Acute Ischemic Stroke: Acute Management and Selection for Endovascular Therapy

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Abstract

Stroke is a medical emergency and expeditious treatment is critical to reducing permanent disability or death. Acute management of patients suffering from acute ischemic stroke (AIS) requires early recognition of symptoms, rapid assessment and stabilization (hyperacute workup), and appropriate selection of patients for reperfusion with intravenous alteplase and/or mechanical thrombectomy. Established stroke protocols which involve both prehospital emergency medical services and in-hospital multidisciplinary stroke teams have been shown to be crucial to reducing the long term, devastating effects of stroke.

Keywords
- stroke
- acute management
- intravenous alteplase
- mechanical thrombectomy
- interventional radiology

Despite recent advances in stroke prevention and acute stroke treatment, stroke remains the fifth most common cause of death in the United States as well as the number one cause of long-term disability. Although the incidence of stroke has decreased over the past decade, the absolute number has increased with a rising mean age within this population. Approximately 85% of strokes are caused by an ischemic event.[1–3] Neuronal death occurs within minutes of oxygen deprivation, resulting in an irreversible "core" infarction. The nonfunctioning tissue surrounding the core infarct, termed the ischemic "penumbra," retains just enough blood flow to avoid cell death. This collateral blood flow is the result of a complex network of vascular anastomoses within the brain, including large artery-to-artery connections in the circle of Willis to smaller artery-to-artery pial connections as well as external-to-internal carotid anastomoses. The conversion of penumbra to core infarct is time and collateral dependent and thus requires rapid diagnosis and therapy. Several recent clinical trials have demonstrated overwhelming evidence that rapid reperfusion achieved with endovascular treatment leads to improved outcomes.[4–13]

Acute medical and endovascular treatments have advanced significantly in the past two decades with strides made in triage models, imaging diagnosis, and the availability of new thrombectomy devices. A multidisciplinary team, optimized workflow, rapid diagnosis, and effective treatment options culminate in judicious early therapy that is aimed to minimize infarct size and permanent disability.[14,15]

Acute management of this life-threatening disease can be broken down into two primary phases: hyperacute workup and acute therapy, with a goal centered on earliest possible treatment. Hyperacute workup refers to the process that occurs immediately after a stroke is recognized, and acute therapy refers to therapeutic interventions that restore blood flow to the ischemic cerebral territory.

Hyperacute Workup

Emergency Services Activation

To provide rapid and effective management for an acute ischemic stroke (AIS), a comprehensive system of care is necessary, beginning from community education of stroke recognition to all facets of pre- and in-hospital management.[16] Emergency medical service (EMS) used by stroke patients is associated with earlier evaluation and therapy by stroke specialists.[17] EMS prioritization to an appropriate designated stroke center is needed to ensure rapid and appropriate care: patients suspected of having AIS should be transported to the

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nearest facility with the capability of administering intravenous (IV) alteplase and/or performing endovascular stroke treatment (i.e., primary stroke centers and thrombectomy capable/comprehensive stroke centers).[4]

The EMS responder should begin initial stroke assessment in the field to allow for early diagnosis if stroke is suspected. Validated and standardized stroke screening tools include the FAST (Face, Arms, Speech Test), Los Angeles Prehospital Stroke Screen (LAPSS), Los Angeles Motor Scale (LAMS), Rapid Arterial Occlusion Evaluation (RACE), EMS Vision Aphasia Neglect (VAN) score, Field Assessment Stroke Assessment for Emergency Destination (FAST-ED), Ambulance Clinical Triage for Acute Stroke Treatment (ACT-FAST), and Cincinnati Prehospital Stroke Scale (CPSS). A prehospital notification allows for mobilization of hospital resources and personnel prior to patient arrival, streamlining workflow when the patient arrives.[4,18]

In addition to early recognition and transfer to the nearest appropriate stroke center, EMS responders must ensure stability of the patient, beginning with evaluation of airway, breathing, and circulation (ABCs). Patients with diminished consciousness are at risk for aspiration and hypoventilation and may require intubation for airway protection and to maintain oxygenation. Oxygen therapy should be administered to maintain blood oxygen saturation of $\geq$ 94%.[4]

Analogous setups for comprehensive systems of care and prehospital notification with rapid assessment in the field are seen in ST-elevation myocardial infarction (STEMI) and trauma services, but in the case of AIS, time can be in fact more critical and the workup is usually more complicated, and thus resource intensive.

Initial Hospital Assessment (Emergency Room)

An organized and established protocol for the evaluation of a stroke patient is needed for the assessment of patients arriving to the emergency room. A designated, multidisciplinary stroke team, including an emergency physician, neurologist, neurointerventionalist, radiologist, radiology techs, nurses, pharmacy, laboratory personnel, and transport, allows rapid evaluation and triage of patients for acute therapy.[19,20]

As patients may clinically deteriorate during transition from the field to the emergency room, assessment could begin with stabilizing the patient (ABCs). Due to autoregulatory function that maintains brain perfusion via collaterals, most patients suffering from AIS are hypertensive when presenting to the emergency room. However, to avoid hemorrhage or other complications from acute therapies, systemic and diastolic blood pressure should be maintained at <185/110 mm Hg, usually with the use of IV nicardipine and/or labetalol. Any concurrent fever (temperature > 100.4°F or 38°C) should also be identified and controlled.[4]

Once stabilized, a focused history should include the time the patient was last known well to establish the time of ischemic stroke onset. The time from stroke onset to presentation is a major determinant of eligibility of acute therapies. Since the patient is often unable to provide a reliable time of symptom onset, information from family, caretakers, or paramedics at the scene is extremely useful for determining if the patient is within a treatment window. When patients are found in the morning with stroke symptoms (i.e., "wake up stroke"), the last known well is defined as the time at which a family member or caretaker can confirm the patient was at his baseline neurological status.

