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Review Article

Acute ischemic stroke: management approach

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ABSTRACT

A stroke, or brain attack, happens when blood flow to the brain is stopped. It is an emergency situation. The brain needs a constant supply of oxygen and nutrients in order to work well. If blood supply is stopped even for a short time, this can cause problems. Brain cells begin to die after just a few minutes without blood or oxygen. Stroke is the second most common cause of death worldwide and the most important cause of physical weakness, with a growing occurrence in developing countries. Ischemic stroke is the most common type of stroke which occurs due to arterial block and managed by fast reperfusion with endovascular thrombectomy and intravenous thrombolysis. The first step in stroke management is initial identification of patients with stroke and triage to centers accomplished of transporting the suitable treatment, as fast as conceivable. Mobile stroke units, tele stroke and artificial intelligence are technologies playing an important role in recognizing and treating stroke. Stroke system-of-care models remain to streamline the distribution of definitive revascularization in the age of mechanical thrombectomy. Overall, in the present review, we emphasized the pathophysiology, diagnosis and management of acute ischemic stroke (AIS).

Keywords: AIS, Anticoagulant therapy, Antithrombotic agent

INTRODUCTION

Stroke is defined by the world health organization as a clinical syndrome consisting of rapidly developing clinical signs of focal (or global in case of coma) disturbance of cerebral function lasting more than 24 hours or leading to death with no apparent cause other than a vascular origin.[1] Stroke is classified broadly into three categories; ischemic stroke, haemorrhagic stroke and subarachnoid haemorrhage. Ischemic stroke occurs due to blockage of blood vessel which limits the blood supply to the brain whereas haemorrhagic stroke occurs due to rupture of blood vessel leading spillage of blood in the intracranial cavity.[2] Depending on the site of blood spillage the haemorrhagic stroke could be classified as intracerebral haemorrhage or subarachnoid haemorrhage. Approximately 60-80% of all strokes is ischemic. This article is dedicated to AIS and its management.

Stroke is the second leading cause of death worldwide, with 6.2 million dying from stroke in 2015, an increase of 830,000 since the year 2000. Globally, 68% of all strokes are ischemic and 32% are haemorrhagic.[3] In 2020, 1 in 6 deaths from cardiovascular disease was due to stroke.[4] Every 40 seconds, someone in the United States has a stroke. Every 3.5 minutes, someone dies of stroke. Every year, more than 795,000 people in the United States have a stroke. About 610,000 of these are first or new strokes. About 185,000 strokes-nearly 1 in 4-are in people who have had a previous stroke.[5] Numbers from the USA differ a little with 87% of all strokes being ischemic, 10% haemorrhagic and about 3% being subarachnoid haemorrhage.[6] In 2016, the lifetime global risk of stroke from age 25 years onward was 25%, an increase of 8.9% from 1990. Nearly 7 million Americans age 20 or older report having had a stroke, and the prevalence is estimated to rise by 3.4 million adults in the next decade,

representing 4% of the entire adult population.[7] Conversely, case-specific disability-adjusted life-years due to stroke are falling, likely due to better prevention and treatment, but overall disease burden will continue to climb as the population ages, and stroke is likely to remain the second most common disabling condition in individuals aged 50 or older worldwide. India has the highest burden of acute coronary syndrome (ACS) in the world and the three most common risk factors for ACS are smoking (40%), high blood pressure (38%), and diabetes (30%).[8] Taking account of the above mentioned data and considering the fact that stroke shares common risk factors with ACS, we can safely assume that India has a very high incidence of stroke as well.

A stroke, or cerebrovascular accident, is an abrupt onset of a neurologic deficit that is attributable to a focal vascular cause. Thus, the definition of stroke is clinical, and laboratory studies including brain imaging are used to support the diagnosis. The clinical manifestations of stroke are highly variable because of the complex anatomy of the brain and its vasculature. Cerebral ischemia is caused by a reduction in blood flow that lasts longer than several seconds. Neurologic symptoms are manifested within seconds because neurons lack glycogen, so energy failure is rapid. If the cessation of flow lasts for more than a few minutes, infarction or death of brain tissue results. When blood flow is quickly restored, brain tissue can recover fully and the patient's symptoms are only transient: this is called a transient ischemic attack (TIA). The definition of TIA requires that all neurologic signs and symptoms resolve within 24 h without evidence of brain infarction on brain imaging. Stroke has occurred if the neurologic signs and symptoms last for >24 h or brain infarction is demonstrated. A generalized reduction in cerebral blood flow due to systemic hypotension (e.g., cardiac arrhythmia, myocardial infarction, or haemorrhagic shock) usually produces syncope. If low cerebral blood flow persists for a longer duration, then infarction in the border zones between the major cerebral artery distributions may develop. In more severe instances, global hypoxia-ischemia causes widespread brain injury; the constellation of cognitive sequelae that ensues is called hypoxic-ischemic encephalopathy. Focal ischemia or infarction, conversely, is usually caused by thrombosis of the cerebral vessels themselves or by emboli from a proximal arterial source or the heart. Intracranial haemorrhage is caused by bleeding directly into or around the brain; it produces neurologic symptoms by producing a mass effect on neural structures, from the toxic effects of blood itself, or by increasing intracranial pressure.

