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STROKE (JF MESCHIA, SECTION EDITOR)

Endovascular Thrombectomy for Acute Ischemic Stroke

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Abstract

Purpose of Review To review the current evidence supporting the use of endovascular thrombectomy (EVT) for the treatment of acute ischemic stroke (AIS) due to anterior circulation large vessel occlusion (LVO).

Recent Findings Recent advances in AIS management by EVT have led to significant reduction in morbidity and mortality in selected patients with LVO within the anterior circulation. Until recently, use of EVT was strictly based on time criteria, within 4.5 to 12 h of symptom onset with many patients presenting with "wake-up" stroke who were not considered for EVT. The positive results of the DAWN and DEFUSE-3 trials have shown benefit in extending the therapeutic window for EVT to 24 and 16 h, respectively, after last known normal (LKN) time in the setting of large ischemic penumbra. These trials represent a paradigm shift in contemporary treatment of AIS, changing from a purely time-based decision to treat to an individualized decision based on clinical and radiographic findings of salvageable tissue.

Summary Overall, acute stroke management has evolved considerably over the years from intravenous thrombolysis to include EVT, with paralleled improvements in patient selection and thrombectomy devices. Since the results of the DAWN and DEFUSE-3, EVT is now considered the standard of care in select patients with anterior circulation LVO up to 24 h from LKN time. Despite these developments, post-stroke disability remains pervasive and further studies are warranted in establishing the role of EVT in posterior circulation and distal vessel occlusions, with need for development of new and effective techniques for revascularization of small vessels.

Keywords Acute ischemic stroke · Endovascular · Thrombectomy · DAWN · DEFUSE 3 · Stent retrievers

Introduction

Stroke is the fifth leading cause of death and the number one cause of serious long-term disability in the USA [1, 2]. Every 3 min and 42 s, someone dies of an acute stroke and about 62% of stroke deaths occur outside of a hospital [2]. Geographic disparities in stroke mortality, known as the "stroke belt" in the southeastern USA, have existed since the 1940s, and

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despite some improvements, these disparities continue [3]. On average, the stroke belt has demonstrated an estimated 30% higher stroke mortality than the rest of the country, while it is nearly 40% higher in the "stroke buckle" regions of North Carolina, South Carolina, and Georgia [4]. Poor functional outcome after an acute stroke can be attributed to the failure in recognizing key symptoms and presenting late to the hospital, often beyond the therapeutic window for management. The estimated total direct medical stroke-related costs from 2015 to 2035 are projected to double from $36.7 to $94.3 billion [5].

Recent advances in acute ischemic stroke (AIS) treatment with endovascular thrombectomy (EVT) have demonstrated significant reduction in stroke morbidity and mortality. Historically, the first approved treatment for AIS in 1996 was thrombolysis by intravenous tissue plasminogen activator (IV-tPA). After that, Prolyse in Acute Cerebral Thromboembolism II (PROACT II) demonstrated improved clinical outcomes at 90 days with intra-arterial thrombolysis (IAT) with prourokinase for middle cerebral artery (MCA) occlusions within 6 h of stroke onset. The Interventional Management of Stroke Studies (IMS) suggested that combining IV and IA-tPA was safe and clinically useful in AIS treatment, while the results of five published trials revolutionized the treatment of large vessel occlusions (LVO) amenable to endovascular treatment (EVT) [6–10]. The positive results of the DAWN and DEFUSE-3 trials represent a paradigm shift in contemporary treatment of AIS, moving from a strictly time-based treatment decision to a physiologic-based decision made from advanced imaging characteristics suggestive of salvageable brain, or a so-called clinical-radiographic mismatch. Compared to prior stroke trials, DAWN sought to reach more stroke patients by extending the window for EVT to stroke victims that were previously considered ineligible for EVT. In this review, we provide a brief overview of the landmark EVT trials along with patient selection criteria based on neurovascular imaging, current EVT techniques, unresolved issues, and complications related to EVT.