Patients presenting with stroke symptoms often suffer from other serious medical conditions. A focused history is critical to identify any disease processes which are contributing to their acute deterioration and to rule out any stroke mimics (i.e., hypoglycemia, drug intoxication, and seizure). Oxygen saturation and finger stick glucose level are required prior to initiation of any acute therapy. Additional laboratory studies can be obtained; however, their results should not delay urgent imaging or therapy, which may include electrocardiogram, complete blood count, troponin, coagulation panel, basic metabolic panel, and pregnancy. If respiratory failure is suspected, an arterial blood gas and chest radiograph can also be obtained.[4]

As of October 2014, AHA target stroke best practice strategies implement protocols for EMS to transport AIS patients directly to imaging, with the aforementioned workup performed by EMS on the way to the hospital as well as by the emergency room physician while on the EMS gurney on the way to the computed tomography (CT) scanner (direct to CT scanner, or DCCT protocol). These best practices are associated with significant improvements from door to reperfusion therapies.[21–24]

Stroke Scales and Neuroimaging

At this point, the key to understanding further hyperacute workup is a ready knowledge of standardized scales, terminology, and neuroimaging that is widely used in stroke therapy.

The National Institute of Health Stroke Score (NIHSS) is a standardized scale that can quantify the degree of neurological impairment (►**Table 1**). The NIHSS can be reliably used by all healthcare providers and is obtained during a focused physical exam at this stage of the workup. The NIHSS consists of 11 tests with scores ranging from 0 to 42. Stroke severity is described as mild, moderate, and severe for NIHSS scores of <5, 5 to 9, and $\geq$10, respectively. Frequent reassessment with the NIHSS is useful to monitor for clinical deterioration or improvement. Some ischemic vascular territory syndromes are not well reflected in the NIHSS, particularly posterior circulation strokes.[4,25,26]

The modified Rankin scale (mRS) is a tool used to measure the degree of disability related to performing daily activities in patients with a prior stroke or neurological disability (►**Table 2**). Assessment of the baseline mRS in a patient prior to acute stroke presentation should be considered prior to intervention. In general, patients with a baseline mRS greater than 2 are less likely to achieve a significant improvement in functional status following acute intervention.[27]

Neuroimaging plays a pivotal role in determining the best treatment pathway for patients suffering from AIS by ruling out hemorrhage and stroke mimics, identifying the location of embolus, and determining the presence of ischemic core versus penumbra. All patients with suspected acute stroke should have a noncontrast CT (NCCT) of the head, which is

Table 1 National Institutes of Health Stroke Scale (NIHSS)

	Tested Item	Score—Response
1A	Level of consciousness	0—Alert 1—Drowsy 2—Obtunded 3—Coma or unresponsive
1B	Orientation questions (2)	0—Answers both correctly 1—Answers one correctly 2—Answers neither correctly
1C	Response to commands (2)	0—Performs both tasks correctly 1—Performs one correctly 2—Performs neither correctly
2	Gaze	0—Normal horizontal movements 1—Partial gaze palsy 2—Complete gaze palsy
3	Visual fields	0—No visual field defect 1—Partial hemianopia 2—Complete hemianopia 3—Bilateral hemianopia
4	Facial movement	0—Normal 1—Minor facial weakness 2—Partial facial weakness 3—Complete unilateral palsy
5	Motor function (arm) a. Left b. Right	0—No drift 1—Drift before 10 s 2—Falls before 10 s 3—No effort against gravity 4—No movement
6	Motor function (leg) a. Left b. Right	0—No drift 1—Drift before 10 s 2—Falls before 10 s 3—No effort against gravity 4—No movement
7	Limb ataxia	0—No ataxia 1—Ataxia in one limb 2—Ataxia in both limbs
8	Sensory	0—No sensory loss 1—Mild sensory loss 2—Severe sensory loss
9	Language	0—Normal 1—Mild aphasia 2—Severe aphasia 3—Mute/global aphasia
10	Articulation	0—Normal 1—Mild dysarthria 2—Severe dysarthria
11	Extinction/ Inattention	0—Absent 1—Mild loss (1 sensory modality lost) 2—Severe loss (2 modalities lost)

Notes: Score 0 = no stroke, score 1–4 = minor stroke, score 5–15 = moderate stroke, score 15–20 = moderate to severe stroke, score 21–42 = severe stroke.

