Stroke management

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Introduction

Scope of the guidelines

These National Clinical Guidelines for stroke cover the management of patients with acute stroke and the secondary prevention of stroke. Primary prevention of stroke, rehabilitation and subarachnoid hemorrhage are excluded from the scope of these guidelines. These guidelines cover the management of stroke in adults (over 18 years) from onset to chronic care and focus on patients with a new clinical event (first stroke or recurrent stroke).

Goal and objectives of the guidelines

The primary goal of the guidelines is to continuously improve the quality of care in patients with stroke nationally. Our intention is closing the gap between best practice and actual practice.

The objective of the guidelines is to provide clinicians and administrators with explicit statements, where evidence is available, on the best way to manage specific problems. Local health service facilities (e.g. hospitals, nursing homes, etc.) will need to add detail.

The guidelines are directed primarily at practising clinicians involved in management of patients with stroke. Their aim is to help clinicians, at any level – primary, secondary or tertiary – to make the best decisions for each patient, using the evidence currently available. The focus is on the more common clinical questions faced in day-to-day practice. The guidelines may be used by all health professionals or health care planners involved in the management of the patients with stroke.

The secondary objectives of the guidelines are to identify areas where gaps in knowledge or lack of evidence exist and to stimulate research in each area.

The guidelines are concerned with the management of patients who present with a new clinical event that might be stroke. Stroke in this context is defined as 'a clinical syndrome characterized by rapidly developing signs and symptoms of focal or at times global loss (as in subarachnoid hemorrhage or brain stem involvement) of cerebral brain functions, lasting more than 24 hours or leading to death, with no apparent cause other than of vascular origin.'

While appraisal of evidence forms the basis of the development of these guidelines, we wish to clarify some points:

- Evidence related to drugs is generally stronger, because it is methodologically easier to study each intervention in contrast to studying complex intervention like occupational therapy, health education or nursing care. These do not necessarily mean that interventions with so called strong evidence are more important than those where the evidence is weak.
- We believe that highest level of evidence is not always required to make strong recommendation. If the intervention is safe, logic is strong and effect is obvious, the level of evidence desirable to make strong recommendation may be lower than the highest.
- We recognize that many areas of clinical importance may not have evidence available to construct guidelines, and the recommendations represent a consensus from the working group on such areas.

The working group is aware of recent developments in evaluating levels of evidence and strength of recommendations, and also that the GRADE methodology has been adopted by more than 25 organizations around the world including the WHO. The group endorses the use of GRADE methodology (Guyatt and Oxman)[1] for this purpose and will incorporate this in the next version of the guidelines.

Context and use

These guidelines should be taken as statements to inform the clinician, not as rigid rules. Practitioners may need to deviate from the guidelines in individual cases but such deviations should be justifiable and justified.

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The guidelines may be used to inform decisions on standards of good practice and are likely to be used for audit of stroke services. Before the guidelines are used as 'standards', it is important to ensure that the relevance and appropriateness of the guidelines are discussed in the context proposed.

These guidelines do not cover specific management of associated illnesses like diabetes mellitus, cardiac problems and others as these may addressed by guidelines from related organizations or are generally expected from a physician.

Guidelines for Organization of Services for Stroke Care

Stroke care may be organized at three levels - a basic stroke care facility, a primary stroke care facility and a comprehensive stroke care facility. The basic stroke care facility should be the minimum setup at district hospitals; primary stroke care facility should be mandatory for all medical colleges and multispeciality hospitals; and well-equipped hospitals including some medical colleges should develop comprehensive stroke care facilities. The basic stroke facility may not have artificial ventilators, echocardiography and carotid Doppler facility, primary stroke care facilities may have these facilities but not neurosurgery, MRI or angiography. Comprehensive stroke care facilities should have all these facilities.

Recommendations

Patient care services

Acute stroke team

- At a minimum, includes a physician and another health care professional (i.e., nurse, physician). In addition, a physiotherapist is essential for rehabilitation.
- Team personnel should have experience, expertise and special interest in diagnosis and treatment of stroke patients.
- Team should be available 24 × 7 and a member of the team should be at patient bedside within 15 minutes of being called.

Written care protocols

- Protocols should be made available for rt-PA use in acute stroke.
- Protocols for emergency care, diagnostic tests, stabilization of vital functions and use of medication should be made available.
- Protocols should be reviewed and updated at least once a year.

Emergency medical services (EMS) should be developed and upgraded for stroke care at the hospital or district level to include transport and triage of patients from peripheral medical centers.

Emergency department

- ED personnel should be trained to diagnose and treat all types of stroke.
- ED should have good communication with the EMS and the acute stroke team
- ED personnel should undergo educational activities related to stroke diagnosis and management at least twice a year.

Stroke unit

- Should consist of a hospital unit with specially trained staff and a multidisciplinary approach to treatment and care of stroke patients.
- Should be able to admit patients in the unstable phase, monitor the vital and neurological parameters, diagnose the etiology and subtype, treat and discharge patients with advice on physiotherapy and secondary prevention.
- Should transfer severely ill and stuporous patients including those with raised intracranial pressure (ICP) and with unstable cardiopulmonary status to intensive care.
- Should consider using telemedicine to improve access to treatment in rural and remote areas.

Neurosurgical services

- Comprehensive stroke care facilities should have 24 × 7 on call neurosurgeon to evaluate and operate in cases requiring such consultation and neurosurgery.
- A primary stroke care facility should have neurosurgical care available as early as possible (<2 hours). The patient should either be transferred to a neurosurgical care facility or should be able to call in a neurosurgeon within 2 hours.
- A written protocol for transfer plan should be available.
- The hospital with neurosurgical facility should be having 24 hours operating facility and support personnel (anesthesia, radiology, laboratory services, etc.).

