

Investigation and early treatment of Acute Stroke

BACKGROUND: Stroke is defined by sudden loss of brain function due to interference to the blood supply of the brain or from compression of the brain related to intracerebral or subarachnoid hemorrhage. It is important to recognize that appropriate evaluation and management of patients with stroke can reduce the associated morbidity and risk of recurrence.

METHODS: We review the guidelines for management of patients with ischemic stroke, intracerebral and subarachnoid hemorrhage provided by American Heart Association. We provide a concise account of the general principles of evaluation and management of patients who present with acute stroke.

RESULTS: Since the availability of thrombolytic therapy, it is important to screen all patients with acute stroke for eligibility to receive intravenous (or intraarterial) thrombolysis. Familiarity to mandatory aspects about history, neuroimaging, and laboratory work-up is helpful in expedient decision-making. Appropriate diagnostic tests are important to detect an underlying predisposing condition that can result in recurrent ischemic events. Depending upon the predisposing condition, long-term antiplatelet or anticoagulant therapy can reduce the risk of recurrence.

CONCLUSION: Efforts directed towards appropriate evaluation and management of patients with acute stroke can reduce the associated morbidity and risk of recurrence.

ABSTRACT

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INTRODUCTION

Stroke is defined by a sudden loss of brain function resulting from interference to the blood supply of the brain or from compression of the brain related to intracerebral or subarachnoid hemorrhage. Stroke is the third leading cause of death and the most important cause of disability in the United States. The following article will address the important issues that a clinician faces when evaluating a patient with acute stroke.

Classification of stroke

Stroke is broadly classified into ischemic and hemorrhagic stroke. About 84% of all strokes are ischemic and 16% are hemorrhagic (1). Ischemic strokes result from an interruption of blood flow to the brain from occlusion of the blood

vessel. Hemorrhagic strokes result from bleeding into either the parenchyma of the brain or cerebrospinal spaces such as ventricles or subarachnoid space.

Table 1.

CONDITIONS THAT CAN RESEMBLE ACUTE STROKE

- Intracranial mass lesions (tumors, abscess, arteriovenous malformation)
- Infections (meningitis, encephalitis)
- Demyelinating disease (multiple sclerosis)
- Seizures with post-ictal paralysis
- Complex migraine
- Hypertensive encephalopathy
- Hypoglycemia
- Presyncope or syncope

Presenting symptoms of stroke

The most common symptoms of stroke include visual loss, difficulty in speech, weakness of the face (facial drooping), weakness of the upper and/or lower extremities, numbness affecting one side of the body, vertigo, imbalance, headache, or sudden loss of consciousness. A sudden onset of severe headache (often described as the worst headache of the life) is usually the presenting symptom of subarachnoid hemorrhage. Acute changes in the level of consciousness are usually seen with hemorrhagic strokes including intracerebral or subarachnoid hemorrhage.

ACUTE EVALUATION OF PATIENTS WITH STROKE

Initial assessment of stroke

In the era of thrombolytic therapy, an important issue to be addressed is the time of onset of stroke symptoms. Every attempt should be made to identify what was the time of onset from either the patient or one of the witnesses present at the time of symptom onset. In the patients in whom there is no clearly defined time of onset available, attempts should be made to identify the last time the patient was seen intact. Patients with ischemic stroke presenting within three hours of symptom onset may be candidates for intravenous thrombolysis (2). Patient presenting between three and six hours after symptom onset can be candidates for intra-arterial thrombolysis (3). The patient or the family should also be inquired if the patient has had any symptoms similar to this episode in the past. It is not uncommon for the patients to have presented with previous transient ischemic attacks in similar fashions prior to suffering a major ischemic stroke. The patient's past medical history pertinent to the risk factors that predispose to stroke should be identified. These risk factors include hypertension, diabetes mellitus, cigarette smoking, hyperlipidemia, or underlying heart disease. Because most of the therapies such as thrombolytics, anticoagulants, or antiplatelet therapy increase the risk of patient to develop bleeding, it is important to identify any underlying conditions that predispose the patient to a higher risk of bleeding associated with the use of these medications. These include any recent surgical procedures (within one month), history of gastrointestinal bleeding, underlying hematological abnormalities such as thrombocytopenia, previous hemorrhagic stroke, or use of anticoagulant or antiplatelet medication.

Other conditions that can resemble a stroke

Certain conditions may mimic the presentation of an acute stroke (see table 2). These include seizures with postictal

paralysis, intracranial mass lesions such as tumors, metabolic conditions such as hypoglycemia, or complex migraine with or without the characteristic headaches.