Table 2 Modified Rankin's Scale (mRS)

Score	Description
0	No symptoms
1	No significant disability: able to perform activities despite noticeable neurological deficits. Independent living
2	Slight disability: unable to perform most previous activities, but capable of functioning independently
3	Moderate disability: no longer able to live independently, but capable of walking with no assistance
4	Moderately severe disability: unable to attend to own bodily needs without assistance, incapable of walking without assistance
5	Severe disability: requires constant nursing care and attention, bedridden, incontinent
6	Death

Note: The mRS measures functional independence on a seven-grade scale (0–6).

essential for excluding the presence of hemorrhage. In addition to blood evaluation, NCCT is useful for checking the presence of other findings in the setting of acute infarction, such as a hyperdense vessel sign, which indicates the presence of a thrombus within an artery or extensive cytotoxic edema from early infarction. A NCCT of the head is obtained as soon as possible in the patient's hyperacute workup phase, ideally within 20 minutes after arriving to the emergency room.[4]

The Alberta Stroke Program Early CT Score (ASPECTS) is a quantitative tool used for assessing middle cerebral artery (MCA) territory ischemic changes from an NCCT. The ASPECTS system includes 10 regions of interest in the MCA territory, spanning from the basal ganglia to the cortex (►**Fig. 1**). The score is determined by subtracting one point for each area of ischemic change, as seen by loss of gray-white matter differentiation or hypoattenuation. Of note, this assessment tool does not apply to strokes outside of the MCA territory, such as the posterior circulation.[28] Instead, newer scales, such as the posterior circulation ASPECTS (pc-ASPECTS), utilize analogous regions of interests within the posterior circulation, including the thalamus, cerebellum, posterior cerebellar artery, and pons, to quantify ischemia in basilar artery occlusions. Although this scale was originally developed utilizing CT, magnetic resonance imaging (MRI) with diffusion-weighted imaging (DWI) can also be used, especially with greater accuracy in identifying posterior lesions.[29,30]

Following NCCT, several additional noninvasive imaging studies are available which help guide the decision for intervention. CT angiography (CTA) of the head allows for detection of intracranial large vessel occlusion (LVO) or stenosis with excellent sensitivity and specificity. CTA of the neck, performed in conjunctional with CTA of the head, is useful for evaluating the aortic arch anatomy and extracranial stenosis or occlusion. CTA has become a standard test for patients with suspected LVO not only to identify location of thrombus but also to evaluate the thoracic and cervical vascular anatomy for preintervention planning.

CT perfusion (CTP) is another valuable tool that guides the decision to perform thrombectomy. CTP is performed by monitoring the first pass of a contrast bolus throughout the cerebral circulation. Flow rates of up to 8 mL/s are preferred, and thus large IV bore access is necessary. By measuring the time it takes for the contrast to increase attenuation within the

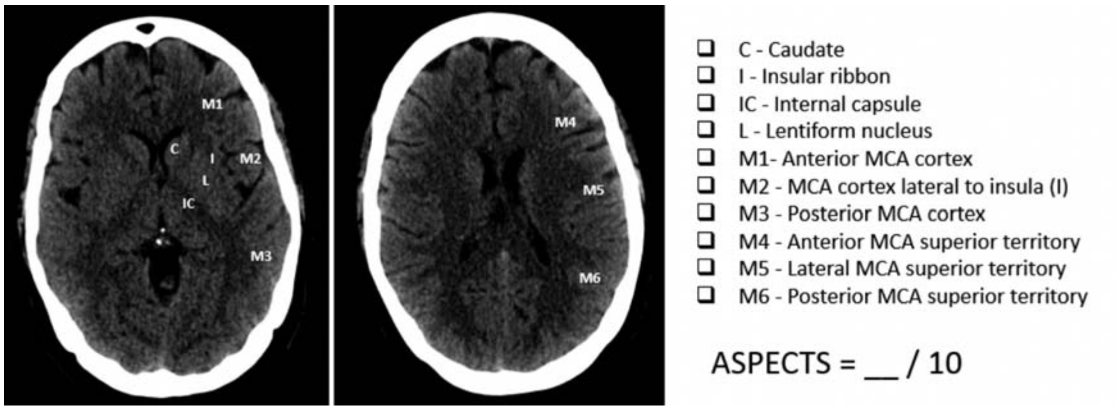

Fig. 1 Alberta Stroke Program Early CT Score (ASPECTS). A simple and reliable 10-point scale to quantify ischemic changes in the middle cerebral artery (MCA) territory. Ischemic changes (loss of gray-white matter differentiation or hypoattenuation) in each of the areas listed earlier (each a single point) is subtracted from a total of 10 to give a final score. A score of 10 signifies no ischemic changes seen on noncontrast head CT.

intracranial arteries and veins over a series of scans, perfusion analysis software generates a map of brain cerebral blood flow (CBF), cerebral blood volume (CBV), mean transit time (MTT), time to peak opacification (TTP), and time to maximum of residue function (Tmax).[31–34] Perfusion imaging is performed after NCCT to avoid contrast contamination and, with the advent of 320 multi-slice detector CT scanners, whole brain perfusion imaging can now be achieved in 1 minute or less.[35] In general, these maps can be used to make an estimate of the size of a core infarction and ischemic penumbra. Regions of severely reduced CBV or CBF correspond to core infarction, whereas regions with prolongation MTT or Tmax with preserved CBV correlate to penumbra in patients with AIS (►**Fig. 2**). The automated volumetric software for estimated core and penumbra, such as RAPID (iSchemaView), Viz.ai, and Brainomix, currently utilize empirical cutoff values of CBF $<$ 30% as core and Tmax $>$ 6 seconds as penumbra, but protocols may vary by instutition.[11] Additional comprehensive review of perfusion imaging is outside the scope of this article.

