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REVIEW ARTICLE

Emergency Neurological Life Support: Acute Ischemic Stroke

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Abstract Acute ischemic stroke is a neurological emergency that can be treated with time-sensitive interventions, including intravenous thrombolysis and endovascular approaches. Extensive study has demonstrated that rapid assessment and treatment are essential to improving neurological outcome. For this reason, acute ischemic stroke was chosen as an Emergency Neurological Life Support protocol. The protocol focuses on the first hour following the onset of neurological deficit.

Keywords Ischemic stroke · Tissue plasminogen activator · Protocol · Algorithm · ENLS

Introduction

According to 2002 World Health Organization statistics, cerebrovascular disease is the second cause of death worldwide, with an estimated 6.2 million deaths per year—coming a close second to ischemic heart diseases (7.3 million deaths per year). In the United States, ~800,000 strokes occur annually, of which nearly 25 % are recurrent strokes [1]. Although there are many new advances in the treatment of stroke, it is crucial that proper diagnosis and management occur as soon as possible, since the later therapies are instituted, the less the chance of successful intervention.

The Emergency Neurological Life Support (ENLS) suggested algorithm for the initial management of acute ischemic stroke is shown in Fig. 1. Suggested items to complete within the first hour of evaluating a patient with acute ischemic stroke are shown in Table 1.

Clinical Suspicion of Stroke

Acute stroke is suspected when a patient exhibits the sudden onset of a neurological deficit. In the absence of an obvious seizure, the deficit can most likely be attributed to stroke or transient ischemic attack (TIA). In countries that treat stroke as an emergency, paramedical personnel are typically the first to evaluate the patient (Fig. 2). The standard treatments are to perform routine airway, breathing, and circulation (ABC) assessments, administer supplemental oxygen, and transport the patient.

Some prehospital systems can call ahead to the receiving hospital, and many transfer the patient, preferentially to stroke centers. Once the patient arrives to an emergency department (ED), he or she is rapidly given a clinical assessment and then imaged, typically with non-contrast computed tomography (CT). Similarly, many regional arrangements have been made for "telestroke" consultation in order to expedite the administration of thrombolytic agents, followed by transfer to a stroke center if possible.

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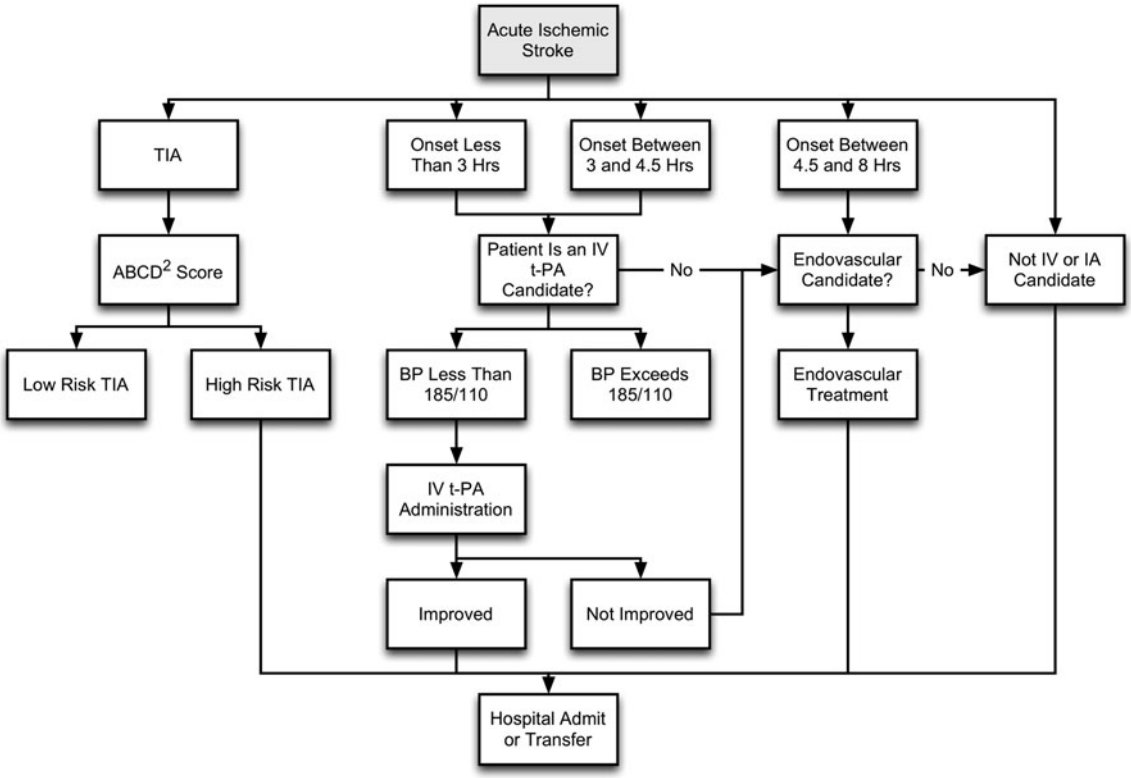