Initial clinical examination

A detailed assessment of level of consciousness, verbal interaction, or response to physical stimulation (if verbal response is nonproductive) should be evaluated. The language func-

Table 2.

SELECTION OF PATIENTS FOR INTRAVENOUS THROMBOLYSIS

❖ Eligible patients include:

- ◆ Symptom onset within 3 hours of evaluation
- ◆ The diagnosis is established by a physician with expertise in diagnosis of stroke and computed tomographic scan of the brain is assessed by physicians with expertise in reading this imaging study.

❖ Thrombolytic use should be avoided in the following patients:

- ◆ Computed tomographic scan demonstrates early changes of a recent major infarction such as sulcal effacement, mass effect, edema, or possible hemorrhage.
- ◆ Current use of oral anticoagulants or a prothrombin time greater than 15 seconds (International Normalized Ratio [INR] greater than 1.7).
- ◆ Use of heparin in the previous 48 hours and a prolonged partial thromboplastin time.
- ◆ A platelet count less than 100 000/mm³.
- ◆ Another stroke or a serious head injury in the previous 3 months
- ◆ Major surgery within the preceding 14 days
- ◆ Pretreatment systolic blood pressure greater than 185 mm Hg or diastolic blood pressure greater than 110 mm Hg
- ◆ Rapidly improving neurological signs.
- ◆ Isolated, mild neurological deficits, such as ataxia alone, sensory loss alone, dysarthria alone, or minimal weakness.
- ◆ Prior intracranial hemorrhage.
- ◆ Blood glucose less than 50 mg/dL or greater than 400 mg/dL.
- ◆ Seizure at the onset of stroke.
- ◆ Gastrointestinal or urinary bleeding within the preceding 21 days.
- ◆ Recent myocardial infarction.

tions should be evaluated in terms of comprehension, repetition, fluency (expression), and naming of objects. The patient should be evaluated for orientation as well as neglect. A detailed cranial nerve exam should be performed to look for any new cranial nerve deficits.

Examination of the motor system should include assessment of tone and strength in all major muscle groups. Certain tests such as evaluation of fine finger movements, pronator drift and lag in wrist rolling are helpful in the patients with subtle deficits. To evaluate for pronator drift, the patient is asked to extend his or her hand in front with the palms facing upwards. Patients in whom a minor stroke has affected one side would tend to pronate the affected arm. The patient can also be asked to rapidly roll their wrists over each other and the affected arm usually shows a lag in the wrist rolling movements. Sensation should be assessed by testing the patient's ability to perceive pinprick bilaterally. Coordination tests such as finger-to-nose testing is also important in the patients with cerebellar or brainstem deficits. Gait should be evaluated in terms of balance as well as strength in the muscles involved. Deep tendon reflexes can be evaluated; however, absence of reflexes on the affected side is the most common finding observed in the initial period.

Immediate neuroimaging and laboratory tests

A laboratory profile evaluating for complete blood count, coagulation profile including prothrombin time and activated partial thromboplastin time, and serum chemistry including sodium, potassium, glucose, chloride, and bicarbonate should be evaluated. The patient should have a 12-lead EKG to evaluate for underlying cardiac rhythm disturbances or coronary ischemia. A non-contrast computed tomographic scan is mandatory in the evaluation of any patient with stroke. The differentiation between ischemic and hemorrhagic stroke cannot be made in the absence of a non-contrast computed tomographic scan. The only exceptions are patients in whom a magnetic resonance imaging can be performed in the acute period following the onset of stroke symptoms.

Non-contrast computed tomographic scan

The computed tomographic scan differentiates between ischemic and hemorrhagic stroke (4). In the patients without hemorrhagic stroke, it is important to evaluate for early evidence of ischemic injury. This evaluation should usually be performed in conjunction with a neuroradiologist or a neurologist. Early signs such as obliteration of the sulcal spaces, breakdown of the gray-white matter junction in the brain parenchyma, or obliteration of deep nuclei such as basal ganglia should be identified. At times, a thrombus can be visualized in the middle cerebral artery, a sign which is known as the dense middle artery sign. In the patients with hemorrhagic stroke, it is important to identify the location of bleeding i.e., whether the bleeding is intraparenchymal, intraventricular or in the subarachnoid space. The presence of any mass effect demonstrated by compression of ventricles and shift of pineal glands should be visualized as well. Hydrocephalus is the condition where the ventricles may be dilated because of impairment of cerebrospinal fluids drainage. This condition should also be identified because rapid treatment with intraventricular catheter may improve the condition of the patient.