MRI is also an excellent tool for the diagnosis of acute hemorrhagic and ischemic stroke. In fact, MRI DWI has superior sensitivity compared with NCCT for the detection of stroke and is the accepted standard for defining acute infarction. Magnetic resonance angiography (MRA) provides excellent detection of intracranial large vessel stenosis and occlusion, and magnetic resonance perfusion (MRP) imaging is also available, providing intracranial vascularity maps analogous to its CT counterpart. There are several barriers to widespread use of MRI to triage stroke patients, most commonly limited availability, longer image acquisition time, higher cost, lack of safety screening, and patient intolerance or contraindication.[36,37] By overcoming these barriers, several institutions use MRI as their primary neuroimaging selection tool in AIS, which can be particularly useful in patients presenting late or with an unknown time of onset.[10,38–41]

Acute Therapy

Intravenous Alteplase

The goal of acute therapy for ischemic stroke is to restore blood flow to the brain that is not already infarcted. Early treatment and reperfusion are key factors to improve outcomes in stroke.

Once hemorrhagic stroke is excluded by initial head NCCT, the first-line therapy for reperfusion is IV alteplase (recombinant tissue plasminogen activator or tPA; Genentech, South San Francisco, CA). Alteplase binds to fibrin in a thrombus and initiates fibrinolysis by converting plasminogen to plasmin, which, in turn, dissolves fibrin. The effectiveness of IV alteplase for ischemic stroke is time dependent, and thus, it is critical that it is administered as early in the treatment process as possible. According to current guidelines, patients presenting 3 to 4.5 hours or less from the time of onset of stroke symptoms are candidates for this therapy.[4,42–45] Recent trials such as MR WITNESS and WAKE-UP have studied extending the window further with imaging triage utilizing MRI.[46,47]

In addition to being within the specified timeframe, patients must be 18 years or older and not meet a long list of exclusion criteria (►**Table 3**). Note that there are a few special considerations for patients presenting between 3 and 4.5 hours, based on the ECASS-3 trial.[44] These criteria are rapidly screened in the field as well as in the emergency room, and the decision to administer IV tPA occurs immediately after obtaining the NCCT, once intracranial hemorrhage and mimics have been ruled out. The guidelines of acute stroke management call for treatment as early as possible ("time is brain"). Therefore, despite the list of exclusion criteria mentioned in ►**Table 3**, there are relative exceptions for common workup "bottlenecks." For example, in a patient whose hematologic laboratory values are not yet available by the time the NCCT is obtained (i.e., complete blood cell count or international normalized ratio), IV alteplase can still be administered if there is no suspected history of a bleeding diathesis or anticoagulation use. The only laboratory value required is glucose, to exclude an easily reversible stroke mimic, which should be maintained above 60 mg/dL. Per current guidelines, the goal of initiating IV alteplase is within 60 minutes of arriving to the emergency room (door to needle, DTN), but frequently, DTN in established workflows is far less.[4]

Alteplase requires a dedicated IV line, and the dose is calculated by the patient's body weight (0.9 mg/kg), with a maximum dose of 90 mg. A total of 10% of the dose is given as a bolus over 1 minute and the remainder is infused over