Support services

- Neuroimaging: All levels of stroke care facilities should have the capability of performing or access to either a cranial computed tomography (CT scan) or magnetic resonance imaging (MRI) scan within 30 minutes of the order being written with experienced physicians or a radiologist to interpret the imaging reports.
- Laboratory services to perform routine blood tests, coagulation studies, ECG and chest roentgenograms with 24-hour services. The lab results should be available within 45 minutes of being ordered.
- Commitment and Support of the Organization/Institution should be available toward the stroke care facility and the stroke unit should have a designated medical director/ incharge with expertise in stroke.
- Educational programs periodically and annual programs for the stroke team should be instituted and public education about prevention, recognition and management of stroke should be carried out.

Evidence: Albers,[2] Alberts,[3] Audebert,[4] Calvet,[5] Evans,[6] Intercollegiate Stroke Working Party,[7] Katzan,[8] Koton,[9] LaMonte,[10] Prabhakaran,[11] Purroy,[12] Ronning,[13] Silva,[14] Stavem,[15] Stroke Unit Trialists' Collaboration.[16]

Acute Phase Care

Admission to hospital

Most patients with stroke should be admitted to a hospital because their neurological condition may worsen over the first

few days, they may develop non-neurological complications (e.g., aspiration pneumonia), and urgent investigations (like CT scan) may be required.

Recommendations

Patients with acute stroke (onset within last 72 hours or altered consciousness due to stroke) should be admitted to hospital for initial care and assessment. Circumstances where a physician might reasonably choose *not to* admit selected patients with stroke include the following:

- Individuals with severe pre-existing irreversible disability (e.g., severe untreatable dementia), or terminal illnesses (e.g., cancer), who have options to be cared at lower level health care facility.
- Alert patients with mild neurological deficits (not secondary to ruptured saccular aneurysm) who are identified more than 72 hours after onset of symptoms, who can be evaluated expeditiously as outpatients, and who are unlikely to require surgery, invasive radiological procedures or anticoagulation;
- Patients with mild neurological deficits in whom a history and examination is consistent with lacunar stroke syndrome, and a CT scan that either is normal or shows old lacunar infarcts. However, they should be evaluated expeditiously as outpatients.

Diagnosis and management of resolved or rapidly resolving acute neurological event

- Patients who are first seen after fully resolved or rapidly resolving neurological symptoms need diagnosis to determine whether in fact the cause is vascular (about 50% are not) and then to identify treatable causes that can reduce the risk of stroke (greatest in first 7-14 days).
- Any patient who presents with transient symptoms suggestive of a cerebrovascular event should be considered to have had a transient ischemic attack (TIA), unless neuroimaging reveals an alternative diagnosis.
- All such patients except those with transient monocular blindness should have imaging of brain, either CT scan or MRI. Patients presenting with transient monocular blindness (amaurosis fugax) must have a complete ophthalmological examination to exclude primary disorders of the eye before diagnosis of TIA.
- Patients who have had a TIA should be assessed as soon as possible for their risk of subsequent stroke using a validated scoring system, such as $ABCD^2$ (Refer to Appendix -1).
- All patients with history of TIA should be started on aspirin 150 or 300 mg daily or Clopidogrel (75 mg) once a day in case of aspirin allergy; and those at high risk of stroke ($ABCD^2$ score of 4 or above) should be assessed at primary or comprehensive stroke care facility within 24 hours for further management (as indicated under heading 'Secondary Prevention'). Those at lower risk should be assessed within 1 week of onset of symptoms.
- Patients with crescendo TIA (two or more TIAs in a week) should be treated as being at high risk of stroke, even though they may have $ABCD^2$ score of 3 or below.
- Patients who have had a TIA but who present more than one week after their last symptom has resolved should be treated as those with $ABCD^2$ score of 3 or below.
- All patients with TIA should be managed as indicated under the heading 'Secondary Prevention'.

Evidence: Bray,[17] Cucchiara,[18] Lavallee,[19] Rothwell.[20]

Diagnosis of acute persistent cerebrovascular event

The aims of emergent evaluation are to:

- Separate stroke (a vascular event) from other causes of rapid onset neurological dysfunction (stroke mimics);
- Provide information about pathology (hemorrhage vs. ischemia);
- Give clues about the most likely etiology;
- Predict the likelihood of immediate complications; and
- Plan appropriate treatment.
- It should be recognized that 'stroke' is primarily a clinical diagnosis and that the diagnosis should be made with special care:
  - In the young;
  - If the sensorium is altered in presence of mild to moderate hemiparesis;
  - If the history is uncertain; or
  - If there are other unusual clinical features such as gradual progression over days, unexplained fever or papilloedema.

History, physical examination and common investigations

- History should follow usual routine. Special attention should be paid to onset of symptoms, recent stroke, myocardial infarction, seizure, trauma, surgery, bleeding, pregnancy and use of anticoagulation/insulin/antihypertensive, history of modifiable risk actors: Hypertension, diabetes, smoking, heart disease, hyperlipidemia, migraine and history of headache or vomiting, recent child birth and risk of dehydration.
- Physical examination should be on usual lines with special attention to ABC (airway, breathing, circulation), temperature, oxygen saturation, sign of head trauma (contusions), seizure (tongue laceration), carotid bruits, peripheral pulses, cardiac auscultation, evidence of petechiae, purpura or jaundice.
- Validated stroke scales like NIHSS may be used to determine the degree of neurological deficit.
- All patients should have neuroimaging, complete blood count, blood glucose, urea, serum creatinine, serum electrolytes, ECG and markers of cardiac ischemia. Selected patients may require liver function tests, chest radiography, arterial blood gases, EEG, lumbar puncture, blood alcohol level, toxicology studies or pregnancy test.
- All patients should have their clinical course monitored and any patient whose clinical course is unusual for stroke should be reassessed for possible alternative diagnosis.