Fig. 1 ENLS acute ischemic stroke protocol

Table 1 Acute ischemic stroke checklist for the first hour

☐ Labs: CBC, platelets, chemistries, PT/PTT, glucose
☐ IV access
☐ Supplemental oxygen to maintain sats >94 %
☐ Activate stroke code system (if available)
☐ NIHSS
☐ Administer t-PA if eligible

As shown in Fig. 2, imaging is essential to confirm the correct diagnosis and exclude cerebral hemorrhage. Treatment should then proceed according to one of three ENLS protocols (shaded in gray): subarachnoid hemorrhage, intracerebral hemorrhage, or acute ischemic stroke. If the CT is free of hemorrhage, then a presumptive ischemic stroke or TIA is present.

The diagnosis of acute ischemic stroke is based on the presence of new and typically sudden focal neurological findings (facial weakness, arm/leg weakness, aphasia, neglect, visual field disturbance, and ataxia) lasting longer than 24 h, and on an imaging study—typically CT or magnetic resonance imaging (MRI) of the brain—that shows acute ischemic infarction.

When confronted with a patient whose focal symptoms have begun within the preceding few hours, it should be assumed that the patient will eventually be diagnosed with stroke. Most TIAs are brief, typically lasting less than 20 min. Therefore, if the patient is still manifesting physical signs of a stroke in the ED, those signs likely indicate a stroke.

In some centers, patients may be screened immediately upon arrival, then taken directly to CT or MRI based on symptoms of facial weakness, dysarthria, gaze preference, limb weakness, or other focal findings. However, there are a number of stroke mimics, including seizure, hypoglycemia, sepsis or fever, migraines, and Bell's palsy.

To determine optimal treatment, consideration should be given to the following:

Time of Onset

One of the chief criteria used to select patients for vascular reperfusion therapy is the duration of stroke symptoms, since treatment delays lead to a lower likelihood of a good outcome and higher risk of hemorrhage. The time the patient was last known to be without neurological deficits must be established from the patient or a bystander. If the patient went to bed and awoke with the stroke, the time of onset is considered to be when the patient went to bed.

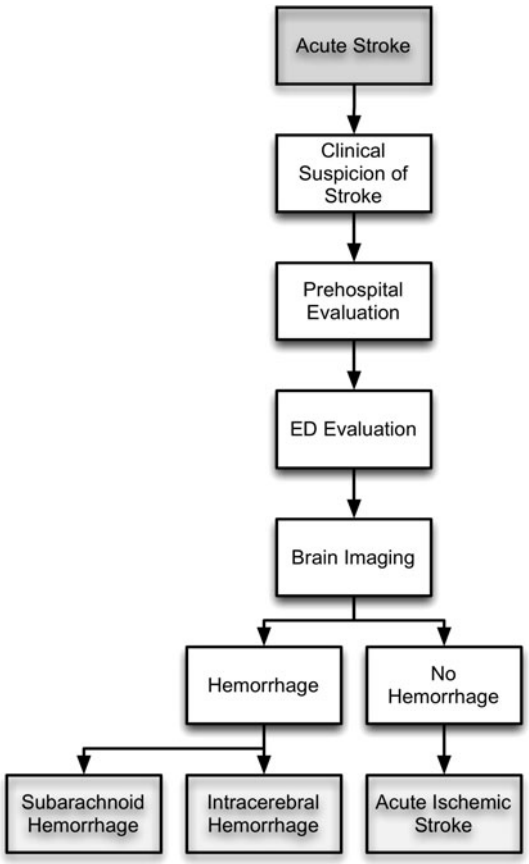

Fig. 2 The clinical suspicion of stroke algorithm assumes the patient is outside of the hospital when stroke occurs. Based on the results of brain imaging, the patient can be triaged to one of the three ENLS protocols shaded in *gray* (*bottom*)