Brief Review of Recent Trials

Several randomized EVT trials (SYNTHESIS, IMS III, and MR RESCUE) were reported in 2013 and failed to demonstrate improved patient outcomes following EVT [11–13]. Lessons from these studies led to the design of several studies with more stringent selection criteria. Although vascular reperfusion had been demonstrated earlier, it was not until the emergence of 5 prospective randomized controlled trials (RCTs) in 2015 that the benefits of EVT were clearly demonstrated in selected patients with AIS [6–10]. The decision for EVT was still based strictly on time criteria, within 4.5 to 12 h of symptom onset. Patients with late-presenting stroke symptoms, unwitnessed stroke onset, or stroke symptoms discovered upon awakening were not eligible for EVT based on these studies. Recently, the DAWN and DEFUSE-3 trials showed benefit in extending the therapeutic window to 24 and 16 h, respectively, after last known normal (LKN) time [14••, 15••]. These landmark EVT trials are summarized in Table 1. The HERMES collaboration [16] was an effort to pool patient-level data for 1287 patients from the 5 positive EVT trials including MR CLEAN, ESCAPE, REVASCAT, SWIFT PRIME, and EXTEND-IA to assess whether EVT was efficacious across the various included populations. EVT was shown to reduce disability at 90 days, and the number-needed-to-treat with EVT to reduce disability by one level on the modified Rankin Scale (mRS) for one patient was 2.6.

Patient Selection Criteria for EVT

Patient selection is crucial for improving the outcomes of EVT. Clinically, patients with National Institutes of Health Stroke Scale (NIHSS) > 6 or with a lower score and significant aphasia should be considered for EVT [17]. Imaging criteria continue to evolve with implementation of variable modalities from non-contrast computed tomography (NCCT) and magnetic resonance imaging (MRI) to CT/MR angiogram (CTA/MRA) and CT/MR perfusion (CTP/MRP) [17]. Favorable imaging parameters include an Alberta Stroke Program Computed Tomography Score (ASPECTS) of 6–10, a significant area of mismatch on CTP or MRP, a core infarct < 70 ml, and evidence of anterior circulation LVO with good collaterals on CTA/MRA [18]. Patients with these criteria presenting within 24 h from LKN should be considered for EVT without delay. Outside these established parameters, the decision to pursue EVT is often clinician-dependent with a variety of influencing factors that differ among centers and clinicians.

Optimizing Patient Selection for Endovascular Treatment in Acute Ischemic Stroke (SELECT) is a multicenter, observational, prospective study implementing a protocol to obtain imaging and clinical variables known to affect clinical outcomes after EVT. The goal of the study is to evaluate and compare the selection criteria currently utilized for EVT and identify the criteria that will provide the highest predictive ability in selecting patients with anterior circulation LVO. The study enrolled 500 patients (250 for EVT and 250 for control) ≤ 8 h from LKN time and collected imaging and clinical data, and follow-up data at 90 days. Patients with CTA-proven LVO in the internal carotid artery (ICA) or M1/M2 middle cerebral artery (MCA) location, NIHSS ≥ 6 points, and mRS score 0–1 were included. Primary outcome measure comprised of functional outcome at 90 days, while secondary outcome measures included rate of reperfusion and safety at 90 days as measured by the incidence of hemorrhage, mortality, hematoma, infection, or vascular injury. The study started recruiting participants in 2016 and was completed in May 2018 [19].