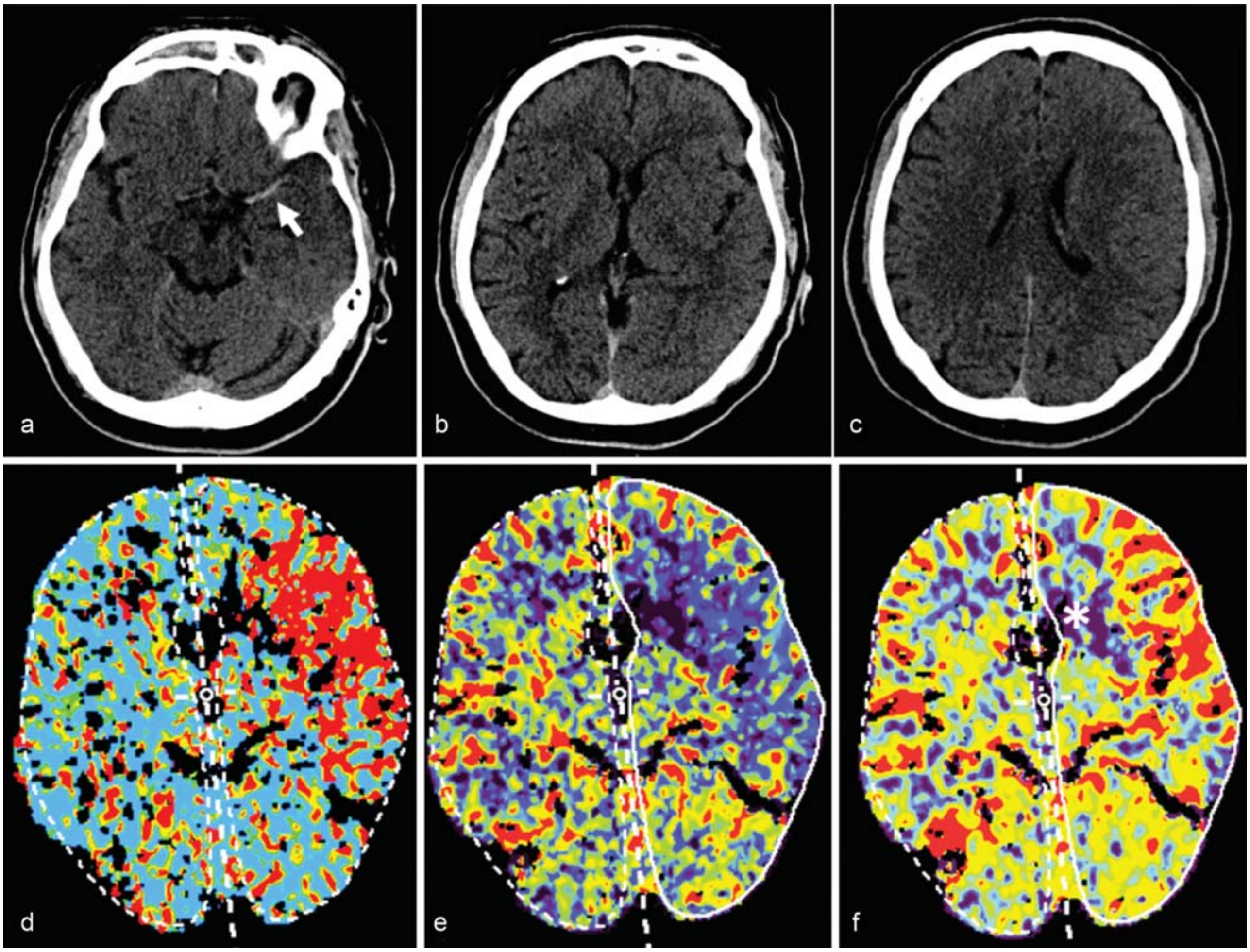

Fig. 2 ASPECTS and CT perfusion imaging. A 57-year-old male presented with acute right hemiplegia and aphasia, NIHSS 24, with a last known well of 4 hours prior to arrival. A noncontrast CT of the head was obtained (a–c), which demonstrates a hyperdense left MCA vessel sign (white arrow), no intracranial hemorrhage, and no ischemic changes in the MCA territory, ASPECTS = 10. CTA (not shown) and CTP imaging were obtained, demonstrating (d) increased MTT, (e) decreased CBF, and (f) maintained CBV, with the exception of the lentiform nucleus and caudate head (*), corresponding to a small core infarct within a large area of MCA territory ischemic penumbra. ASPECTS, Alberta Stroke Program Early CT Score; NIHSS, National Institute of Health Stroke Scale; CTA, computed tomographic angiography; MCA, middle cerebral artery; CTP, computed tomography perfusion; MTT, mean transit time; CBF, cerebral blood flow; CBV, cerebral blood volume.

1 hour.[4] Some countries, such as Japan, may utilize smaller doses of alteplase in treatment regimens to decrease potential complications, the most feared being intracerebral hemorrhage (6%).[48,49] Other complications include systemic bleeding (2%) and angioedema (1–8%).[49] Blood pressure should be maintained at <180/105 mm Hg for at least the first 24 hours after treatment, and treatment with antiplatelets or anticoagulation should be avoided for 24 hours, unless there are special circumstances such as cervical or intracranial stenting.[4]

Mechanical Thrombectomy

Regardless of IV alteplase administration, consideration for mechanical thrombectomy (MT) should be performed. It is paramount to understand that IV alteplase and MT are not mutually exclusive and both therapies often occur simultaneously. MT physically removes the embolus, immediately restoring blood flow to the ischemic territory of the occluded artery, preventing further infarction within the penumbra. At the time of writing this article, MT is indicated for patients with an LVO presenting up to 24 hours from symptom onset.[4,11] As with IV alteplase, treatment with MT should also be initiated as quickly as possible.

To determine if the patient has an LVO, a noninvasive angiographic study is performed—CTA or MRA. As mentioned previously, the preferred modality is CT due to its availability and quicker acquisition times compared with MR. It is important that appropriate large-bore IV access lines are obtained in the emergency room so that there is no delay in treatment and imaging. As with laboratory bottlenecks when administering IV alteplase, a serum creatinine is not needed to proceed with these contrast-enhanced studies.[4] Perfusion imaging (-CTP/MRP) is usually included in this step of decision analysis to differentiate areas of ischemic brain versus core infarct.