ISCHEMIC STROKE CLASSIFICATION

According to the multicenter trial of acute stroke treatment (TOAST) there are three kinds of ischemic stroke: large vessel stroke, small vessel stroke or lacunar stroke, and cardioembolic stroke.

Large artery strokes could be due to thrombotic or embolic occlusion of the major arteries of the brain like the internal carotid artery, middle cerebral artery, anterior cerebral artery or the vertebrobasilar system. Lacunar strokes are more often due to involvement of smaller or the perforating blood vessels supplying the deeper structures of the brain.

Risk factors: non modifiable and modifiable

Non modifiable risk factors: Include age, race, sex, ethnicity, history of migraine headaches, fibromuscular dysplasia, hereditary: family history of stroke or TIAs.

Modifiable risk factors: Include hypertension, diabetes mellitus, cardiac disease (see below), high cholesterol, previous stroke, carotid stenosis, hyperhomocystinemia, lifestyle issues (smoking, excessive alcohol intake, tobacco use, illicit drug use, physical inactivity), obesity, oral contraceptive use/postmenopausal hormone use.

Smoking is possibly the most substantial adaptable risk influence. Smokers are two to four times more probable to suffer a stroke, not to indicate an advanced injury and mortality proportion than non-smokers after a stroke.[9] Majority of the ischemic strokes seen in patients with cardiovascular disease are embolic. Embolic strokes may arise directly from the heart or the aorta. Following is the list of conditions that carry a high risk for the embolic strokes.[9]

Arrhythmias: Atrial fibrillation and paroxysmal atrial fibrillation, sick sinus syndrome, sustained atrial flutter.

Valvular heart disease: Rheumatic mitral or aortic valve disease, bioprosthetic and mechanical heart valves, fibrous nonbacterial endocarditis (i.e., Libman-Sacks endocarditis), antiphospholipid syndrome, cancer (marantic endocarditis), systemic lupus erythematosus, infective endocarditis.

Thrombus and structural lesion: Papillary fibroelastoma, left atrial myxoma, atrial or ventricular thrombus.

Structural heart disease: Recent myocardial infarction (within one month), chronic myocardial infarction together with ejection fraction<28%, congestive heart failure with ejection fraction <30%, dilated cardiomyopathy.

Surgical: Coronary artery bypass graft (CABG) surgery; conditions which have been associated with embolic stroke but lack definitive evidence are mitral annular calcification, patent foramen ovale, left atrial smoke on echocardiogram, atrial septal aneurysm, left ventricular aneurysm and aortic arch atheroma. Genetic diseases, storage diseases, traumatic vascular diseases are well known causes of stroke which are beyond the scope of this article.

PATHOPHYSIOLOGY OF ISCHEMIC STROKE

Acute occlusion of an intracranial vessel causes reduction in blood flow to the brain region it supplies. The magnitude of flow reduction is a function of collateral blood flow, and this depends on individual vascular anatomy (which may be altered by disease), the site of occlusion, and systemic blood pressure. A decrease in cerebral blood flow to zero causes death of brain tissue within 4-10 min; values <16-18 mL/100 gm tissue per minute cause infarction within an hour; and values <20 mL/100 gm tissue per minute cause ischemia without infarction unless prolonged for several hours or days.[7] If blood flow is restored to ischemic tissue before significant infarction develops, the patient may experience only transient symptoms, and the clinical syndrome is called a TIA. Another important concept is the ischemic penumbra, defined as the ischemic but reversibly dysfunctional tissue surrounding a core area of infarction. The penumbra (Figure 1) can be imaged by perfusion imaging using MRI or CT. The ischemic penumbra will eventually progress to infarction if no change in the flow occurs, and hence, saving the ischemic penumbra is the goal of the revascularization therapies.