Table 1 Landmark endovascular revascularization trials in acute ischemic stroke

	MR CLEAN [10]	ESCAPE [9]	SWIFT PRIME [6]	EXTEND-IA [7]	REVASCAT [8]	DAWN [14••]	DEFUSE-3 [15••]
Study type	PROBE	PROBE	PROBE	PROBE	PROBE	PROBE	PROBE
(*N* =)	502	316	196	70	206	206	182
Age	≥ 18	≥ 18	18–80	≥ 18	18–85	≥ 18	18–90
Treatment arm	IA UK/tPA/device + IV-tPA	Stent retriever + IV-tPA	Stent retriever + IV-tPA	Stent retriever + IV-tPA	Stent retriever + IV-tPA	Trevo retriever + IV-tPA	Trevo Retriever/Solitaire revascularization device/Penumbra thrombectomy system + IV-tPA
Control arm	IV-tPA	IV-tPA	IV-tPA	IV-tPA	IV-tPA	IV-tPA	IV-tPA
Premorbid condition	None	Barthel index ≥ 90	mRS 0–1	mRS 0–1	mRS 0–1	mRS 0–1	mRS 0–2
Median time from stroke onset to groin puncture (min)	260	200	224	210	269	60—randomization to puncture	28—randomization to puncture
Inclusion criteria							
NIHSS	≥ 2	> 5	8–29	None	≥ 6	≥ 10	≥ 6
Vessel occlusion	ICA, M1, M2, A1, or A2	MCA trunk and immediate branches and intracranial ICA	Intracranial ICA, M1, or both	ICA or MCA	Intracranial ICA or M1	Intracranial ICA and/or MCA-M1	ICA or M1; carotid occlusions can be cervical or intracranial, without or without tandem MCA lesion
Neuroimaging modalities and specific criteria	CT, MRI, CTA, MRA, DSA No specific criteria	NCCT, mCTA Small infarct core (ASPECTS 6–10); good-to-moderate collateral flow	NCCT, CTA, MRA, MR DWI, CTP, MRP Small infarct core (ASPECTS > 5)	NCCT, CTA, CTP Evidence of salvageable tissue and ischemic core < 70 ml on CTP	NCCT, MR DWI Absence of large ischemic core; ASPECTS > 7 on NCCT or > 6 on MRI DWI	NCCT, MRI, MRA, CTA, MR DWI, CTP < 1/3 MCA territory involved Clinical imaging mismatch: Group A—age ≥ 80, NIHSS ≥ 10, infarct volume < 21 ml Group B—age < 80, NIHSS ≥ 10, infarct volume < 31 ml Group C—age < 80, NIHSS ≥ 20, infarct volume 31–51 ml	CTA, MRA, CTP, MRP, MR DWI Target mismatch profile: initial infarct volume (ischemic core) < 70 ml, a ratio of volume of ischemic tissue to initial infarct volume of ≥ 1.8, and absolute volume of potential reversible ischemia (penumbra) ≥ 15 ml
Outcome (EVT vs control)							
TICI 2b/3 (%)	58.7	72.4	88	86	65.7	84—Modified TICI ≥ 2b 72.6—original TICI ≥ 2b 10.4—TICI 3	13—TICI 2a 57—TICI 2b 19—TICI 3

Table 1 (continued)

	MR CLEAN [10]	ESCAPE [9]	SWIFT PRIME [6]	EXTEND-IA [7]	REVASCAT [8]	DAWN [14••]	DEFUSE-3 [15••]
mRS 0–2 at 90 days (%)	32.6 vs 19.1 ($P < 0.05$)	53 vs 29.3 ($P < 0.001$)	60 vs 35 ($P < 0.001$)	71 vs 40 ($P = 0.01$)	44 vs 28 (OR 2.1)	49 vs 13 (PPS > 0.999); utility-weighted mRS mean score—5.5 vs 3.4 (PPS > 0.999); NNT—2 and 2.8 for lower disability and functional independence, respectively	45 vs 17 (OR 2.67; $P < 0.001$)
Symptomatic ICH (%)	7.7 vs 6.4	3.6 vs 2.7	0 vs 3	11 vs 15	1.9 vs 1.9	6 vs 3	7 vs 4
Mortality (%)	18.9 vs 18.4	10.4 vs 19	9 vs 12	9 vs 20	19 vs 16	19 vs 18	14 vs 26

ASPECTS Alberta Stroke Program Early Computed Tomography Score, *CT* computed tomography, *CTA* computed tomography angiography, *CTP* computed tomography perfusion, *DWI* diffusion-weighted imaging, *IA* intra-arterial, *ICA* internal carotid artery, *IV-tPA* intravenous recombinant tissue-plasminogen activator, *M1* first segment of middle cerebral artery, *M2* second segment of middle cerebral artery, *mCTA* multiphasic computed tomography angiography, *MRA* magnetic resonance angiography, *MRP* magnetic resonance perfusion, *mRS* modified Rankin Scale, *NCCT* non-contrast computed tomography, *NIHSS* National Institute of Health Stroke Scale, *NNT* number-needed-to-treat, *PPS* posterior probability of superiority, *TICI* thrombolysis in cerebral infarction

Neurovascular Imaging for EVT

Rapid neurovascular imaging is pivotal in identifying eligible patients for EVT. Recent advancements in neuroimaging have allowed for improved assessment of risks/benefits of EVT and appropriate triage of patients based on specific clinical and radiological features.