Vital Signs

Pulse oximetry should guide supplemental oxygen to achieve an oxygen saturation ≥94 %. Hyperoxia may be detrimental in stroke, so there is no need for high flow oxygen [2]. If the patient is not hypoxic, supplemental oxygen is not needed.

Laboratory Examination

An adequate laboratory examination includes capillary blood glucose (CBG), complete blood count (CBC) with platelets, chemistries, prothrombin time/partial thromboplastin time (PT/PTT), and beta-human chorionic gonadotrophin (HCG) for women. However, if a patient is deemed a candidate for tissue plasminogen activator (t-PA) and there is no reason to suspect abnormal laboratory test results, t-PA should be administered without waiting for these laboratory values to prevent further delay [2]; at a minimum, a CBG should be performed prior to t-PA administration, since it can be completed quickly.

Imaging

There should be a goal of completing non-contrast head CT scan or MRI within 25 min of the patient's arrival. Chest X-ray is no longer routinely recommended during the acute phase of the workup [2].

Activate Stroke Team

If available, the stroke code system should be activated. The team should evaluate the patient within 10–15 min of the call.

NIHSS

The National Institutes of Health Stroke Scale (NIHSS) is a standardized method for examiners to reproducibly and quantifiably assess a patient's stroke symptoms. This is the preferred scoring system and may be used by a variety of non-neurological medical providers [2]. Scores range from zero (non-measurable) to 42 (devastating stroke).

The scale has some limitations, especially in scoring brainstem strokes. While many physicians use an NIHSS of four (4) as a threshold to treat an acute ischemic stroke with t-PA, this is not an absolute cut off. Therefore, careful documentation should be recorded when treating patients with NIHSS scores below 4.

Health care providers wishing to learn how to perform the NIHSS and receive certification may visit: http://learn.heart.org/ihtml/application/student/interface.heart2/nihss.html.

The NIHSS score may also be used as a guideline to predict risk of intracerebral hemorrhage (ICH) in patients who are given t-PA, as shown in Table 2. However, despite this increased risk of hemorrhage, patients in all NIHSS strata benefit from t-PA.

Onset <3 h

If the time from stroke symptom onset is less than 3 h, it should be confirmed that there are no other contraindications for IV t-PA (Table 3). One particularly relative

Table 2 Risk of intracerebral hemorrhage with IV t-PA treatment [3]

NIHSS score	Risk of intracerebral hemorrhage (%)
0–10	2–3
11–20	4–5
>20	17

Table 3 Eligibility and contraindications for use of IV t-PA

Diagnosis of ischemic stroke causing measurable neurological deficit
Neurological signs should not be clearing spontaneously
Neurological signs should not be minor and isolated
Caution should be exercised in treating a patient with major deficits
Symptoms of stroke should not be suggestive of subarachnoid hemorrhage
No head trauma or prior stroke in the previous 3 months
No myocardial infarction in the previous 3 months
No gastrointestinal or urinary tract hemorrhage in the previous 21 days
No major surgery in the previous 14 days
No arterial puncture at a non-compressible site or lumbar puncture in the previous 7 days
No history of previous intracranial hemorrhage
Blood pressure not elevated (systolic <185 mmHg and diastolic <110 mmHg)
No evidence of active bleeding or acute trauma (fracture) on examination.
Not taking an oral anticoagulant or, if anticoagulant being taken, INR <1.7
If receiving heparin in previous 48 h, aPTT must be in normal range
Platelet count $<100{,}000$ mm^3
Blood glucose concentration <50 mg/dL (2.7 mmol/L)
No seizure with postictal residual neurological impairments
CT does not show a multilobar infarction (hypodensity $>1/3$ cerebral hemisphere)
Patient or family members understand the potential risks and benefits from treatment
No dabigatran, apixaban, or rivaroxaban use for chronic anticoagulation for conditions such as atrial fibrillation. (At the time of this publication, there is little information on assessing influence or levels of these medications in patients with acute stroke. Currently, use of t-PA is NOT recommended in patients with recent use of these products.)