Patient Selection

Careful patient selection is crucial for optimizing outcomes in MT, while potentially avoiding major complications. With

Table 3 Contraindications to IV alteplase therapy for patients 18 years and older, who present within 4.5 hours of stroke symptom onset

IV alteplase: exclusion criteria
Historical
Ischemic stroke within 3 mo. Severe head trauma within 3 mo. History of intracranial hemorrhage
History of arterial puncture at noncompressible site in the previous 7 d. Intra-axial malignancy
Cerebral or spinal surgery within 3 mo
Clinical
Symptoms that suggest possible subarachnoid hemorrhage
Persistent blood pressure elevation (systolic $\geq$ 185 mm Hg, diastolic $\geq$ 110 mm Hg) Serum glucose < 50 mg/dL
Active internal bleeding
Stroke related to aortic arch dissection. Symptoms that suggest infective endocarditis. History of bleeding diathesis
Hematologic
Platelets < 100,000/mm^3 INR > 1.7
PT > 15 s; aPTT > 40 s
Use of a direct thrombin inhibitor/direct factor Xa inhibitor
Therapeutic doses of LMWH received within 1 d (not prophylactic doses)
Imaging
Intracranial hemorrhage
Extensive edema from acute infarct (i.e., greater than one-third of MCA territory)
Relative contraindications (between 0 and 3 h)
Intracranial neoplasm, arteriovenous malformation, or unruptured aneurysm (>10 mm). Major surgery or serious trauma within the previous 14 d
Dural puncture within 7 d
Gastrointestinal malignancy or hemorrhage within 3 wk
Relative contraindications (between 3 and 4.5 h)
Age > 80 y
Oral anticoagulant use regardless of INR. Severe stroke (NIHSS > 25)
Combination of both previous ischemic and diabetes mellitus

Abbreviations: aPTT, partial thromboplastin time; INR, international normalized ratio; IV, intravenous; LMWH, low-molecular-weight heparin; MCA, middle cerebral artery; NIHSS, National Institute of Health Stroke Scale; PT, prothrombin time.
Note: Considerations between 3 and 4.5 hours, which are relative contraindications based on the ECASS3 trial and should be individualized to each patient's presentation.

current guidelines, it is estimated that only 15% of patients who present with AIS are actually eligible for thrombectomy.[50] The primary goal of selection is to identify patients who have (or do not have) a small area of core infarction but have a significant salvageable penumbra. The criteria for selection are both time and perfusion based and are summarized in ►**Fig. 3**. The decision to proceed with MT is made immediately after obtaining necessary imaging, usually while the patient is in the CT scanner room, even prior to the patient getting off the table.

General criteria. Per trials, selection is based on age ($\geq$18 years). Baseline functional status, or prestroke disability (mRS), is an extremely important consideration in addition to age and comorbidities. In the landmark clinical trials,[7–13] only anterior circulation occlusions were included, with the vast majority in the M1 segment of the MCA or distal internal carotid artery (ICA) terminus. However, in high-volume stroke centers with experienced operators, embolectomy is not limited to just the ICA or proximal MCA. Leslie-Mazwi et al eloquently defined an emergent large vessel occlusion (ELVO) as "an acute vascular occlusion that impairs cerebral perfusion, results in significant clinical deficit, and is accessible for endovascular thrombectomy." This definition expands the scope of ELVO to include distal MCA branches (M2 and M3 segments), anterior cerebral artery branches (A1 and A2 segments), and the posterior circulation (basilar artery and P1 segment of the posterior cerebral artery).[51,52]

Early window: within 6 hours—"Rule of 6's." For patients who present within 6 hours of onset, who have an NIHSS $\geq$ 6 and ASPECTS $\geq$ 6, MT is now the standard of care. Perfusion imaging is not required but may be beneficial. Although most large-volume centers now include CTP as a part of their standard workup, CTP can be unreliable in the early treatment window and should not be used to exclude patients, the reasoning of which is discussed later in this article.