NCCT is the first-line and most cost-effective imaging tool used in the setting of an acute stroke [20]. NCCT is critical to help guide the decision for IV-tPA after excluding intracranial hemorrhage. In patients with early AIS, NCCT may appear normal or can show subtle findings such as hypodensity due to cytotoxic edema, loss of gray-white differentiation, cortical swelling, hyperdense MCA sign, or effacement of sulci. When NCCT is performed < 6 h after stroke onset, the prevalence of early CT findings is 61% and the sensitivity of NCCT continues to increase 24 h after AIS [21]. Early evidence of infarction on CT suggests a worse prognosis and is associated with poor functional outcome [21]. Patients unlikely to recover after thrombolytic therapy may be identified using ASPECTS on NCCT, which is a standardized method for quantifying topographically early ischemic changes in the anterior circulation [22]. ASPECTS is calculated using 2 standard axial CT cuts—one at the level of the thalamus and basal ganglia and the other just rostral to the basal ganglia—and by dividing the MCA territory into 10 regions (Table 2) with 1 point subtracted from 10 for ischemic changes noted in each region. A normal NCCT has an ASPECTS of 10, while a patient with diffuse ischemic changes across the MCA territory has a score of 0. In a study of 156 patients with anterior circulation ischemia treated with IV-tPA, an ASPECTS of ≤ 7 was associated with functional dependence and death at 3 months. The sensitivity and specificity of ASPECTS in predicting functional outcome were 78% and 96% for AIS and 90% and 61% for symptomatic ICH [22]. Nonetheless, ASPECTS is not applicable to lacunar strokes or strokes outside the MCA territory, such as strokes of the brainstem or cerebellum.

Table 2 ASPECTS score

	Axial CT cuts	Regions
Ganglionic ASPECTS	At the level of the caudate head or below	M1–M3, insula, caudate nucleus, lentiform nuclei, internal capsule
Supraganglionic ASPECTS	Above the level of the caudate head, including the body and tail of the caudate nucleus	M4–M6

ASPECTS Alberta Stroke Program Early Computed Tomography Score, *CT* computed tomography

Advanced Neurovascular Imaging

MR diffusion-weighted imaging (DWI), non-invasive angiogram (CTA/MRA), and perfusion imaging represent advanced imaging tools for triage of AIS once NCCT excludes hemorrhage or large established infarct. MRI can identify stroke subgroup patients that may benefit from EVT [23], and various MRI sequences are combined (DWI, apparent diffusion coefficient [ADC], fluid-attenuated inversion recovery [FLAIR], and gradient echo [GRE]) to provide details on infarct size and chronicity (acute, subacute, chronic) [24]. Patient limiting factors regarding the utility of MRI include the following: reduced availability afterhours, extensive time required for imaging, presence of implanted metallic objects (e.g., pacemaker), need for sedation in anxious patients, risk of gadolinium-induced nephrogenic systemic fibrosis in patients with end-stage renal disease. MRI limiting factors include table weight capacity and bore diameter capacity. Transfer to another facility with an open MRI would not be feasible due to time constraints. However, in centers where MRI is readily available, protocols utilizing T1 and T2 sequences with DWI, perfusion-weighted imaging (PWI), and GRE are reliable in diagnosing both acute ischemic and hemorrhagic strokes emergently and obviate the need for emergent CT [25]. In one study, the MRI protocol utilized solely during EVT triage had a total imaging time of 5 min and 10 s and included DWI, GRE, MRA time-of-flight, and MRP sequences [26]. DWI offers greater sensitivity (91–100%) and specificity (86–100%) in estimating the volume of infarcted tissue < 6 h from symptom onset [27] and can detect ischemia within 3 to 30 min of symptom onset [28–30]. In the setting of subacute ischemic stroke, DWI changed the management in 14% of cases by clarifying the diagnosis and localizing the vascular territory [31]. The presence of multiple DWI lesions on baseline imaging is associated with an increased risk of early recurrence [32–34], while multiple DWI lesions of variable ages are an independent predictor of future ischemic events [35].

CTA and MRA are non-invasive advanced imaging modalities that provide information about blood vessels in three dimensions and can identify the site of vascular occlusion, proximal access, and degree of collateral circulation. The American Society of Intervention and Therapeutic Neuroradiology/Society of Interventional Radiology (ASITN/SIR) grading scale is widely used to assess collateral circulation [36]. While CTA requires the use of IV contrast and exposure to radiation, MRA time-of-flight technology can be used to visualize blood flow within the vasculature without IV contrast. CTA can be completed in seconds, while MRA may take several minutes. In patients with chronic kidney disease, pregnancy, or allergy to IV contrast, CTA is generally avoided and time of flight MRA is preferred. When performed within 24 h, DWI with MRA improves early diagnostic accuracy of ischemic stroke subtypes [37]. Limitations of MRA are similar to those mentioned earlier with MRI. In the setting of intracranial LVO, the sensitivity and specificity for CTA range from 92 to 100% and 82 to 100% and from 86 to 97% and 62 to 91% for contrast-enhanced MRA, respectively [38]. Conventional digital subtraction angiography (DSA) remains the gold standard to assess collateral circulation given the small caliber of these vessels. However, its routine use for diagnostic purposes is limited by its invasive nature and long procedural times [39].

