be evaluated by testing for improvements of the NIHSS by at least 4.¹⁰⁶ Continue collateral support for at least 24 hours with a gradual weaning thereafter. Failure to withstand weaning may require initiation of oral hypertensive agents such as fludrocortisone.¹⁰⁵ Note, however, that the AHA guideline dismisses volume expansion in the treatment of AIS.⁴

Symptomatic ICH: Hemorrhagic transformation represents a continuum in reperfusion injury with breakdown of the blood-brain barrier. Symptomatic ICH refers to the contemporaneous neurologic worsening (NIHSS increase of 4 from baseline) with corresponding radiologic evidence of hemorrhage within 36 hours from treatment initiation.³² The relevance of hemorrhagic transformation is based on the radiologic appearance and is graded according to the European-Australasian Acute Stroke Study II (ECASS II) criteria with PH being symptomatic (► **Table 11**).¹⁰⁷ Though petechial hemorrhagic infarction is ischemic in nature, parenchymal hematomas are due to reperfusion injury.¹⁰⁸ A third type of hemorrhage, extrinsic, that is, remote from the infarct and often multifocal, merits consideration of entities such as coagulopathies or amyloid angiopathy.¹⁰⁸ Management involves reversal of coagulopathy, supportive therapy, and decompressive craniectomy if signs of significant mass effect (PH2) are present.

Malignant infarction: Malignant infarction occurs in 1 to 10% of patients with an MCA stroke leading to depression of sensorium over the 24 to 48 hours. It is one of the most

Table 11 ECASS II hemorrhage grades

Grade	Imaging criteria
HI	• Petechial hyperdensities in the infarct bed but no mass effect
	• HI1
	• HI2
PH	• Homogenously hyperdense hematoma/coagulum
	• PH1
	• PH2

Abbreviations: AIS, acute ischemic stroke; ECASS, European Cooperative Acute Stroke Study; EVT, endovascular treatment; HI, hemorrhagic infarction; PH, parenchymal hematoma.

dreaded complications having a mortality rate of nearly 80%.¹⁰⁹ Favorable neurological outcomes and reduced mortality can still be achieved by decompressive craniectomy, but this needs correct timing.¹¹⁰ Clinical factors that were predictive of impending malignant infarction post-EVT were a high NIHSS (≥ 20 or ≥ 15 for left and right hemispheres respectively), a high admission BP, and hyperglycemia (with failure of control within 48 hours).^{111,112} Radiologically, the strongest predictor was a CT ASPECTS (Alberta Stroke Program Early CT Score) ≤ 5 or a diffusion-weighted imaging (DWI) core volume of > 80 mL with a low sensitivity but high specificity.^{111,113}

Other measures: Patients may be extubated based on the neurologist/anesthetist's assessment. Airway support and ventilator assistance may be continued if there is evidence of continued depressed sensorium or lack of airway protection secondary to bulbar dysfunction. Dysphagia screening with is necessary prior to initiation of oral medications or feeds. Continue supplemental oxygen if peripheral capillary oxygen saturation (SpO_2) is $< 94\%$. Control any hyperthermia with antipyretics. Though hypotension and hypovolemia correction is beneficial, the role of hemodilution, vasodilators, or flow augmentation strategies is controversial. Maintain sugars in the range of 140 to 180 mg/dL while preventing hypoglycaemia.¹⁰⁵ Prevent sICH by maintaining SBP < 140 to 160 mm Hg while avoiding cerebral hypoperfusion with the use of tightly titrated infusion of rapidly acting IV agents such as nicardipine, labetalol, or enalapril.^{105,114}

Aspirin must be started within 24 to 48 hours from onset in all patients with AIS after ruling out hemorrhagic complications.^{4,105} Dual antiplatelets (with clopidogrel) are beneficial in patients with minor stroke for secondary stroke prevention. Glycoprotein 2b/3a inhibitors such as abciximab are contraindicated. Anticoagulation has no role of in AIS with ELVO but may be indicated in extracranial nonocclusive thrombi.¹⁰⁵

Posttreatment Imaging

Posttreatment imaging is aimed at establishing the size of the final infarct and the presence of hemorrhage.¹¹⁵ Apart from age, the final infarct volume (FIV) is a better predictor of neurologic outcomes than even revascularization grade.¹¹⁶ Indeed, revascularization achieves good outcomes only because it reduces FIV. In cases of incomplete recanalization, a 24-hour CT may underestimate FIV due to ongoing infarction. The role of the 24-hour CT is to rule out hemorrhagic transformation. A 7- or 30-day CT/fluid-attenuated inversion recovery (FLAIR) is best to look for the FIV because infarct growth is insignificant beyond this point.^{117,118} Parenchymal contrast medium staining may be differentiated from ICH by means of serial noncontrast CTs, susceptibility-weighted imaging (SWI), or dual-energy CT.¹⁰⁵

Quality Control

The joint statement by the American Society of Neuroradiology with the Society for Neurointerventional Surgery and others have given training and quality control guidelines for the interventional neuroradiologist.¹¹⁹ As a basic minimum, interventionists are expected to achieve successful

recanalization of TICI 2b/3 in at least 60% of cases, embolization to new territories in $< 15\%$ of cases, and an sICH (i.e., PH) rate of $< 10\%$.

Conclusion

Significant improvements have been made in clinical outcomes following AIS with ELVO, largely due to advances in endovascular techniques. Apart from endovascular radiology, interventionists must be competent in aspects of vascular neurology, diagnostic stroke radiology, and cerebrovascular neurosurgery to make the best decision for the patient. Further progress is dependent on evolving improved devices and techniques, a harmoniously integrated multidisciplinary team, enhanced transport systems, and increased public awareness.

Conflict of Interest

None.

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