contraindication in Table 3 is the issue of "clearing neurological deficit." Some patients will clear to near or full recovery without t-PA, while others may improve somewhat from a severe stroke but then fail to clear further. If a patient has plateaued or still has significant stroke symptoms and no other contraindication, treatment should proceed as it would otherwise.

Common reasons to avoid administering intravenous (IV) t-PA are time (duration from first symptom >4.5 h), recent surgery, current bleeding at a non-compressible site, as well as large area of cerebral infarction that is already apparent as low density on the brain CT or diffusion weighted MRI study ($>1/3$ of the middle cerebral artery (MCA), territory).

Patients with major neurological deficits have a high risk of poor outcome, regardless of whether t-PA is administered. In these cases, realistic expectations and risks associated with either choice should be discussed with the patient's family members, and a joint decision should be made. While a contraindication of glucose greater than 400 has been removed, it should be noted that high glucose may be a stroke mimic and can be associated with worse outcome. Similarly, the presence of fever should prompt a reconsideration of the diagnosis. For example, a simple urinary tract infection can bring back old, subclinical stroke symptoms and, once corrected, these stroke-like symptoms resolve.

Onset Between 3 and 4.5 h

In the U.S., t-PA has not yet been approved by the Food and Drug Administration for use between 3 and 4.5 h, though it has been approved in Europe and Canada. However, t-PA use in the U.S. in this time window has been endorsed by the American Stroke Association [4] and is widely used.

The inclusion criteria are similar to those of onset <3 h (discussed above), but are modified as noted in Table 4.

Patient is IV t-PA Candidate

After reviewing the inclusion/exclusion criteria for IV t-PA use, the patient is eligible to receive the drug, assuming the current blood pressure (BP) is not excessively elevated. If

Table 4 Additional inclusions to IV t-PA use between 3 and 4.5 h [5]

Meet all criteria of <3 h since onset of stroke
Age $<$ 80 years
No anticoagulant use, regardless of INR
NIHSS $\leq$ 25
No combined history of prior stroke and diabetes

the patient's BP is too high, the risk of intracerebral hemorrhage (ICH) from t-PA is increased.

Systolic BP higher than 185 or diastolic pressure greater than 110 mmHg is too high for IV t-PA administration and requires reduction prior to initiating t-PA. The following medications may be used to lower BP into the range of eligibility for t-PA:

Labetalol

- IV 10 mg every 10 min.
- Consider doubling dose (i.e., 20, 40, and 80) to a maximum total dose of 150 mg, followed by a maintenance infusion.

Nicardipine

- Begin with IV 5 mg/h.
- Titrate up by 2.5 mg/h at 5–15 min intervals to a maximum total dose of 15 mg/h.
- When desired BP has been attained, reduce to 3 mg/h.

If the patient's BP proves refractory to the above medications, the patient is considered to be high risk for ICH and should not be treated with t-PA. However, efforts to reduce BP below 220/120 mmHg should be continued. Permissive hypertension (allowing BP to naturally rise) is allowed for TIA, as it is for non-t-PA treated patients, up to 220/120 mmHg.

It should be noted that while nitroglycerin paste (for patients with no IV access) is listed as an option in the current American Stroke Association guidelines, this agent is not titratable and may lead to BP spikes after administration of t-PA. Therefore, titratable agents like labetalol and nicardipine are recommended as the acute antihypertensives of choice.

BP $<$ 185/110

If BP is below 185/110 (or becomes this low with antihypertensives), it is permissible to proceed with IV t-PA administration.

IV t-PA Administration

After placing two peripheral IV lines, the patient should be weighed rather than use an estimated body weight; t-PA 0.9 mg/kg should be mixed (not shaken), with the total dose not to exceed 90 mg.