Brain imaging should be performed immediately for patients with persistent neurological symptoms if any of the following apply:

- Indication for thrombolysis or early anticoagulation.
- On anticoagulant treatment.
- A known bleeding tendency.
  - A depressed level of consciousness (GCS below 13).
  - Severe headache at onset of stroke symptoms.
  - Papilloedema, neck stiffness, subhyaloid hemorrhage or fever.

Patients with acute stroke without the above indications for

immediate brain imaging, scanning should be performed within 24 hours after onset of symptoms.

Evidence: Intercollegiate stroke working party,[7] Wardlaw.[21]

Immediate specific management of ischemic stroke

All patients with disabling acute ischemic stroke who can be treated within 3 hours (4.5 hours as soon as approved by the Drug Controlling authority) after symptom onset should be evaluated without delay to determine their eligibility for treatment with intravenous tissue plasminogen activator (alteplase).

- Please see Appendix - 2 for detailed recommendation on thrombolytic therapy.
- All acute stroke patients should be given at least 150 mg of aspirin immediately after brain imaging has excluded intracranial hemorrhage (In patients with t-PA, aspirin should be delayed until after the 24-hour post-thrombolysis).
- In patients with large hemispheric infarct (malignant MCA territory infarct), aspirin may be delayed until surgery or decision is made not to operate.
- In dysphagic patients, aspirin may be given by enteral tube.
- Aspirin (at least 150 mg) should be continued until 2 weeks after the onset of stroke symptoms, at which time any antiplatelet or anticoagulant agent is started as indicated in 'secondary prevention'.
- Any patient with acute ischemic stroke who is known to have dyspepsia with aspirin should be given a proton pump inhibitor in addition to aspirin (also see 'secondary prevention').

Evidence: CAST,[22] ECASS III - Hacke,[23] Hill,[24] IST-3 Whiteley,[25] National Institute for Health and Clinical Excellence,[26] NINDS.[27]

Surgery for ischaemic stroke

Patients with middle cerebral artery (MCA) infarction who meet all of the criteria below should be considered for decompressive hemicraniectomy and operated within a maximum of 48 hours:

- Age 60 years or below.
- NIHSS score of above 15.
- Decrease in the level of consciousness to give a score of 1 or more on item 1a of NIHSS, or GCS score between 6 and 13.
- CT scan showing signs of an infarct of at least 50% of the MCA territory, with or without infraction in the territory of anterior or posterior cerebral artery on the same side or diffusion-weighted MRI showing infarct volume >145cm^3.

Patients with large cerebellar infarct causing compression of brainstem and altered consciousness should be surgically managed with suboccipital craniectomy.

Symptomatic hydrocephalus should be treated surgically with ventriculostomy.

Evidence: DECIMAL, DESTINY, HAMLET - Gupta,[28] Jüttler,[29] Vahedi.[30]

Hemodilution and neuroprotection:

- Hemodilution therapy is not recommended for the management of patients with acute ischemic stroke.
- No neuroprotective drug is recommended outside the setting of randomized clinical studies.

Evidence: Davalos,[31] Muir,[32] Shuaib.[33]

Immediate specific management of intracerebral hemorrhage (ICH)

ICH related to antithrombotic or fibrinolytic therapy

- ICH related to intravenous heparin requires rapid normalization of a-PTT by protamine sulphate (1 mg/100 U of heparin) with adjustment of dose according to time elapsed since the last heparin dose: For 30 to 60 min : 0.5 to 0.75 mg; for 60 to 120 min: 0.375 to 0.5 mg, for >120 min 0.25-0.3/mg). Protamine sulfate is given by slow i.v. not to exceed 5 mg/min (maximum of 50 mg). Protamine sulfate may also be used for ICH related to use of subcutaneous low molecular weight heparin.
- Patients with warfarin related ICH should be managed with vitamin K, fresh frozen plasma (FFP) and wherever available prothrombin complex concentrate. Vitamin K (10 mg i.v.) should not be used alone because it takes at least 6 hours to normalize the INR. FFP (15-20 ml/kg) is an effective way of correcting INR, but there is risk of volume overload and heart failure. Prothrombin complex concentrate and factor IX complex concentrate require smaller volumes of infusion than FFP (and correct the coagulopathy faster but with greater risk of thromboembolism).
- Patients with ICH related to thrombolysis should be treated with infusion of platelets and cryoprecipitate as indicated in Appendix-2.

Evidence: Cartmill,[34] Goldstein,[35] Huttner,[36] Fredriksson,[37] Yasaka.[38]

Restarting warfarin

- Patients with a very high risk of thromboembolism (those with mechanical heart valves), warfarin therapy may be restarted at 7-10 days after onset of the index ICH. Those with lower risk may be restarted on antiplatelet therapy.

Evidence: Gubitz 4,[39] Phan.[40]

Surgery for ICH

- Patients with cerebellar hemorrhage (>3 cm in diameter) who are deteriorating neurologically or who have signs of brain stem dysfunction should have suboccipital craniectomy and surgical evacuation of hematoma.
- Patients with supratentorial ICH causing midline shift and/or herniation with impairment of consciousness or deteriorating neurologically should have surgical evacuation of hematoma within 72 hours of onset of symptoms, unless they were dependent on others for activities of daily living prior to the event or their GCS is <6 (unless this is because of hydrocephalus).
- Patients with hydrocephalus who are symptomatic from ventricular obstruction should undergo ventriculostomy.

Evidence: Auer 1989,[41] Mendelow,[42] Prasad,[43] Prasad.[44]

Acute arterial dissection

- Any patient suspected of having arterial dissection should be investigated with appropriate imaging (MRI and MRA).
- People with stroke secondary to arterial dissection should be treated with either anticoagulants or antiplatelet agents. In selected patients, stenting may be indicated.