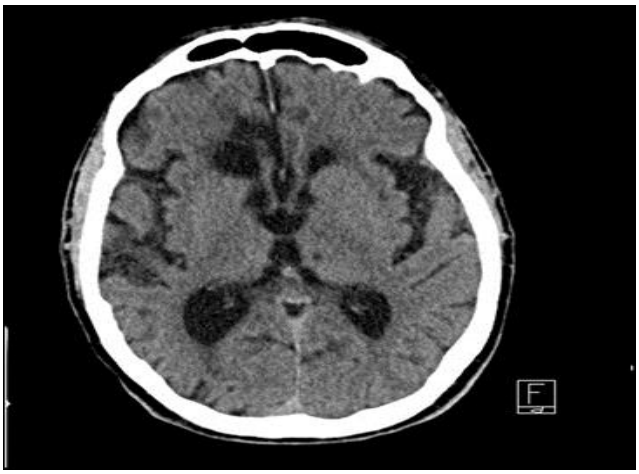

Figure 1: Acute ICA (internal carotid artery) ischemic penumbra due to high-grade CCA (common carotid artery) stenosis (CT perfusion).

Focal cerebral infarction occurs via two distinct pathways: (1) a necrotic pathway in which cellular cytoskeletal breakdown is rapid, due principally to energy failure of the cell; and (2) an apoptotic pathway in which cells become programmed to die. Ischemia produces necrosis by starving neurons of glucose and oxygen, which in turn results in failure of mitochondria to produce ATP. Without ATP, membrane ion pumps stop functioning and neurons depolarize, allowing intracellular calcium to rise. Cellular depolarization also causes glutamate release from synaptic terminals; excess extracellular glutamate produces neurotoxicity by activating postsynaptic glutamate receptors that increase neuronal calcium influx. Ischemia also injures or destroys axons, dendrites, and glia within brain tissue. Free radicals are produced by degradation of membrane lipids and mitochondrial dysfunction. Free radicals cause catalytic destruction of membranes and likely damage other vital functions of cells. Lesser degrees of ischemia, as are seen within the ischemic penumbra, favor apoptotic cellular death, causing cells to die days to weeks later. Fever dramatically worsens brain injury during ischemia, as does hyperglycemia (glucose >11.1 mmol/L [200 mg/dL]),[7] so it is reasonable to suppress fever as well as prevent hyperglycemia as much as possible. The value of induced mild hypothermia to improve the stroke outcomes is the subject of the continuing clinical research.

What are the signs and symptoms of AIS?

Stroke syndromes present clinically as neurologic deficits of sudden onset. Symptoms depend upon the affected region of brain, which in turn is defined by the arterial anatomy involved. Although some features are more or less typical of haemorrhagic forms of stroke, as distinct from ischemic stroke, none are sufficiently discriminatory to allow clinical diagnosis of stroke type. Therefore, brain and neurovascular imaging in the acute phase is required for all strokes. Common symptoms of stroke in the left hemisphere include aphasia, right hemiparesis and right hemianopia, and in the right hemisphere, left hemispatial neglect, left hemiparesis and left hemianopia. The majority (90%) of strokes are supratentorial; as such, the public can be taught to recognize and act upon stroke using the acronym FAST, for facial droop, arm drop, speech disturbance and time to call 911. Posterior circulation or infratentorial stroke has a multitude of additional symptoms, including diplopia, bulbar palsies, dysphagia, unilateral dysmetria and incoordination, as well as reduced levels of consciousness. Although headache or head, facial or neck pain may be an ancillary symptom, stroke is typically painless. The most important historical feature of stroke is the suddenness of its onset.

Remember the 6S method to diagnose stroke: Sudden (symptoms usually start suddenly), slurred speech (speech is not clear, as if drunk), side weak (face, arm or leg or all three can get weak), spinning (vertigo), severe headache, seconds (note the time when the symptoms start and rush to the hospital).

Befast: Balance (loss of balance/dizziness), eyes (disturbance of vision in one or both eyes), face (facial droop), arm (weakness) and speech (difficulty or slurred speech) and time (time to call 911).

All the symptoms need not be present to diagnose stroke. Any of the above-mentioned symptoms can be present and is helpful in diagnosing ischemic as well as haemorrhagic stroke.

Identification of a stroke syndrome is relatively easy: sudden onset of acute neurologic symptoms, peaking within a few minutes, is deemed a stroke until proven otherwise. However, detailed diagnosis and management are highly-dependent upon clinical assessment of the

history and physical examination, because symptoms and signs vary tremendously according to the region of the brain that is affected.

APPROACH TO THE PATIENT

A careful history and neurologic examination can often localize the region of brain dysfunction; if this region corresponds to an arterial distribution, the possible causes responsible for the syndrome can be narrowed. This is of particular importance when the patient presents with a TIA and a normal examination. For example, if a patient develops language loss and a right homonymous hemianopia, a search for causes of left middle cerebral emboli should be performed. A finding of an isolated stenosis of the right internal carotid artery in that patient, for example, suggests an asymptomatic carotid stenosis, and the search for other causes of the stroke should continue.

How is the diagnosis confirmed?