The initial 10 % of the total t-PA dose is given by bolus, then the remainder infused over 1 h. As t-PA is dispensed in 50 and 100 mg bottles, excess t-PA should be drawn off and discarded to avoid accidental overdose.

During the hospital admission or transfer period, there should be continued observation for complications of t-PA, including airway obstruction due to angioedema (consider rapid intubation), hemorrhage (stop t-PA), and sudden deterioration in mental status.

A sudden decline in neurological status during or following t-PA administration may be due to an intracerebral hemorrhage (ICH). This is often accompanied by a marked rise in BP, and a marked rise or fall in BP alone may signal an ICH. In these cases, the following steps should be immediately taken:

- Stop t-PA infusion.
- Obtain STAT head CT scan.
- Notify the neurosurgeon on call; if a neurosurgeon is not available, begin the process of transferring the patient to a facility with neurosurgical capability once CT scan results are available.
- STAT labs: PT, PTT, platelets, fibrinogen, type and cross 2–4 U PRBCs
- Give the following:
  - 6–8 U of IV cryoprecipitate
  - 6–8 U of IV platelets
- Consider 40–80 mg/kg of recombinant factor VIIa IV while waiting for platelets and cryoprecipitate

Improvement During Infusion of t-PA

If the patient improves during administration of t-PA (drop of 4 or more points in NIHSS), it is reasonable to proceed with patient admission or patient transfer, depending on the setting. BP should be carefully monitored during and following IV t-PA administration.

No Improvement Following t-PA Infusion

If the patient does not improve following t-PA (which is often the case), this does not necessarily indicate drug failure: the drug may have successfully opened the occluded intracranial vessel, but it takes time for the brain to

Table 5 Sample acute stroke admission orders

Neuro check q30 min × 6 h, then q1 h[a]; oxygenation to keep O_2 sat >94 %
BP check q15 min × 2 h, then q30 min × 6 h, then q1 h × 16 h
Keep BP after t-PA treatment <180/105 (*Note*: this is lower than pre-treatment values); if no t-PA given, keep BP < 220/120

[a] Bedside swallow test (30 mL water PO) before anything else PO

recover function. However, the possibility still exists that the vessel remains occluded.

Based on an observed lesser ability for t-PA to open larger intracranial vessels, many stroke neurologists refer the patient for endovascular treatment at this stage—especially if the stroke is due to a large vessel intracranial occlusion, demonstrated by computed tomography angiography (CTA) or magnetic resonance angiography (MRA), or on clinical grounds.

Onset Between 4.5 and 8 h: Endovascular Treatment

If the patient has a large vessel occlusion—e.g., MCA, intracranial internal carotid artery (ICA), basilar or vertebral artery—and is within 8 h of the stroke onset, intra-arterial (IA) thrombolysis or thrombectomy treatment may be helpful. Even if the patient was treated with IV t-PA, IA treatments may open a vessel that has not become patent. If the time window is beyond 4.5 h (and therefore precludes IV t-PA) but within 8 h, IA treatment may be an option as well.

Large vessel occlusion can be suspected by seeing a hyper-dense sign (e.g., clot within the vessel) on non-contrast CT, but this sign is insensitive. CTA or MRA is more diagnostic, as is conventional angiography. It is prudent to contact the neurointerventional physician on call, if one is available; if the treating hospital does not have this capability, consideration may be given to transfer to a comprehensive stroke center. Some hospitals use CT perfusion or MR perfusion techniques to select appropriate patients for intervention, looking for ischemic penumbra; this practice is not well established.

Exclusions for IA thrombolysis include the absence of a large vessel occlusion on CTA or MRA, lack of consent from the patient or surrogate, or large area of infarction already present on the brain imaging study.

Hospital Admission or Transfer

Assuming there are no complications of t-PA or IA therapy, Table 5 lists the orders that should be considered while waiting for the patient be admitted.