CTP and MRP provide an excellent estimation of salvageable tissue and can recognize the presence and location of LVO with correlating angiographic imaging studies. In one study, MRP and DWI alone were found to have a sensitivity of 96% and specificity of 98% for accurate EVT triage where DWI identified the presence of small core infarction and MRP delineated salvageable tissue and identified the presence and location of LVO [26]. Multimodal CT utilizes 3 techniques, including NCCT, CTA, and CTP, and when combined, it improves detection of acute infarction and decreases door to EVT time [40–43]. Perfusion imaging utilizes IV contrast boluses and times its passage through the brain to obtain a whole brain blood perfusion map [44]. It quantifies the amount of contrast agent reaching the brain tissue after a fast IV bolus. Integrating the amount of contrast entering the brain during the first pass followed by the time course of arrival into the tissue and subsequent washout allows construction of cerebral blood volume (CBV), relative cerebral blood flow (rCBF), and mean transit time (MTT) maps. The average transit time for blood through a specific region of the brain is the MTT and depends on the time required for the contrast to travel from the arterial inflow to the venous outflow, while the time to maximum (Tmax) is the time to peak and reflects a delay in the arrival of the contrast bolus to ischemic tissue [24]. Alternatively, arterial spin labeling is a non-ionizing MRI technique for measuring tissue perfusion by magnetically labeling arterial water protons as an endogenous tracer and identifies perfusion defects and diffusion-perfusion mismatches [45].

The utility of perfusion imaging has been advocated by several practices for years. EXTEND IA and SWIFT PRIME utilized CTP per protocol and patients were noted to have better outcomes compared to other studies that utilized NCCT with ASPECTS and CTA, including REVASCAT and ESCAPE [6–9]. Similarly, the DAWN and DEFUSE-3 trials provided level 1 evidence for utilization of perfusion imaging in patient selection for EVT and demonstrated positive results [14••, 15••]. Similarly, patients who had a favorable perfusion profile compared to those that did not and underwent EVT had better outcomes in the CRISP study [46]. On the contrary, other studies reported no significant difference in clinical outcomes when CTP was utilized compared to NCCT [47, 48].

Brief Review of Current Techniques

EVT for managing AIS from LVO are evolving alongside the rapidly evolving technology. Most of the currently deployed techniques involve the use of either a third-generation stent retrieval device, a technique of direct aspiration, or a multimodal approach combining the two techniques such as "Solumbra." The most significant variations among the current techniques include sedation modality, device selection, decision to use a balloon guide catheter (BGC), and technical nuances in stent deployment and retrieval. A recent review from an anonymous survey of 80 Society of Neurointerventional Surgery members regarding EVT techniques reported that direct aspiration without a BGC was the favored technique (41.1%) followed by the Solumbra technique without a BGC (32.4%) and lastly the Solumbra with a BGC (11.8%) [49]. While some prefer using the initial technique for every patient, the selected technique needs to be based on the location and extent of the vascular occlusion with suspected clot characteristics, such as clot length and surmised composition. Such algorithms may include removing softer clots with a stent retriever without aspiration versus removing more fibrin-rich clots with Solumbra technique, but more studies are needed to elucidate which technique is best for each patient.

Sedation Modality

Three RCTs, the 128-patient General or Local Anesthesia in Intra-Arterial Therapy trial (GOLIATH), the 150-patient Sedation Versus Intubation for Endovascular Stroke Treatment trial (SIESTA), and the 90-patient Anesthesia During Stroke trial (AnStroke), have been published since 2017 comparing the outcomes of EVT with conscious sedation versus general endotracheal anesthesia (GETA) [50–52]. All 3 trials concluded that there was similar efficacy and safety margins. The GOLIATH trial reported no significant difference in procedural time, post-operative pneumonia, length of stay, or reperfusion rate in either group. The SIESTA trial reported increased rate of hypothermia (32.9% vs 9.1%; $P < 0.001$), delayed extubation (49.3% vs 6.5%; $P < 0.001$), and pneumonia (13.7% vs 3.9%; $P = 0.03$) in the GETA group. Both the SIESTA and the AnStroke trials reported no significant difference in overall mortality or neurological outcome in either group. There was a 14.3–15.6% conversion from conscious sedation to GETA with movement and severe agitation being the most common reasons for conversion to general anesthesia. A meta-analysis of these 3 trials and 19 observational studies reported no difference in procedural time, but a higher likelihood of death or respiratory complications in the GETA group [53]. In our practice, we attempt conscious sedation first and convert to general anesthesia in patients who are agitated and poorly cooperative and in patients who develop emesis to prevent aspiration. Larger studies are needed to provide recommendations on superiority of either anesthesia modality.