Brain and neurovascular imaging are required for diagnosis. The current standard is non-contrast computed tomography (CT) of the head because it is fast and widely available. When interpreted by an expert, head CT can rule in a diagnosis of haemorrhagic stroke (intracerebral or subarachnoid haemorrhage) with over 95% accuracy. Head CT can also rule in a diagnosis of major stroke in about two-thirds of cases in which ischemic changes are evident, but it is highly insensitive to the diagnosis of minor stroke. Small-volume ischemic change is simply beyond the resolution of CT; therefore, a "normal" scan in the scenario of minor stroke neither confirms nor excludes ischemia. Magnetic resonance imaging (MRI) has greater spatial resolution to detect brain ischemia in TIA or minor ischemic stroke and is the modality of choice to make an inclusive imaging diagnosis of minor stroke in cases where the deficits are very mild (Figure 2).

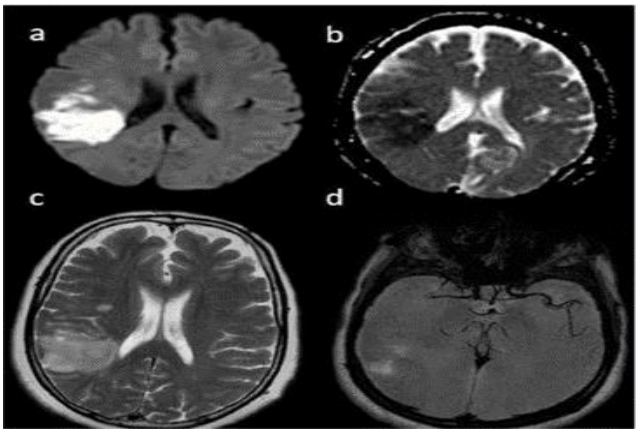

Figure 2 (A-D): Some of the brain advanced sequences: Diffusion-weighted imaging (DWI), apparent diffusion coefficient (ADC) map, T2 weight image, and dark blood magnetic resonance angiography (MRA).

For all presentations of acute stroke syndrome, we recommend CT angiography immediately following non-contrast head CT. Identification of the occluded intracranial vessel and evaluation of the extracranial carotid, extracranial vertebral, aortic arch and proximal great vessels is required for management of both TIA or minor stroke and major ischemic stroke, if not immediately then over the next several days. In cases of haemorrhagic stroke, intracranial CT angiography will identify intracranial aneurysm as the cause of subarachnoid haemorrhage or show the source of bleeding in intracerebral haemorrhage as a "spot" sign. Although MRI has greater sensitivity for the small-volume ischemia observed in TIA or minor stroke, it is used only in situations where there is no time pressure to offer treatment, typically as follow-up imaging. Unlike the situation for acute coronary syndromes, where serum troponin and electrocardiography (ECG) are helpful diagnostic biomarkers, similar blood or simple electrophysiological tests are not available in stroke. Imaging is the biomarker.

Management of acute stroke

The most important factor in the management of AIS is time. The patient with ischemic stroke loses 190,0000 brain cells every minute, about 14000,000,000 nerve connections are destroyed every minute and 12 km (7.5 miles) of nerve fibres are lost every minute. The brain ages 3.6 years for every hour it is deprived of the blood supply.[10]

Pre-hospital scales

Numerous scales occur in assistance to EMS (emergency medical services) in recognizing patients with large vessel occlusion (LVO). Documentation is the vital first step in receiving the right patient to the right treatment more rapidly and, as the consequence is contingent on time to reperfusion, might recover consequences.[11] About 20 prehospital scales occur; nearly of the greatest common scales used are the Los Angeles motor scale (LAMS), Cincinnati prehospital stroke severity scale (CPSS) and rapid arterial occlusion evaluation scale (RACE).[12-15] Numerous scales were intended originally to recognize patients with stroke as conflicting to circumstances that impersonate a stroke, but approximate values were exactly intended for documentation of patients with stroke with LVO (for instance, aphasia, vision, neglect or VAN).[16] Though, current meta-analysis originates considerable heterogeneity of sensitivity and specificity between studies.[12] The assumption of this meta-analysis recommended that the National Institutes of health stroke scale (NIHSS), VAN and LAMS obligated the best prognostic worth for LVO but that additional testing in dissimilar populations is required. Residents in dissimilar settings (urban versus rural) could also have advantage from dissimilar scales; for instance, triage in rural areas might necessitate an extra precise scale that might involve an alteration for the time and distance.

Simple alteration of the face arm speech-time (FAST) or the LAMS groove might support to stratify the risk of an LVO, but neither has remained prospectively authenticated in the prehospital location.[17]

There are two modalities of treatment available for treatment of AIS. Intravenous thrombolysis and mechanical thrombectomy.