Evidence: Arauz,[45] Desfontaines,[46] Han,[47] Lyrer.[48]

Cardioembolic stroke

- Patients with disabling ischemic stroke who are in atrial fibrillation should be treated with aspirin 300 mg for the first 2 weeks before starting anticoagulation.
- In patients with prosthetic valves who have disabling cerebral infarction and who are at significant risk of hemorrhage transformation, anticoagulation treatment should be stopped for one week and aspirin 150-300 mg should be substituted.
- Some experts, despite lack of evidence, recommend starting heparin within 48 hours of onset of cardioembolic stroke, except in patients with large infarctions.

Evidence: Butler,[49] Evans,[50] Hart,[51] Intercollegiate Stroke Working Party,[7] Scottish Intercollegiate Guidelines Network.[52]

Cerebral venous thrombosis

- Patients suspected to have stroke due to cerebral venous thrombosis should be investigated by MRI/MRV/CTV only if not diagnosed by CT scan.
- Patients diagnosed with stroke due to cerebral venous thrombosis (with or without hemorrhagic infarct or secondary cerebral hemorrhage) should be given full-dose anticoagulation (initially heparin and then warfarin [INR 2-3]) unless there are contraindications.

Evidence: Bousser,[53] Stam.[54]

Physiological Homeostasis (Oxygen, temperature, blood pressure, glucose)

Supplemental oxygen therapy

- Patients should receive supplemental oxygen if their oxygen saturation drops below 95%.

Evidence: Chiu,[55] Ronning.[56]

Management of body temperature

Recommendation

- Temperature should be monitored every 4 hours for at least first 48 hours and preferably as long as the patient is in the ward.
- Fever (>37.5ºC) should be treated with paracetamol. The search for possible infection (site and cause) should be made.
- Hypothermia <34ºC should be avoided as it can lead to coagulopathies, electrolyte imbalance, infection and cardiac arrhythmias.

Evidence : Castillo,[57] Fukuda,[58] Hajat,[59] Reith.[60]

Management of blood pressure

Ischemic stroke

- In acute ischemic stroke, paraenteral antihypertensive medication should be recommended only if there is a hypertensive emergency with one or more of the following serious concomitant medical issues:
  - hypertensive encephalopathy
  - hypertensive nephropathy
  - hypertensive cardiac failure/myocardial infarction
  - aortic dissection
  - pre-eclampsia/eclampsia
  - intracerebral hemorrhage with systolic blood pressure (SBP) over 200 mmHg.

- Antihypertensive medication should be withheld in ischemic stroke patients unless SBP is >220 mmHg or the mean arterial blood pressure (MAP) is >120 mmHg. Lowering by approx 15% during the first 24 hours is recommended.
- Except in hypertensive emergency, lowering of blood pressure should be slow and with use of oral medications.
- Sublingual use of antihypertensives is not recommended.
- Blood pressure reduction to 185/110 mmHg or lower should be considered in people who are candidates for thrombolysis.

Intracranial hemorrhage

- If SBP is >200 mmHg or MAP is >150 mmHg (recorded twice, two or more minutes apart), then blood pressure should be aggressively treated with parenteral antihypertensives (e.g., labetolol or nitroglycerin).
- If SBP is >180 mmHg or MAP is >130 mmHg (up to 150 mm Hg), then a modest reduction is advised with rapidly acting oral or parenteral medication or nitroglycerin patch.
- Target BP should be 160/90 or MAP of 110 mmHg.

Evidence: Ahmed,[61] Bath,[62] Horn,[63] Schrader.[64]

Management of blood glucose

Recommendation

- The blood glucose level should be maintained between 70 and 190 mg/dL. Elevated blood glucose >140 mg/dL should be managed with insulin administration using the sliding scale in the first week of stroke onset.
- Hypoglycemia should be monitored and accordingly 20% glucose (50 ml bolus) should be administered.

Evidence: Bruno,[65] Gray,[66] National Institute for Health and Clinical Excellence.[67]

Cerebral edema and increased intracranial pressure

Until more data are available

- Corticosteroids are not recommended for the management of cerebral edema and increased ICP following stroke.
- In patients whose condition is deteriorating secondary to increased ICP, including those with herniation syndromes, various options include: Hyperventilation, mannitol, furosemide, CSF drainage and surgery. If CT scan (first or repeat one after deterioration) suggests hydrocephalus as the cause of increased ICP, then continuous drainage of CSF can be used.
- Initial care includes mild restriction of fluids, elevation of head end of the bed by 20 to 30 degrees and correction of factors that might exacerbate increased ICP (e.g. hypoxia,

hypercarbia and hyperthermia).
- Hyperventilation acts immediately (reduction of the pCO_2 by 5-10 mmHg lowers ICP by 25-30%) but should be followed by another intervention to control brain edema and ICP. Hyperventilation can cause vasoconstriction that might aggravate ischemia. An intravenous bolus of 40 mg furosemide may be used in patients whose condition is rapidly deteriorating. If required, furosemide 20 mg (once daily) may be continued for the first week, Acetazolamide 250 mg (BD) may be added in those not responding to other treatment methods.
- Strict intake-output chart must be maintained to avoid dehydration.
- Mannitol (0.5 gm/kg IV given over 20 minutes) can be given every 6-8 hours. If clinically indicated, dose frequency may be increased to every 4 hours, but then the central venous pressure should be monitored and kept between 5 and 12 mmHg to prevent hypovolemia. This may be continued for 3-5 days.

Evidence: Bereczki,[68] Broderick,[69] Qizilbash,[70] Tyson.[71]

General Early Supportive Care

Position
- Patients should be advised to undertake activities like sitting, standing or walking only with caution. An occasional patient, who deteriorates on assuming sitting or standing posture, should be advised bed rest.
- Non-ambulatory patient should be positioned to minimize the risk of complications such as contractures, respiratory complications, shoulder pain and pressure sores etc.