Stent Retrievers

Stent retrievers are cylindrical devices that consist of a self-expanding stent mounted on a wire and deployed within the thrombus through a catheter. They immediately push the clot against the arterial walls and re-establish blood flow to the brain in 80 to 90% of cases. The stent is typically deployed for a few minutes to engage the thrombus within its tines and the wire is pulled back to retrieve the thrombus. Since 2015, several large RCTs provided evidence that EVT with a third-generation device is superior to medical management. There are now several devices available with the Solitaire (ev3/Covidien, Irvine, CA) and Trevo (Stryker Neurovascular, Fremont, CA) being the most commonly used in recent trials including MR CLEAN, ESCAPE, REVASCAT, SWIFT PRIME, EXTEND-IA, DAWN, and DEFUSE-3. The EmboTrap II (Cerenovus, Irvine, CA) recently obtained FDA approval and appears in early reports to have equivalent safety and efficacy [54, 55]. There is insufficient data to determine superiority of any single device with several active clinical trials for newer devices.

Direct Aspiration

This thrombectomy technique utilizes a large bore distal access catheter with suction applied at the face of the clot. Compared to stent retrievers, using A Direct Aspiration First Pass Technique (ADAPT) may be as effective with comparable functional outcomes. A retrospective study reported significantly higher rate of good clinical outcome (mRS 0–2) at 90 days in anterior circulation LVO using the ADAPT technique versus stent retrieval (55.6% vs 30.9%; $P = 0.015$) [56]. Another retrospective analysis reported equivalent TICI 2b/3 reperfusion and 90-day mRS scores with a reduction in procedural time and material costs ($6000–$7000 per case) when using the ADAPT technique first [57]. In 2017, The Contact Aspiration Versus Stent Retriever for Successful Revascularization (ASTER) multicenter study found no significant difference in reperfusion rates (mTICI 2b/3 85.4% [$n = 164$] vs 83.1% [$n = 157$]; OR, 1.20; 95% CI 0.68–2.10; $P = 0.53$) with similar occurrence of adverse events (symptomatic ICH in 5.3% vs 6.5% and new AIS in a different vascular territory in 5.3% vs 8.5%) [58].

Combined Modality Techniques

Combined techniques are commonly used in modern clinical practice especially for patients with long segment occlusions and for intracranial ICA occlusions. The "switching strategy" is a modality in which a direct aspiration first pass is made followed by a stent retrieval to remove any residual thrombus. This modality was first reported in 2013 with improved recanalization and no significant difference in time, complications, or hemorrhage rates [59]. The most commonly used technique is Solumbra, which derives its name from the simultaneous use of the Solitaire stent retriever and the Penumbra aspiration system [60]. The technique is frequently described in the literature with many variations in practice using different stent retrieval devices and different guide catheters with or without a BGC.

The theoretical benefit of combining stent retrievers with catheter aspiration is that the stent can allow immediate restoration of flow through the occlusion after deployment and the continuous suction through an aspiration catheter will minimize distal emboli preventing new stroke in distal territories. The large bore aspiration catheter can also provide another tool for removal of additional clots. The flow typically stops within the catheter when a clot is engaged, and the catheter is pulled back proximally until restoration of good blood flow. The catheter is aspirated to wash out any potential debris and distal access can be re-established from it making subsequent thrombectomy attempts more efficient [61]. Although techniques for clot retrieval are rapidly evolving, there is a growing number of combined modality techniques using stent retrievers and aspiration with slight modifications to improve outcomes. Indeed, there are several variables with clots including size, consistency, and distributions with too few studies to determine superiority of any single technique. Three of the most recently published are as follows: Continuous aspiration prior to intracranial vascular embolectomy (CAPTIVE) [62], Aspiration-Retrieval Technique for Stroke (ARTS) [63], and Stent-Retriever Assisted Vacuum-locked Extraction (SAVE) [64, 65].