Once the clinical diagnosis of an acute stroke is made the following steps need to be followed: Ensure that the patient is medically stable, evaluate for reversible causes of neurological symptoms, determine the nature of stroke (ischemic vs haemorrhagic), treatment of stroke, determine the causes of stroke.

Ensure the patient is medically stable: never forget the ABC

In the treatment of acute stroke time is of the essence. Medical stability of the patient should be established as soon as possible so that stroke management can proceed. Airway, breathing and circulation need to be assessed like in every medical emergency. Large strokes, intracranial haemorrhage, strokes affecting posterior circulation present with loss of consciousness, bulbar dysfunction and sometimes respiratory distress. Hypoxia should be avoided at all costs and intubation should be considered if the airway is not protected or the patient needs ventilator support.

Evaluation of reversible causes of neurological symptoms

As per the stroke guidelines, finger stick glucose is an essential test before thrombolysis is started.

Following tests can be considered in special patient groups, however none of them should delay the start of thrombolytic therapy if indicated unless the patient has a history of bleeding disorder, is taking anticoagulants or has history of thrombocytopenia: Electrocardiogram (this should not delay the non-contrast brain CT), complete blood count including platelets, troponin, prothrombin time and international normalized ratio (INR), activated partial thromboplastin time, ecarin clotting time, thrombin time, or appropriate direct factor Xa activity assay (if the patient is taking new oral anticoagulants).

Once the acute management of stroke is done other lab tests can be done such as liver function, kidney function etc.

Determine the nature of stroke (Ischemic vs haemorrhagic)

Plain head CT scan is sufficient to rule out intracranial haemorrhage. Systems should be established so that brain imaging studies can be performed within 20 minutes of arrival in the ED in at least 50% of patients who may be candidates for IV alteplase and/or mechanical thrombectomy (door to imaging time).[18]

Depending on the time of onset of symptoms further studies can be conducted to aid in management.

If the patient presents within first 6 hours of symptoms onset: CT scan should be combined with CT angiogram of the brain and the neck to rule out large vessel occlusion. CT angiogram should not be delayed to wait for serum creatinine. Whenever possible CT angiogram should be completed with the CT scan to save time for possible mechanical intervention. MRI or MR angiogram or MR perfusion is not indicated within the first 6 hours of symptom onset.

For patients presenting between 6 hours and 24 hours of symptom onset: In selected patients with AIS within 6-24 hours of last known normal who have large vessel occlusion in the anterior circulation, obtaining CT perfusion, Diffusion weighted-MRI, or MRI perfusion is recommended to aid in patient selection for mechanical thrombectomy.

Intravenous thrombolysis

As recommended by AHA/ASA (American heart association/ American stroke association) intravenous tPA infusion is treatment modality of choice for patients presenting within first 3 hours of onset of symptoms. The treatment window can be extended to 4.5 hours for eligible patients.[19] Use of intravenous alteplase is based on the landmark national institute of neurological disorders and stroke (NINDS) tPA trial which showed that patients who received tPA were at least 30% more likely to have minimal or no disability at 3 months on the assessment scales. Outcome measures were in favour of the group that received tPA (global odds ratio for a favorable outcome, 1.7; 95% confidence interval, 1.2 to 2.6).[20] A pooled analysis of ATLANTIS, ECASS, and NINDS was published in 2004 which showed that the tPA window could be extended to 4.5 hours with reasonable benefit to the patient. The European cooperative acute stroke study III (ECASS-III) definitively established the efficacy of tPA within 3-4.5-hour window. ECASS-III showed that patients who received tPA within 3-4.5-hour window had a better chance to a favorable outcome with an odds ratio of 1.42 (95% CI 1.02-1.98, p=0.04).[21]

Intravenous tPA infusion can only be given to eligible patients and there are strict indications and contraindications as per stroke guidelines published in 2018.[18]

The checklist includes some FDA-approved indications and contraindications for administration of IV rtPA for acute ischemic stroke (Table 1). Recent guideline revisions have modified the original FDA approved indications. A physician with expertise in acute stroke care may modify this list.

Table 1: Administration of intravenous recombinant tissue plasminogen activator (rtPA) for AIS.

S. no.	Variables
1	**Indications**
	Clinical diagnosis of stroke
	Onset of symptoms to time of drug administration ≤ 4.5 hrs.
	CT scan showing no haemorrhage or edema of > 1/3rd of the MCA territory.
	Age ≥18 years.
2	**Contraindications**
	Sustained BP > 185/110 mm Hg despite treatment.
	Bleeding diathesis.
	Recent head injury or intracerebral haemorrhage.
	Major surgery in preceding 14 days.
	Gastrointestinal bleeding in preceding 21 days.
	Recent myocardial infarction.
3	**Relative contraindications**
	Only minor or rapidly improving stroke symptoms (clearing spontaneously)
	Pregnancy
	Seizure at onset with postictal residual neurological impairments.
	Major surgery or serious trauma within previous 14 days.
	Recent gastrointestinal or urinary tract hemorrhage (within previous 21 days)
	Recent acute myocardial infarction (within previous 3 months)

Onset time is defined as either the witnessed onset of symptoms or the time last known normal if symptom onset was not witnessed.