Evidence : Turkington,[72] Tyson.[71]

Swallowing
- Please see Appendix- 3 for detailed recommendation on bedside swallowing assessment.
- All conscious patients should have assessment of the ability to swallow. A water swallow test performed at the bedside is sufficient (e.g. 50 ml water swallow test)
- Testing the gag reflex is invalid as a test of swallowing.
- Patients with normal swallow should be assessed for the most suitable posture and equipment to facilitate feeding. Any patient with abnormal swallow should be fed using a nasogastric tube.
- Gastrostomy feeding should be considered for patients who are unable to tolerate nasogastric tube.
- Patients with altered sensorium should be given only intravenous fluids (Dextrose saline or normal saline) for at least 2-3 days.

Evidence: Dennis,[73] Hamidon,[74] Norton,[75] Paciaroni,[76] Smithard.[77]

Oral care
- All stroke patients should have an oral/dental assessment including dentures, signs of dental disease, etc., upon or soon after admission.
- For patients wearing a full or partial denture, it should be determined if they have the neuromotor skills to safely wear and use the appliance(s).
- An appropriate oral care protocol should be used for every patient with stroke, including those who use dentures. The oral care protocol should address areas including frequency of oral care (twice per day or more), types of oral care products (toothpaste, floss and mouthwash) and specific management for patients with dysphagia.
- If concerns are identified with oral health and/or appliances, patients should be referred to a dentist for consultation and management as soon as possible.

Evidence: Brady.[78]

Early mobilization
- Passive full-range-of-motion exercises for paralyzed limbs can be started during the first 24 hours.
- All patients should be referred to a physiotherapist/ rehabilitation team as soon as possible, preferably within 48 hours of admission.
- The patient's need in relation to moving and handling should be assessed within 48 hours of admission.

Evidence: Fang,[79] Richards.[80]

Nutrition
- Every patient should have his/her nutritional status determined using valid nutritional screening method within 48 hours of admission.
- Nutritional support should be considered in any malnourished patient.

Evidence: Davalos,[81] Gariballa,[82] Milne,[83] National Institute for Health and Clinical Excellence.[84]

Management of seizures
- Patients with seizure, even single should be treated with loading dose of phenytoin (15-20 mg/kg) followed by maintenance dose 5 mg/kg per day for a period of at least 3 months. If needed, carbamazepine or sodium valproate may be added. Status epilepticus should be treated as per its guidelines. At present there is insufficient data to comment on the prophylactic administration of anticonvulsants to patients with recent stroke.

Evidence: Meierkord,[85] Passero,[86] Vespa.[87].

Venous thromboembolism
Prophylaxis
- Patients with paralyzed legs (due to ischemic stroke) should be given standard heparin (5000 units subcutaneous b.d.) or low-molecular weight heparin (with appropriate prophylactic doses as per agent) to prevent deep vein thrombosis (DVT).
- For those who cannot tolerate heparin, aspirin given for treatment is of some prophylactic value.
- In patients with paralyzed legs (due to ICH), routine physiotherapy and early mobilization should be carried out to prevent leg vein thrombosis.
- Early mobilization and optimal hydration should be maintained for all acute stroke patients.
- CLOTS trial data does not support the routine use of thigh

length graduated compression stockings for prevention of DVT.

Treatment
- Standard heparin (5000 U i.v.) or low molecular weight heparin (with appropriate therapeutic doses as per agent) should be started initially. When standard heparin is used, a prior baseline complete blood count and a-PTT should be done and a rebolus (80 U/kg/h) and maintenance infusion (18 U/kg/h) should be given (target a-PTT of 1.5 times the control value).
- Anticoagulation (warfarin 5 mg once daily) should be started simultaneously unless contraindicated and the dose should be adjusted subsequently to achieve a target INR of 2.5 (range 2.0-3.0), when heparin should be stopped.

Evidence: Berge,[88] CLOTS,[89] Gubitz.[39]

Bladder care
- An indwelling catheter should be avoided as far as possible and if used, indwelling catheters should be assessed daily and removed as soon as possible.
- Intermittent catheterization should be used for urinary retention or incontinence.
- The use of portable ultrasound is recommended as preferred non-invasive method for assessing post-void residual urine.

Evidence: Thomas[90]

Bowel care
- Patient with bowel incontinence should be assessed for other causes of incontinence including impacted feces with spurious diarrhea.
- Patients with severe constipation should have a drug review to minimize use of constipating drugs, be given advice on diet, fluid intake and exercise (as much as possible), be offered oral laxatives and be offered rectal laxatives only if severe problems remain.

Evidence: Coggrave[91]

Infections
- Development of fever after stroke should prompt a search for pneumonia, urinary tract infection or DVT.
- Prophylactic administration of antibiotics is not recommended.
- Appropriate antibiotic therapy should be administered early (after taking relevant culture specimens).

Evidence: Chamorro.[92]

Discharge planning
- Discharge planning should be initiated as soon as a patient is stable.
- Patients and families should be prepared and fully involved.
- Care givers should receive all necessary training in caring for it.
- Patients should be given information about discharge issues and explained the need for and timing of follow up after discharge.

Evidence: Grasel,[93] Langhorne,[94] Larsen.[95]

Secondary Prevention

This includes measures to reduce the risk of recurrence of stroke in patients who have had TIA or stroke. These guidelines apply to vast majority of patients with TIA or stroke, although some of the recommendations may not be appropriate for those with unusual causes of stroke, like trauma, infections, etc.

Every patient should be evaluated for modifiable risk factors within one week of onset. This includes:
- Hypertension
- Diabetes mellitus
- Smoking
- Carotid artery stenosis (for those with non-disabling stroke)
- Atrial fibrillation or other arrhythmias
- Structural cardiac disease

In any patient where no risk factor is found, consideration for investigating for rare causes may be given. The investigations may include anti-phospholipid antibodies, protein C,S and anti-thrombin III.