ACUTE MANAGEMENT OF PATIENTS WITH STROKE

The following issues need to be addressed at the time of initial evaluation of patients with stroke:

Intubation and mechanical ventilation

It is important to recognize that the patients may have severe neurological deficits or altered their level of consciousness that places them at risk for hypoventilation, hypoxia and aspiration pneumonia. Such secondary injuries worsen the neurological injury caused by ischemic stroke and therefore should be prevented by aggressive monitoring and treatment. During the initial evaluation, the patient's oxygenation should be monitored using transcutaneous oxygen saturation monitor. Special attention should be paid to the patient's level of consciousness and cranial nerve deficits. Patients with altered levels of consciousness or severe cranial nerve deficits are at high risk for respiratory complications and should be intubated electively.

Cardiovascular monitoring and treatment

All patients with acute stroke when they present to the emergency room should be placed on EKG monitoring for continuous monitoring of heart and automated cuff for regular measurements of blood pressure. Patients with acute stroke commonly present with elevated blood pressure. In the patients with ischemic stroke who present with elevated blood pressure, the elevation in blood pressure is the protective response initiated by the brain to increase blood flow to the brain to limit ischemic injury. Therefore, aggressive treatment to lower blood pressure should be avoided. The American Heart Association recommends lowering of blood pressure if the initial systolic blood pressure is greater than 220 mm Hg or mean arterial pressure is greater than 130 mm Hg (4,5). Intravenous medication should be used for better titration and rapid response when treating acute hypertension. Intravenous labetalol (a and b blocker) and hydralazine (direct vasodilator) are the most common medications used in treatment of acute blood pressure. Use of medications such as nitroglycerin or nitrates should be avoided because they can lead to precipitous drop in blood pressure, which can worsen the ischemic injury in the brain. Intravenous nitroprusside can raise intracranial pressure because of intracranial venodilation and should only be considered once intravenous labetalol or hydralazine have failed. In the patients with intracerebral hemorrhage or subarachnoid hemorrhage the blood pressure should be lowered in order to prevent expansion of the hematoma or rebleeding into the subarachnoid space. Blood pressure should be maintained below 180 mm Hg systolic and 105 mm Hg diastolic values in patients with intracerebral hemorrhage (6,7).

Intracranial mass effect and elevated intracranial pressure

In the patients who present with hemorrhagic stroke it is not uncommon to find clinical symptoms of raised intracranial pressure and mass effect such as transtentorial herniation consisting of asymmetrical pupillary dilatation and decreased level of consciousness. These patients should be emergently intubated and mechanically ventilated. Hyperventilation and

intravenous mannitol should be used to treat elevated intracranial pressure. Routine use of hyperventilation and mannitol is discouraged given the adverse effects of each of these modalities.

Neurological and neurosurgical consultations

In the event a stroke is suspected in any patient presenting to the emergency room, the neurologist should be notified for expedited evaluation and consideration of possible treatment options. A neurosurgeon should be involved in the care if the patient has intracerebral or subarachnoid hemorrhage.

Intravenous thrombolysis

A randomized trial demonstrated the benefit of intravenous alteplase (a recombinant tissue plasminogen activator) in the patients with ischemic stroke when administered within three hours of symptom onset (2). A more detailed account is provided in another article in this issue by Khan et al. The criteria for use of intravenous alteplase are listed in the **table 2**. Intravenous alteplase is given in a dose of 0.9 mg/kg; 10% is given as intravenous bolus followed by 90% of

the dose given as intravenous infusion over 60 minutes. Intravenous thrombolysis can result in intracranial hemorrhages if the eligibility criteria are not carefully evaluated. Therefore, it is important to obtain all the pertinent investigations including the computed tomographic scan, laboratory measurements of coagulation profiles, platelet counts, and blood pressure measurements prior to decision-making. The patients who present between three and six hours may be considered for intraarterial thrombolysis. Intraarterial thrombolysis consists of catheter placement via a femoral artery insertion into the affected blood vessels in the brain. In the PROACT II trial (3), the patients who received prourokinase and intraprocedural heparin had a superior outcome when treated within six hours of symptom onset as compared to placebo-treated patients.