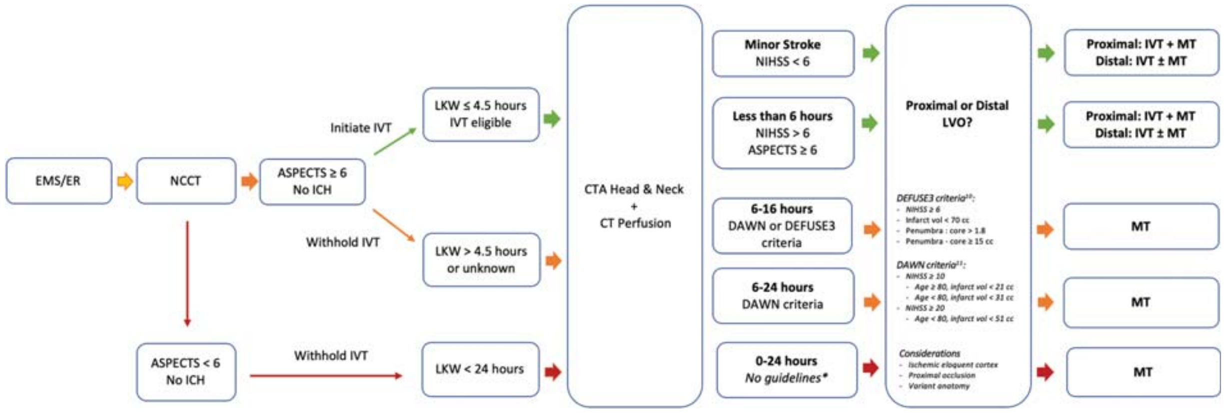

Fig. 3 Management flow chart for acute ischemic stroke. ASPECTS, Alberta Stroke Program Early CT Score; NCCT, noncontrast computed tomography; CTA, computed tomographic angiography; MT, mechanical thrombectomy; ICH, intracranial hemorrhage; IVT, intravenous thrombolysis; LKW, last known well; LVO, large vessel occlusion; MCA, middle cerebral artery; ICA, internal carotid artery; NIHSS, National Institute of Health Stroke Scale. *No standardized guidelines are currently available for low ASPECTS, but individualized patient decision making is necessary.

Extended window: between 6 and 24 hours. The extended treatment windows were established in early 2018, when the DEFUSE3 and DAWN trials demonstrated superior functional outcomes in patients treated with MT and standard care versus standard care alone between 6 to 16 hours and 6 to 24 hours from symptom onset, respectively.[10,11]

Perfusion imaging is key in patients presenting in this time window to identify a significant penumbra–core mismatch. In centers with dedicated perfusion imaging and automatic volumetric software for infarct determination (i.e., RAPID, Viz.ai, and Brainomix), criteria from DAWN and DEFUSE3 trials allow for selection based on core infarct volumes, age, and stroke scale. Both DAWN and DEFUSE3 criteria can be applied to patients presenting up to 16 hours, and DAWN criteria can be applied to any patient up to 24 hours.[10,11]

In the DEFUSE3 trial, patients had to have a target mismatch profile on CT or MRI perfusion utilizing RAPID software (iSchemaView), summarized as the following criteria:

1. Initial infarct volume (ischemic core) of less than 70 mL.
2. A ratio of volume of ischemic tissue to infarct volume of 1.8 or more.
3. An absolute volume of potentially reversible ischemia (penumbra) of 15 mL or more.[10]

In the DAWN trial, patients had to have a mismatch between the severity of the clinical deficit and the infarct volume, summarized as the following criteria:

1. In patients 80 years or older, with an NIHSS of 10 or higher, infarct volume less than 21 mL.
2. In patients younger than 80 years, with an NIHSS between 10 and 19, infarct volume less than 31 mL.
3. In patients younger than 80 years, with an NIHSS of 20 or higher, infarct volume between 31 and 51 mL.[11]

At centers where perfusion imaging is not readily available, tailored MR imaging is also an accepted form of penumbra assessment. There are several different techniques for assessing core/penumbra mismatch. These include DWI–FLAIR (fluid-attenuated inversion recovery) mismatch, where FLAIR is considered to represent core infarct, as well as DWI–perfusion mismatch and DWI–clinical mismatch, in which DWI is traditionally considered to represent core infarct.[53–59]

Several studies have investigated protocols to significantly decrease workflow times by implementing direct transfer to angiography suite protocols, especially in the setting of interhospital transfers (i.e., to a comprehensive stroke center). In these protocols, some of the earlier-mentioned imaging can be performed in the angiography suite by performing cone beam CT if not already performed. In a study by Mendez et al, median door to puncture times were decreased to 17 minutes compared with 70 minutes in a cohort of over 200 patients.[60] In addition to reducing workflow times, these studies have also shown significant improvements in clinical outcome at 90 days.[60–62]

Operators must have an in-depth understanding of neuroimaging to make quick but appropriate decisions on reperfusion therapy in select clinical scenarios. For example, CTP is susceptible to artifacts especially in cases of poor IV access, patient motion, or poor cardiac output.[33] In some cases, particularly in early presentations, CTP may overestimate core infarct size (aka “ghost core”), which could incorrectly deny patients from receiving life-altering therapy.[63,64] For this reason, when the CTP and the ASPECTS are discordant, it is reasonable to proceed to thrombectomy if ASPECTS score is acceptably high, usually ≥ 6.

Along these same lines, it is important to point out that selection criteria for MT are still evolving. Strictly following the current AHA guidelines based on the landmark 2015 trials, DAWN, and DEFUSE3, the number needed to treat (NNT) to achieve benefit at 90 days is less than 3. With such a low NNT, it is likely that there are subgroups of patients who have been currently excluded but would have benefitted from MT. For example, the HERMES collaboration showed that patients with ASPECTS of 3 to 5 derived significant benefit from MT despite slightly higher rates of symptomatic intracranial hemorrhage.[6] There are also several smaller, retrospective studies which have found statistically significant increases in functional independence (mRS: 0–2) with MT despite low baseline ASPECTS or relatively large CTP core volume.[65–68]

If a patient is a candidate for MT, he or she is immediately transported from the CT scanner directly to the angiography suite, which should be ready to accept the patient. The current goal to initiate thrombectomy is 90 minutes from arrival to the emergency room.[4] Many high-volume centers can now achieve 60 minutes or less, with more efficient, streamlined workflows.[8]

Following acute therapy, patients are then monitored in the intensive care unit, ideally a dedicated neurosciences intensive care unit, where further care is continued. The hyperacute and acute workflows are summarized in ►**Fig. 4**.