Evidence: Coull,[96] Johnston,[97] Koton,[98] Lovett.[99]

Antiplatelet therapy
- All patients with ischemic stroke or TIA should receive antiplatelet therapy unless there is indication for anticoagulation.
- Aspirin (30-300 mg/day) or combination of aspirin (25 mg) and extended release dipyridamole (200 mg) twice or clopidogrel (75 mg OD) are all acceptable options for initial therapy. The clinician should be guided by his own preference coupled with the affordability and tolerance of the patient.
- In children, the maintenance dose of aspirin is 3-5 mg/kg per day.
- Combined aspirin-extended release dipyridamole as well as clopidogrel is marginally more effective than aspirin in preventing vascular events.
- The combination of aspirin and clopidogrel increases the risk of hemorrhage and is not recommended unless there is indication for this therapy (i.e., coronary stent or acute coronary syndromes).
- Addition of proton pump inhibitor should not be routine and should only be considered when there is dyspepsia or other significant risk of gastrointesinal bleeding with aspirin.

Evidence: CAPRIE,[100] CHARISMA Bhatt *et al*,[101] ESPS,[102] ESPS-2,[103] ESPIRIT,[104] MATCH – Fisher.[105]

Anticoagulation
- Anticoagulation should be started in every patient with atrial fibrillation (valvular or non-valvular) unless contraindicated, if they are likely to be compliant with the required monitoring and are not at high risk for bleeding. Aspirin also provides some protection if there are constraints to the use of oral anticoagulation. [Table 1].

- Anticoagulation should be considered for all patients who have ischemic stroke associated with mitral valve disease, prosthetic heart valves, or within 3 months of myocardial infarction.
- Anticoagulation should not be started until brain imaging has excluded hemorrhage, and 14 days have passed from the onset of a disabling ischemic stroke (except when a demonstrable intracardiac thrombus is present).
- Anticoagulation should not be used for patients in sinus rhythm unless cardiac embolism is suspected.
- For effective anticoagulation target, INR is 2.5 (range 2.0-3.0) except for mechanical cardiac valves (3.0: range 2.5-3.5).

Evidence: Antithrombotic Trialists' Collaboration,[106] De Schryver,[107] ESPRIT,[104] Hankey,[108] Ringleb,[109] Saxena.[110]

Blood pressure lowering

- Blood pressure lowering treatment is recommended for all patients with history of TIA or stroke. The benefit extends to persons with or without a history of hypertension. The treatment should be initiated (or modified) prior to discharge from hospital in hospitalized and at the time of first medical assessment in non-hospitalized patients.
- An optimal target for these patients is 130/80 mmHg, but for patients known to have bilateral severe (>70%) internal carotid artery stenosis, SBP of 150 mmHg may be appropriate.
- The optimal drug regimen is uncertain; however the available data supports the use of diuretics or the combination of diuretics and an ACEI.

Evidence: ALLAHAT,[111] Blood Pressure Lowering Treatment Trialists' Collaboration,[112] EXPRESS – Rothwell,[113] HOPE,[114] PROGRESS.[115]

Carotid intervention

- Patients with TIA or non-disabling stroke and ipsilateral 70-99% internal carotid artery stenosis (measured by two concordant non-invasive imaging modalities or on a catheter angiogram) should be offered carotid endarterectomy or stenting (see below) within 2 weeks of the incident event unless contraindicated.
- Carotid intervention is recommended for selected patients with moderate (50-69%) stenosis in symptomatic patients.
- Carotid ultrasound / angiogram should be performed on all patients who would be considered for carotid endarterectomy or angioplasty.
- Carotid endarterectomy should be performed by a surgeon with a known perioperative morbidity and mortality of <6%.
- Carotid angioplasty and/or stenting should be considered for patients who are not operative candidates for technical, anatomic or medical reasons or when adequate surgical expertise is not available.
- Carotid intervention is not recommended for patients with mild (<50%) stenosis.
- All those with carotid stenosis should receive all secondary prevention measures, whether or not they receive carotid intervention.

Evidence: Cina,[116] ECST,[117] Ederle,[118] Fairhead,[119] NASCET - Eliasziw,[120] Inzitari,[121] Paty,[122] Rothwell.[123]

Lipid lowering therapy

- All patients with history of TIA or ischemic stroke should be treated with a statin if they have a total cholesterol of > 200 mg%, or LDL cholesterol > 100 mg%.
- The treatment goals should be a total cholesterol of <200 mg%, and LDL cholesterol of <100 mg% (<70 mg% for very high risk individuals).
- Treatment with statin therapy should be avoided or used with caution in patients with history of hemorrhgic stroke.

Evidence: Baigent,[124] Collins,[125] HPS,[126] SPARCL - Amarenco.[127,128]

Lifestyle measures

- All patients who smoke should be advised to stop smoking and to avoid environmental smoke.
- All patients who can do regular exercise should be advised to do so for at least 30 minutes each day. They should be advised to start with low intensity exercise and gradually increase to moderate levels (sufficient to become slightly breathless).
- All patients should be advised to use low fat dairy products and products based on vegetable and plant oils, and reduce intake of red meat.
- Patients' body mass index or waist circumference should be measured, and those who are overweight or obese should be offered advice and support to lose weight.
- All patients, but especially those with hypertension, should be advised to reduce their salt intake by not adding extra table salt to food, using as little as possible in cooking, and avoiding preserved foods, pickles etc. and choosing low salt foods.
- Patients who drink alcohol should be advised to keep within recognized safe drinking limits of no more than three units per day for men and two units per day for women.

Evidence: Brunner,[129] He,[130] Hooper,[131] Lancaster,[132] Rice,[133] Silagy,[134] Toole,[135] Wang.[136]

Appendix-1

ABCD and ABCD2 Prognostic score to identify people at high risk of stroke after a TIA. It is calculated based on:

A – age (≥60 years, 1 point).

B – blood pressure at presentation (≥140/90 mmHg, 1 point).