Stent Deployment Techniques

The classic deployment of a stent retriever involves a simple unsheathing of the stent by pulling back the microcatheter allowing the stent to passively expand within the thrombus. The Active Push Deployment (APD) and Push and Fluff Technique (PFT) have been described as possible improvements in classic stent deployment in which the stent is pushed out of the microcatheter, increasing radial expansion and possibly further increasing vessel wall apposition. The PFT technique was described using the Trevo device, which is completely radiopaque allowing the entire structure to be visualized during opening and reported higher rates of first-pass recanalization (54% vs 32.6%; $P < 0.01$) and lower number of passes. In vitro analysis showed PFT with improved wall apposition and up to 75% greater device diameter [66]. Similarly, the APD technique showed widening of the Trevo and Solitaire devices in a retrospective review of 130 patients treated with multiple devices with TICI 2b/3 reperfusion in 88% of patients and 65% with complete reperfusion [67].

The bare wire thrombectomy (BWT) technique describes complete retraction of the microcatheter before clot retrieval to increase aspiration catheter's effectiveness [68]. The SAVE technique describes a distally placed stent retriever with 2/3 of the stent distal to the clot combined with a proximal aspiration catheter, which are removed as a unit. Early reports for the SAVE technique have been very successful especially for terminal ICA clots. A retrospective study reported first-pass mTICI 3 reperfusion in 23/32 patients (72%) with a mean groin puncture to reperfusion time of 36.0 min ± 15.8 and mTICI 3 in 25/32 cases (78%) with a maximum of 3 attempts. Successful reperfusion (mTICI ≥ 2b) was achieved in all patients [64, 65, 69]. In our practice, we attempt to advance the suction catheter over the microcatheter for direct aspiration of the clot to reduce the required technical steps and to improve the time interval for revascularization. When this proves difficult with tortuous anatomy, we use a stent retriever as an anchor and by pulling on the microcatheter and straightening its course, advancement of the suction catheter against the clot is remarkably facilitated. We also attempt to retrieve the clots locally by pulling the stent retriever in the suction catheter and avoid pulling them against the blood flow. Additional clots are retrieved with the suction catheter still against the clot and the catheter is retrieved slowly under aspiration until restoration of flow. This is followed by aspiration of the catheter until the catheter is free of clots and decision to obtain another pass is based on contrast injection while the suction catheter is maintained close to the occlusion site.

Balloon Guide Catheters

BGCs can also be used to obtain flow arrest or flow reversal during device retrieval to decrease the chances of thrombus fragmentation and distal migration. Although some studies showed decreased procedure times and increased revascularization rates with first pass, the use of BGC increases the steps for its preparation and deployment and requires a large access (an 8fr sheath) [70]. The Proximal Balloon Occlusion Together with Direct Thrombus Aspiration during Stent Retriever Thrombectomy (PROTECT) technique describes proximal balloon occlusion with flow arrest combined with multimodal thrombus aspiration and stent retrieval thrombectomy. Compared to direct aspiration, the PROTECT technique resulted in shorter procedure times (29 vs 40 min; $P = 0.002$) and higher rate of TICI 3 reperfusion (70% vs 39%) [71]. In our practice, we use BGC in cases with proximal ICA occlusions especially when the occlusion extends over a long segment as these cases have a large clot burden and a high risk of distal embolization.

Future Considerations for Stroke Care

Posterior Circulation

The role of EVT for revascularization of the posterior circulation remains largely unknown. Small series such as the Tama-Registry of Acute Thrombectomy (TREAT) study [72] retrospectively studied 48 patients with acute basilar artery occlusion who underwent EVT with stent retrievers and aspiration devices with successful reperfusion in 98% of patients. More than 41% achieved good outcome (mRS 0–2) while 54.2% achieved moderate outcome (mRS 0–3). Major obstacles continue to face clinicians for establishing EVT selection criteria for posterior circulation. This is related to complex anatomy of the brainstem and higher prevalence of anatomical variation in the posterior circulation compared to the anterior circulation [73]. Moreover, CT and CTP studies have reduced sensitivity in detection of posterior fossa infarcts and posterior circulation ischemic changes particularly in the midbrain, and initial stroke symptoms referable to the posterior circulation may not trigger emergent EVT consideration because of low scoring NIHSS [74]. Therefore, the role of EVT for posterior circulation ischemia still needs to be established.