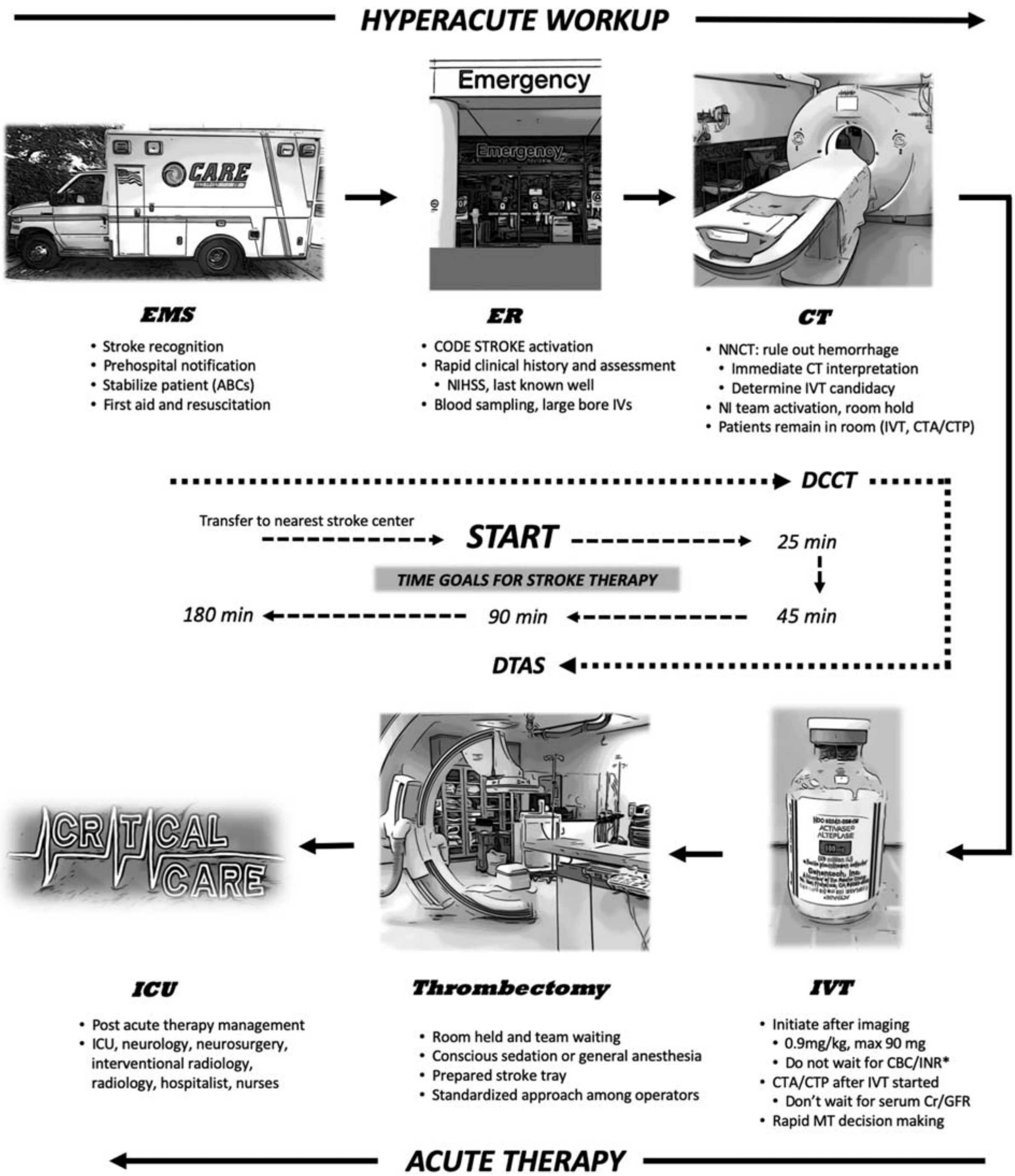

Fig. 4 Graphical flowchart during the acute management of AIS, delineating the hyperacute workup and acute therapies for appropriately selected patients. Standardized goal times are included in the workup, which are often far less in high-volume stroke centers with experienced operators, as well as centers incorporating direct to computed tomography imaging (DCCT) and direct to angiography suite (DTAS) protocols. ABCs, airway, breathing, circulation; NIHSS, National Institute of Health Stroke Scale; NCCT, noncontrast computed tomography; IVT, intravenous thrombolysis; CT, computed tomography; NI, neurointerventional; CTA, computed tomographic angiography; CTP, computed tomography perfusion; MT, mechanical thrombectomy; ICU, intensive care unit. *In patients without suspected bleeding diathesis or anticoagulation use.

Conclusion

The treatment of AIS involves harmonious coordination among many services in a streamlined workflow, with the goal to provide reperfusion to the brain as soon as possible. Advances in endovascular thrombectomy have revolutionized treatment of AIS, and expanding guidelines allow more patients to be treated safely and effectively. Continued preventative medicine and further improvement in technology will continue to decrease stroke-related disability and mortality in the general population.

Conflict of Interest
None.

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