Additional admission orders must address glucose, volume status, body temperature, and catheters:

- Keep glucose <140 mg/dL; consider insulin drip if the patient is diabetic.
- Administer IV fluids 0.5 NS or NS at 1.5 mL/kg/h initially, with a goal of euvolemia.
- Continue telemetry/bedside cardiac monitoring principally to detect atrial fibrillation.
- Treat fever sources with antipyretics (while occasionally used in post cardiac arrest situations as a neuroprotective maneuver, hypothermia has not been sufficiently studied to recommend at present).
- If t-PA was administered, avoid indwelling urinary catheter, nasogastric tubes, and intra-arterial (IA) catheters for 4 h, and do not give anticoagulant/antiplatelet therapy for 24 h.

TIA

The diagnosis of TIA is based on the new onset of focal neurological symptoms and signs that are explainable by a vascular disease (i.e., arterial occlusion of a single or group of arteries adequately explain the patient's signs and symptoms), and these signs and symptoms resolve within 24 h (most TIAs resolve in a much shorter period of time).

However, up to one-third of TIAs have demonstrable injury on MRI [6]. Although these cases are now classified as stroke, it is unlikely that emergency reperfusion therapy should be attempted, since tissue injury is present and all symptoms have resolved. Approximately 50 % of patients with a TIA will have CT findings of a prior cerebrovascular accident (CVA), even though the CVA may have been clinically silent.

$ABCD^2$ Score

The $ABCD^2$ score is an ordinal scale that provides risk prediction of subsequent stroke following a TIA. Table 6 demonstrates how to calculate this score.

Table 6 Calculate $ABCD^2$ score

$ABCD^2$ score	Points
Age > 60 years	1
BP = 140/90 mmHg at initial evaluation	1
Clinical features of the TIA	
Speech disturbance without weakness, or	1
Unilateral weakness	2
Duration of symptoms	
10–59 min, or	1
>60 min	2
Diabetes mellitus in patient's history	1

Table 7 Risk of stroke following TIA with various $ABCD^2$ scores [7]

Total risk	Scores	2 days	7 days	90 days
Low	0–3	1.0	1.2	3.1
Moderate	4–5	4.1	5.9	9.8
High	6–7	8.1	12	18

Add all of the points from above for the total $ABCD^2$ score (0–7). Table 7 lists the estimated risk (%) of a stroke occurring within various time ranges.

Based on this risk stratification, some physicians choose to admit high-risk patients and discharge those at low-risk. There is controversy regarding admission of moderate-risk patients, and this decision follows local practices.

Low-Risk TIA

For low-risk patients ($ABCD^2$ scores 0–3), an outpatient workup in the 1–2 days following score calculation may be most appropriate. Alternately, observation or admission may be an option. In either case, stroke can be prevented by rapid institution of the following regimen [8]:

1. Begin an antithrombotic agent (ASA 325 mg, clopidogrel 75 mg/day, or ASA/extended release dipyridamole).
2. Perform carotid imaging: ultrasound, CTA, or MRA.
3. Consider transthoracic echocardiography; if bilateral infarcts are present on CT or there is high suspicion of cardiac embolic source, and transthoracic echo is normal, obtain transesophageal echocardiograph (TEE).
4. Consider 30-day cardiac monitor to detect intermittent atrial fibrillation.
5. Encourage smoking cessation.
6. Initiate statin (atorvastatin 80 mg/day or equivalent).

If ECG or rhythm strip shows atrial fibrillation, consider starting anticoagulation (oral anticoagulant or low molecular weight heparin) or ASA, depending on CHADS2 score. In these cases, referral to a vascular neurologist or cardiologist is appropriate.

Table 8 Acute ischemic stroke communication regarding assessment and referral

☐ Age
☐ Airways status
☐ Time of onset
☐ NIHSS
☐ Imaging findings
☐ Was t-PA given?

High-Risk TIA

For patients with higher-risk TIAs (scores >3), hospital admission is advisable. In addition to the treatments discussed above, some physicians keep patients on bed rest for a day, with the head flat (in order to maintain brain perfusion). After 24 h, the patient should begin to get out of bed as tolerated with assistance. Permissive hypertension is encouraged (not to exceed 220/120 mmHg), and BP limits should be gradually lowered over 24–48 h.

Communication

When communicating to an accepting or referring physician about this patient, consider including the key elements listed in Table 8.

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