Admission to intensive care or stroke unit

All patients with intracerebral hemorrhage or subarachnoid hemorrhage should be admitted to the intensive care unit. The patients with ischemic stroke should be admitted if they have one of the following: 1. A large ischemic stroke with mass effect and herniation; 2. Received intravenous alteplase or intraarterial thrombolysis because of the risk of intracranial hemorrhage; and 3. Manifested cardiovascular instability such as arrhythmias or cardiac failure.

Use of intravenous heparin

Intravenous heparin has not demonstrated any efficacy in treatment of acute

ischemic stroke. Intravenous heparin can be considered in the patients with cardioembolic sources such as atrial fibrillation, valvular diseases or dilated cardiomyopathy to prevent recurrent embolization. The risk of hemorrhagic conversion of an infarcted brain lesion should be considered. In the patients with large ischemic stroke, intravenous heparin should be used after 72 hours of symptom onset. It should also be remembered that most hemorrhagic conversions related to heparin occur when heparin is used in super-therapeutic doses. Therefore heparin boluses are discouraged and initiation of heparin as a constant infusion is favored. A closed monitoring of activated partial thromboplastin time is mandated when heparin therapy is used.

Use of antiplatelet agents

Aspirin or one of the newer antiplatelet agents such as ticlopidine or clopidogrel should be used in the patients with ischemic stroke. These medications can be initiated within 24 hours of onset of the ischemic symptoms. The role of these medications is to prevent

Table 3.

DIAGNOSTIC EVALUATIONS AND UNDERLYING CAUSES IN PATIENTS WITH ISCHEMIC STROKE.

<u>DIAGNOSTIC TEST</u>	<u>SUSPECTED UNDERLYING ETIOLOGIES</u>
Magnetic resonance angiogram	Intracranial stenosis, extracranial stenosis of the vertebral or internal carotid artery
Carotid Doppler ultrasound	Internal carotid artery stenosis
Transeoophageal or transthoracic echocardiography	Mitral valve disease, left atrial septal aneurysm, patent foramen ovale, left atrial thrombus, left ventricular thrombus, dilated cardiomyopathy, aortic plaque, valvular vegetations
Cerebral angiography	Occlusive diseases of intra- or extracranial arteries, vasculitis, intracranial aneurysm, dissection
Prothrombotic states [protein C, protein S, factor V Leiden, antithrombin III, antiphospholipid antibodies, lupus anticoagulant, homocysteine level, hemoglobin electrophoresis, thrombin time]	Hereditary and congenital deficiencies of proteins S and C, antithrombin III, resistance to activated protein C, anti-phospholipid antibody syndrome, sickle cell disease, homocystinuria and homocysteinemia

recurrent ischemic events and directed more towards long-term secondary prevention.

Aggressive treatment of fever and hyperglycemia

Fever and hyperglycemia have been shown to worsen ischemic injury in the brain. Therefore, particular attention should be directed towards early detection of these conditions. Antipyretics should be used to maintain temperature below 100°C. Regular monitoring of serum glucose with regular insulin coverage is required to maintain levels below 200mg/dl.

SUBACUTE MANAGEMENT OF PATIENTS WITH STROKE

Secondary prevention of recurrent stroke

Patients with ischemic stroke require either antiplatelet or anticoagulant treatment for prophylaxis against recurrent stroke. The selection of the treatment is based on the underlying cause for stroke. In the patients with atherosclerotic diseases involving the intracranial circulation or the carotid arteries, antiplatelet agents should be considered. Surgical options such as carotid endarterectomy should in the patients with moderate-to-severe stenosis of the internal carotid artery. In patients with underlying cardiac abnormalities, anticoagulation should be strongly considered particularly in the patients with valvular diseases, dilated cardiomyopathy, mural thrombi, and cardiac arrhythmias such as atrial fibrillation. In the patients with atrial septal defects and aortic atheromatous plaques, antiplatelet treatment can be used. There is no evidence demonstrating the superiority of anticoagulants over antiplatelet treatment in either atrial septal defects or atheromatous aortic lesions. Secondary prevention of stroke also requires modification of risk factors such as hypertension, cigarette smoking, hyperlipidemia, diabetes mellitus, elevate homocysteine levels, and sedentary lifestyle.

Rehabilitation

Early rehabilitation effort should be initiated when the patient is in the hospital to assess the deficits and initiate early mobilization and stretch in range of motion exercises and prevent medical complications. Intensive rehabilitation can be undertaken once the patient is discharged with the goals to restore mobility and daily activity level skills, language, and cognitive coping strategies.

Support services

It is important to evaluate the patient's transition into the community and evaluate the support network, home safety, and adaptor devices and continue home or outpatient therapy.

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