C – clinical features (unilateral weakness, 2 points or speech disturbance without weakness, 1 point).

D – duration of symptoms (≥60 minutes, 2 points or 10–59 minutes, 1 point).

The calculation of ABCD2 also includes the presence of diabetes (1 point). Total scores range from 0 (low risk) to 7 (high risk).

Appendix - 2

Recommendation on thrombolytic therapy

Prerequisites and criteria for inclusion:

1. Diagnosis of acute ischemic stroke.
2. No evidence of hemorrhage on plain CT scan (NCCT) of brain.
3. Measurable neurological deficit (NIHSS 4-25)
4. Neurological deficits of low NIHSS score but significant functional disability:
   - Aphasias
   - Hemineglect
   - Hemianopia
5. Neurological signs should not be clearing up spontaneously in the evaluation period.
6. Onset of symptoms within 4.5 hours of beginning treatment.
7. Absence of major head trauma or major stroke in the previous 3 months.
8. No myocardial infarction requiring hospitalization in the past 3 months (to prevent hemopericardium)
9. No major gastrointestinal or urinary tract hemorrhage in the past 3 weeks.
10. No major surgery in the previous 14 days.
11. No history of previous intracranial hemorrhage due to aneurysm, angioma or arterio-venous malformations.
12. Diagnosed brain tumor.
13. Blood pressure should be less than 185/110 mm Hg.
14. No evidence of acute bleeding from any site or acute fracture on examination.
15. Not taking oral anticoagulants or if anticoagulants are being taken, INR to be ≤ 1.7
16. If receiving heparin in last 48 hours, a-PTT is to be performed and should be normal (< 35 secs).
17. Platelet count to be assessed if there is clinical suspicion of thrombocytopenia. Platelet count should be ≥ 1,00,000 /μl. If there is no clinical suspicion, platelet count test is ordered, but need not wait for result to start thrombolysis.
18. Arterial puncture at a non-compression site < 7 days.
19. Blood glucose concentration ≥ 50 mg % and ≤ 300 mg%.
20. Seizure at onset to be ascertained whether due to stroke. If there is clinical suspicion of non-vascular postictal deficit, magnetic resonance imaging (MRI) with diffusion-weighted imaging (DWI) to CT with CT angiography (CTA) to be performed to document stroke.
21. NCCT head should not show a large or multilobar hypodensity involving more than 1/3 rd of arterial territory (limited literature suggests increased risk of hemorrhagic transformation).
22. Informed consent from patient or responsible care giver.

Treatment regime for IV thrombolysis with rt-PA in acute ischemic stroke

1. Infuse 0.9 mg/Kg (maximum dose of 90 mg) over 60 minutes with 10% of the dose given as a bolus over 1 minute.
2. Admit the patient to an intensive care unit or a dedicated stroke unit for monitoring.
3. Perform neurological assessments every 15 minutes during the infusion and every 30 minutes thereafter for next 6 hours, then hourly until 24 hours after treatment.
4. If the patient develops severe headache, acute hypertension, nausea or vomiting, discontinue the infusion (if the infusion is still on) and obtain emergency CT scan.
5. Measure blood pressure every 15 minutes for the first 2 hours and subsequently every 30 minutes for the next 6 hours, then hourly until 24 hours after treatment.
6. Increase the frequency of blood pressure measurements if a systolic blood pressure is ≥ 180 mmHg or if a diastolic blood pressure is ≥ 105 mmHg; administer antihypertensive medications to maintain blood pressure at or below these levels.
7. Delay placement of nasogastric tubes, bladder catheters or intra-arterial (IA) pressure catheters.
8. Obtain a follow-up CT scan at 24 hours before starting anticoagulants or antiplatelet agents.

Catheter-Based or intra-arterial (IA) thrombolysis or reperfusion strategies: IA thrombolysis is still under investigation and should be used in well-equipped centers within a framework of research protocol.

Indications

- A significant neurologic deficit expected to result in long-term disability.
- Deficits attributable to large vessel occlusion (basilar, vertebral, internal carotid or MCA M1 or M2 branches).
- Non-contrast CT scan without hemorrhage or showing well-established infarct
- Acute ischemic stroke symptoms with known onset. Treatment initiated within 6-8 hours of established, non-fluctuating deficits due to Anterior Circulation (carotid/MCA) stroke. The window of opportunity for treatment is less well-defined in posterior circulation (Vertebral/Basilar) ischemia and patients may have fluctuating, reversible ischemic symptoms over many hours or even days and still be appropriate candidates for therapy.

Contraindications

1. Intracranial hemorrhage (ICH, SAH, subdural hematoma, etc.)
2. Well-established acute infarct on CT/MRI in the territory to be reperfused ***
3. Major infarction. ***
   - [e.g. > 1/3 cerebral hemisphere]
4. CNS lesion with high likelihood of hemorrhage s/p chemical thrombolytic agents (e.g., brain tumors, abscess, vascular malformation, aneurysm, contusion) ***
5. Suspicion of subarachnoid hemorrhage

The items marked with *** are not contraindications for mechanical clot lysis.

Warnings

These conditions may increase the risk of unfavorable outcomes but are not necessarily a contraindication to treatment:

1. Recent surgery/trauma (< 15 days) ***
2. Recent intracranial or spinal surgery, head trauma, or stroke (< 3 months) ***
3. History of intracranial hemorrhage or brain aneurysm or vascular malformation or brain tumor ***

- [may consider IA catheter-based repurfusion in patients with CNS lesions that have a very low likelihood of bleeding such as small unruptured aneurysms or benign tumors with low vascularity]

4. Active internal bleeding (< 22 days) ***
   - [including arterial puncture at a non-compressible site]
5. Platelets less than 100,000/μl, PTT > 40 sec after heparin use, or PT > 15 or INR > 1.7, or known bleeding diathesis ***
6. Left heart thrombus documented ***
7. Increased risk of bleeding due to any of the following: ***
   - Acute pericarditis
   - Subacute bacterial endocarditis (SBE)
   - Hemostatic defects including those secondary to severe hepatic or renal disease
   - Pregnancy (relative contraindication)
   - Diabetic hemorrhagic retinopathy, or other hemorrhagic ophthalmic conditions
   - Septic thrombophlebitis or occluded AV cannula at seriously infected site
   - Patients currently receiving oral anticoagulants, e.g., Warfarin sodium and INR > 1.7
   - Advanced age
   - Status - post-full dose IV tPA
8. Life expectancy less than 1 year or severe comorbid illness

The items marked with *** are not contraindications for mechanical clot lysis.