In patients without recent use of oral anticoagulants or heparin, treatment with IV rtPA can be initiated before availability of coagulation test results but should be discontinued if INR is >1.7 or PT is abnormally elevated by local laboratory standards.

In patients without history of thrombocytopenia, treatment with IV rtPA can be initiated before availability of platelet count but should be discontinued if platelet count is <100,000/mm³.

aPTT indicates activated partial thromboplastin time; CT, computed tomography; ECT, ecarin clotting time; FDA, food and drug administration; INR, international normalized ratio; IV, intravenous; PTT, partial thromboplastin time; rtPA, recombinant tissue plasminogen activator; and TT, thrombin time.

There are additional relative contraindications for patients in 3-4.5-hour window that determine if the patients are eligible for tPA or not.

A primary goal of achieving door to needle time (DTN) within 60 minutes in ≥50% of AIS patients treated with IV alteplase should be established. It may be reasonable to establish a secondary DTN time goal of achieving DTN times within 45 minutes in ≥50% of patients with AIS who were treated with IV alteplase.[18]

Dose of tPA: As per the guidelines infuse 0.9 mg/kg (maximum dose 90 mg) over 60 minutes, with 10% of the dose given as a bolus over 1 minute (Table 2).

Table 2: Administration of rtPA.

S. no.	Variables
1	IV access with two peripheral IV lines (avoid arterial or central line placement).
2	Review eligibility for rtPA.
3	Administer 0.9 mg/kg IV (maximum 90 mg) IV as 10% of total dose by bolus, followed by remainder of total dose over 1 hr.
4	Frequent cuff BP monitoring.
5	No other antithrombotic treatment for 24 hr.
6	For decline in neurologic status or uncontrolled BP, stop infusion, give neurologic disorders cryoprecipitate, and reimage brain emergently.
7.	Avoid urethral catheterization for >2 hrs.

For treatment within 3 hours of stroke onset, alteplase led to a good outcome for 33% vs 23% for control (odds ratio [OR] 1.75, 95% CI 1.35-2.27). The number needed to treat (NNT) for one additional patient to achieve a good outcome was 10.[22]

For treatment from 3 to 4.5 hours, the proportion with a good outcome in the alteplase and control groups was 35% and 30% respectively (OR 1.26, 95% CI 1.05–1.51, NNT 20).[22]

The benefit of intravenous (iv) defibrinogenating agents and of IV fibrinolytic agents other than alteplase and tenecteplase is unproven; therefore, their administration is not recommended outside a clinical trial. Tenecteplase administered as a 0.4 mg/kg single IV bolus has not been proven to be superior or noninferior to alteplase but might be considered as an alternative to alteplase in patients with minor neurological impairment and no major intracranial occlusion.[18]

Complications of intravenous thrombolysis

Complications related to intravenous r-tPA include symptomatic intracranial haemorrhage, major systemic haemorrhage, and angioedema in approximately 6%, 2%, and 5% of patients, respectively. Guidelines recommend strict blood pressure control and serial neurological exams to diagnose intracranial haemorrhage.[23] In the event that an intracranial haemorrhage is suspected it is recommended to stop alteplase infusion and perform stat labs which include a CBC, PT (INR), aPTT, fibrinogen level, and type

and cross-match. An emergent nonenhanced head CT should be performed to evaluate further. Intravenous cryoprecipitate (includes factor VIII), at a dose of 10 U infused over 10–30 minutes (onset in 1 hour, peaks in 12 hours) should be administered and may be repeated for fibrinogen level of <200 mg/dL. Tranexamic acid or ε-aminocaproic acid may also be used. Stat hematology and neurosurgery consultations should be sought. Supportive therapy should continue.[18] Angioedema should be treated like an allergic reaction and emergent intubation may be needed if breathing difficulty is present. Use antihistamines and steroids are recommended in managing angioedema.[18]

ENDOVASCULAR REVASCULARIZATION

Ischemic stroke from large-vessel intracranial occlusion results in high rates of mortality and morbidity. Occlusions in such large vessels (middle cerebral artery [MCA], intracranial internal carotid artery, and the basilar artery) generally involve a large clot volume and often fail to open with IV rtPA alone.