Distal Occlusions

The challenges of EVT in patients with distal occlusions are multifold. Conventional imaging has limitations in detecting distal vessel occlusions and incorporation of multiphase CTA and advanced perfusion reconstructions can increase the sensitivity and specificity for identification of distal vessel occlusion [75, 76]. Other challenges are related to the heterogeneity of clinical symptoms, disabling versus non-disabling and low versus high eloquence [77–79]. Other challenges are related to the limitations of endovascular devices since suction catheters and stent retrievers may not be used safely and effectively in distal occlusions beyond the M2 segment [77–79]. Currently, there is a promising and growing body of evidence that mechanical thrombectomy is safe and more efficacious than standard of care in M2 occlusions [77–79]. The role of IA-tPA, microwire manipulation of the clots within small vessels, and small suction catheters still needs to be determined.

Tandem Occlusions

Tandem occlusions consist of proximal carotid artery occlusions along with concomitant distal intracranial artery occlusion. These cases are particularly challenging given the amount of clot burden and the variability of the underlying pathology that could be related to carotid dissection, carotid stenosis, or to cardiogenic source with a large thrombus that occludes the ICA. In general, presenting symptoms are related to the distal occlusion within the intracranial circulation and patients present with high NIHSS scores especially with occlusion of the ICA terminus. This is related to reduced anterograde flow in the ACA, which limits the leptomeningeal collateralization to the MCA distal territory and involvement of the proximal M1 with corresponding territory of deep ganglia [80]. Both anterograde (proximal to distal revascularization with treatment of the proximal occlusion before distal revascularization) and retrograde (distal to proximal revascularization with treatment of the distal occlusion prior to the proximal occlusion) methods have been reported for the treatment of tandem occlusions with no unanimity on the optimal strategy to approach these cases [81, 82]. A multimodal approach with use of IV-tPA followed by extracranial ICA angioplasty and intracranial mechanical thrombectomy has been suggested in selected patients [80]. However, AIS related to tandem occlusions pose a significant challenge as they generally have decreased chances of reperfusion due to heavy clot burden and hemodynamic instability resulting in suboptimal drug delivery [83–85]. When the terminus is not occluded, we favor revascularization of the distal occlusion first as it allows to restore the flow in MCA from contralateral supply via retrograde flow from ACA and we tend to utilize a proximal balloon protection to reduce the risk of additional or recurrent distal embolization.

Complications

Data reports a broad range of procedure-related complications from 4 to 31% [6–10, 86–92]. These complications include groin hematoma (RCT 3.6% vs non-RCT 1.4%), spontaneous ICH (RCT 4.0–4.3% vs non-RCT 5.3%), subarachnoid hemorrhage (RCT 2.5% vs non-RCT 2%), intraventricular hemorrhage (RCT 1%), device failure including stent detachment or displacement (non-RCT 1.2%), arterial perforation (RCT 1.3% vs non-RCT 2%), arterial dissection (RCT 2% vs non-RCT 3%), vasospasm (RCT 10% vs non-RCT 4%), carotid-cavernous fistula (non-RCT 2.4%), distal arterial embolization (RCT 6% vs non-RCT 4.5%), early mortality ≤ 7 days (RCT 9% vs non-RCT 9%), and late mortality ≤ 90 days (RCT 15% vs non-RCT 18%) [6–10, 86–89, 93–99]. In addition to the abovementioned complications, there exists the risk of radiation-induced cancer in about 1 in 3000 patients age > 60, owing to the combined radiation from CT, CTA, and endovascular management [100].

Conclusion

Acute stroke management has evolved considerably over the years from IV thrombolysis to include EVT with a variety of techniques. EVT is currently considered standard of care in selected patients with LVO within the anterior circulation. The window of treatment has been extended to patients presenting within 24 h from LKN time. The Randomized Controlled Trial to Optimize Patient's Selection for Endovascular Treatment in Acute Ischemic Stroke (SELECT 2) will further evaluate the safety and efficacy of EVT with stent retrievers (Trevo, Solitaire, EmboTrap) in patients treated within 24 h from LKN time who present with a large core infarct and ASPECTS 3–10, rCBF < 40% (0–100 cc), mismatch volume ≥ 15 cc, and mismatch ratio ≥ 1.8 [101]. The specific imaging criteria and EVT techniques continue to evolve with the advent of new devices using suction catheters and stent retrievers individually or combined to achieve revascularization efficiently and to improve patient outcomes. Despite these developments, disability from stroke remains high and further development is needed in stroke management including optimal imaging modality and revascularization of posterior circulation and distal branches for eloquent brain.

Compliance with Ethical Standards

Conflict of Interest Tasneem F. Hasan, Nathaniel Todnem, Neethu Gopal, David A. Miller, Sukhwinder S. Sandhu, Josephine F. Huang, and Rabih G. Tawk declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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