Endovascular mechanical thrombectomy (Figure 3) has been studied as an alternative or adjunctive treatment of acute stroke in patients who are ineligible for, or have contraindications to, thrombolytics or in those who failed to achieve vascular recanalization with IV thrombolytics. In 2015, the results of six randomized trials were published, all demonstrating that endovascular therapy improved clinical outcomes for internal carotid and MCA occlusions proven by CT angiography (CTA), under 6 h from stroke onset, with or without pre-treatment with IV tissue plasminogen activator (tPA). One study concluded that patients were home nearly 2 months earlier if they received endovascular therapy.[7] A combined meta-analysis of all patients in these trials confirmed a large benefit with endovascular therapy (odds ratio [OR], 2.49; 95% confidence interval [CI], 1.76-3.53; p<0.001).[7] The percentage of patients who achieved modified ranking scores of 0-2 (normal or symptomatic but independent) was 46% in the endovascular group and 26.5% in the medical arm. A more recent meta-analysis reveals a mortality benefit as well with thrombectomy. As with IV rtPA treatment, clinical outcome is dependent on time to effective therapy. The odds of a good outcome exceed 3 if groin puncture occurs within 2 h of symptom onset but is only 2 if 8 h elapse. Over 80% of patients who had vessel opening within 1 h of arrival to the emergency department had a good outcome, whereas only one-third had a good outcome if 6 h elapsed. The outcomes from endovascular therapy are likely improved with IV rtPA treatment prior to thrombectomy if the patient is eligible for rtPA and it is safe to administer. Recent data support replacing IV rtPA with IV tenecteplase because its simple bolus administration makes transporting the patient to an endovascular center less cumbersome. Extending the time window beyond 6 h appears to be effective if the patient has specific imaging findings demonstrating good vascular collaterals (CT perfusion or magnetic resonance [MR] perfusion techniques) and can be treated within 24 h. The clinical mismatch in the triage of wake up and late presenting strokes undergoing neurointervention with Trevo (DAWN) trial reported good outcomes more frequently with endovascular therapy than with medical care alone (47 vs 13%, p<0.0001).[7] The endovascular therapy following imaging evaluation for ischemic stroke 3 (DEFUSE-3) trial confirmed these results (45 vs 17%, p<0.001) if treated up to 16 h from stroke onset. Nonrandomized data of thrombectomy for basilar occlusion have found this treatment to be safe up to 24 h from symptom onset and associated with lower 3-month Rankin scores.

Now that endovascular stroke therapy is proven to be effective, the creation of comprehensive stroke centers designed to rapidly identify and treat patients with large-vessel cerebral ischemia is a major focus internationally. Creating geographic systems of care whereby stroke patients are first evaluated at primary stroke centers (which can administer IV rtPA or tenecteplase) then transferred to comprehensive centers if needed, or directly triaged to comprehensive centers based on field assessment, appears to be an effective strategy to improve outcomes.

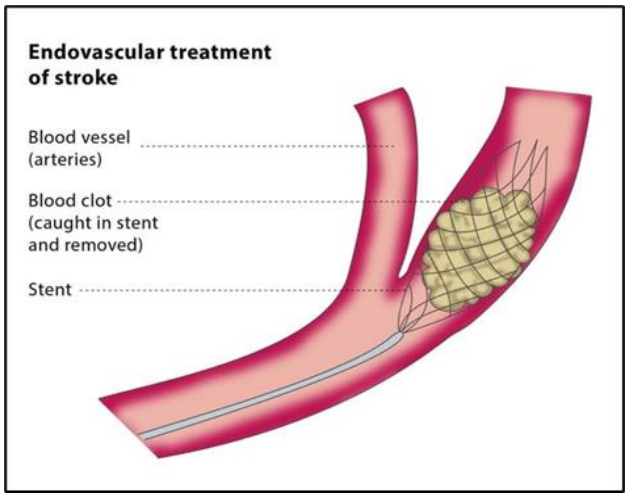

Figure 3: Endovascular treatment of stroke.

ANTITHROMBOTIC TREATMENT

Platelet inhibition

Aspirin is the only antiplatelet agent that has been proven to be effective for the acute treatment of ischemic stroke; there are several antiplatelet agents proven for the secondary prevention of stroke. Two large trials, the international stroke trial (IST) and the Chinese acute stroke trial (CAST), found that the use of aspirin within 48 h of stroke onset reduced both stroke recurrence risk and mortality minimally.[24] Among 19,435 patients in IST, those allocated to aspirin, 300 mg/d, had slightly fewer deaths within 14 days (9.0 vs 9.4%), significantly fewer recurrent ischemic strokes (2.8 vs 3.9%), no excess of haemorrhagic strokes (0.9 vs 0.8%), and a trend toward a

reduction in death or dependence at 6 months (61.2 vs 63.5%). In CAST, 21,106 patients with ischemic stroke received 160 mg/d of aspirin or a placebo for up to 4 weeks. There were very small reductions in the aspirin group in early mortality (3.3 vs 3.9%), recurrent ischemic strokes (1.6 vs 2.1%), and dependency at discharge or death (30.5 vs 31.6%). These trials demonstrate that the use of aspirin in the treatment of AIS is safe and produces a small net benefit. Both proved a decrease in recurrent stroke without a significant increase in haemorrhaging. The recommended dose of aspirin is 325 mg/ day.[25] For every 1000 acute strokes treated with aspirin, ~9 deaths or nonfatal stroke recurrences will be prevented in the first few weeks and ~13 fewer patients will be dead or dependent at 6 months.[7] Combining aspirin with clopidogrel or with ticagrelor following minor stroke or TIA is effective at preventing second stroke. Currently, clopidogrel alone or in combination with aspirin and the intravenous administration of antiplatelet agents that inhibit the glycoprotein IIb/IIIa receptor are class III recommendations. They should not be used outside the setting of clinical trials.[25]

Anticoagulation

Numerous clinical trials have failed to demonstrate any benefit of routine anticoagulation in the primary treatment of atherothrombotic cerebral ischemia and have also shown an increase in the risk of brain and systemic haemorrhage. Therefore, the routine use of heparin or other anticoagulants for patients with atherothrombotic stroke is not warranted. Heparin and oral anticoagulation are likely no more effective than aspirin for stroke associated with arterial dissection. However, there may be benefit of anticoagulation for halting progression of dural sinus thrombosis.

NEUROPROTECTION

Neuroprotection is the concept of providing a treatment that prolongs the brain's tolerance to ischemia. Drugs that block the excitatory amino acid pathways have been shown to protect neurons and glia in animals, but despite multiple human trials, they have not yet been proven to be beneficial. Hypothermia is a powerful neuroprotective treatment in patients with cardiac arrest and is neuroprotective in animal models of stroke, but it has not been adequately studied in patients with ischemic stroke and is associated with an increase in pneumonia rates that could adversely impact stroke outcomes. Hypothermia combined with hemicraniectomy is no more effective than hemicraniectomy with euthermia.

STROKE CENTERS AND REHABILITATION

Patient care in stroke units followed by rehabilitation services improves neurologic outcomes and reduces mortality. Use of clinical pathways and staff dedicated to the stroke patient can improve care. This includes use of standardized stroke order sets. Stroke teams that provide emergency 24-h evaluation of acute stroke patients for acute medical management and consideration of thrombolysis or endovascular treatments are essential components of primary and comprehensive stroke centers, respectively.

Proper rehabilitation of the stroke patient includes early physical, occupational, and speech therapy. It is directed toward educating the patient and family about the patient's neurologic deficit, preventing the complications of immobility (e.g., pneumonia, DVT and pulmonary embolism, pressure sores of the skin, and muscle contractures), and providing encouragement and instruction in overcoming the deficit. Use of pneumatic compression stockings is of proven benefit in reducing risk of DVT and is a safe alternative to heparin. The goal of rehabilitation is to return the patient home and to maximize recovery by providing a safe, progressive regimen suited to the individual patient. Additionally, the use of constrained movement therapy (immobilizing the unaffected side) has been shown to improve hemiparesis following stroke, even years after the stroke, suggesting that physical therapy can recruit unused neural pathways. Controversy exists regarding whether selective serotonin uptake inhibitors improve motor recovery but they may be helpful in preventing poststroke depression. Newer robotic therapies appear promising as well. The human nervous system is more adaptable than previously thought, and developing physical and pharmacologic strategies to enhance long-term neural recovery is an active area of research.

CONCLUSION

Theoretically, comparisons there are in the comprehensive exhibition, pathophysiology and treatment of AIS conditions (since the slightest passing ischemic attack or slight stroke over major ischemic stroke) and acute coronary conditions. Stroke maintenance will have growing significance for neurologists of the forthcoming generations and as a field we have a proportion to suggest, with diagnostic proficiency specifically. Similarly, we could necessitate the advancement of our assistance supplements, such as overall management of intensely ill patients with overall medical difficulties on the acute stroke component or by learning how to achieve mechanical thrombectomy.

Treatment of AIS is period reliant. Effectual and operative stroke maintenance can be contingent on a well-functioning squad from the alternative area to the neurologist and the interventional neurologist. Precise diagnosis, developing treatment to alleviate the patient and precise choice of imagination can make a portion of alteration in the consequence of a patient. Each minute missing in wrong imagination or laboratory test outcomes in diminution of functional consequence can eventually lead to permanent paralysis. Achievement of stroke

management is reliant on the whole squad working effortlessly and professionally. As the periods advance, additional and additional hubs will originate with devoted cardiologists achieve acute myocardial infarction.

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