Prethrombolysis management

1. Start supplementary oxygen if unable to maintain O_2 saturation > 92%. Treat any fever with acetominophen. NPO for any oral intake (e.g., food, medication, etc.).
2. Do not place Foley, nasogastric tube, arterial line or central venous line unless it is necessary for patient safety.
3. Do not place any femoral catheters (venous or arterial).
4. Do not lower blood pressure unless it is causing myocardial ischemia or exceeds 220/120. Use labetolol iv (5-20 mg iv q 10-20 mins). Monitor with non-invasive cuff pressures every 15 mins or continuous arterial pressure monitoring.
5. Do not administer heparin unless recommended by the Acute Stroke Team.
6. Alert interventional neuroradiology and anesthesia about possible case.
7. Alert neuro-ICU and check for bed availability.
   - Consider bypassing CT Angio if risk is increased (e.g., renal failure, acute CHF) and it is unlikely to change treatment decision. Hold metformin 48 hrs after iodinated contrast.
   - Check MRI exclusions (e.g., Severe claustrophobia, implanted pacemaker, metal fragments, shrapnel).
   - Review CT/CTA with interventionalist and stroke team.
   - Obtain written or verbal informed consent for endovascular procedure and general anesthesia from patient or appropriate caregiver. If no individual is available for consent, consider emergency consent procedures.
   - If time permits, obtain STAT DWI-MR imaging but do not delay time to treatment.

Guidelines for management of blood pressure prior and perithrombolysis:

- Pretreatment
  - Systolic > 185 mmHg or diastolic > 110 mmHg
    - Labetalol 10-20 mg IV over 1-2 min
    - If labetalol is not available, oral captopril (12. 5 mg) and repeat at intervals of 15 minutes or clonidine (0.1 mg)
  - if still elevated,
    - May repeat or double labetalol every 10 min to maximum dose of 300 mg, or give initial labetalol dose, then start labetalol drip at 2-8 mg/min
    - Nicardipine 5 mg/h IV infusion as initial dose and titrate to desired effect by increasing 2.5 mg/h every 5 min to maximum of 15 mg/h
    - If blood pressure is not controlled by labetolol or nicardipine, consider sodium nitroprusside or rule out other cause of acute hypertension such as hypertensive urgency

- During/after treatment
  - Monitor blood pressure
  - Check blood pressure every 15 min for 2 h, then every 30 min for 6 h, and finally every hour for 16 h
  - Diastolic > 140 mmHg
  - Sodium nitroprusside 0.5 mcg/kg/min IV infusion as initial dose and titrate to desired blood pressure
  - Systolic > 230 mmHg or diastolic >121 – 140 mmHg
  - Option 1
    - Labetalol 10 mg IV for 1-2 min
    - May repeat or double labetalol every 10 min to maximum dose of 300 mg, or give initial labetalol dose, then start labetalol drip at 2-8 mg/min
  - Option 2
    - Nicardipine 5 mg/h IV infusion as initial dose and titrate to desired effect by increasing 2.5 mg/h every 5 min to maximum of 15 mg/h; if blood pressure is not controlled by labetolol or nicardipine, consider sodium nitroprusside.
  - Systolic 180 – 230 mmHg or diastolic 105 - 120 mmHg
    - Labetalol 10 mg IV for 1 - 2 min
    - May repeat or double labetalol every 10 - 20 min to maximum dose of 300 mg or give initial labetalol dose, then start labetalol drip at 2 - 8 mg/min

For acute stroke onset during or immediately after diagnostic or therapeutic angiography/ or coronary and cardiac interventions

If a femoral arterial sheath is still in place, DO NOT REMOVE IT. The sheath should remain sutured in place while t-PA is given. Consider IA urokinase if the sheath can be accessed and the Interventional Neuroradiology staff is available. If not, consider giving t-PA i.v. at full dose 0.9 mg/kg. In all cases, leave the sheath in place and check STAT a-PTT. Observe the groin site closely and follow hematocrit and vital signs for evidence of acute blood loss. If a hematoma forms or there is evidence of blood loss, notify vascular surgery and apply pressure until hemostasis is achieved. If bleeding continues, t-PA can be reversed with FFP, cryoprecipitate and platelets. Vascular surgery may choose to surgically repair the artery. If no bleeding occurs, the sheath can be removed after 24 hours. If heparin cannot be held for sheath removal, vascular surgery will surgically close the vessel in the operating room.

Bleeding after t-PA

1. For suspected symptomatic hemorrhage after t-PA or other plasminogen activator has been given:
   - Hold administration of IV t-PA if still infusing until Brain CT completed and shows no evidence of bleeding.
   - Exclude other possible causes of neurologic worsening or acute hemodynamic instability.

2. For confirmed symptomatic hemorrhage on head CT:
   - Consult neurosurgery for possible intervention.
   - Check STAT values: CBC, PT, a-PTT, platelets, fibrinogen and D-dimer.
   - If fibrinogen < 100 mg/dL, then give cryoprecipitate 0.15 units/kg rounded to the nearest integer. If still bleeding at 1 hr and fibrinogen level still less than 100 mg/dL, repeat cryoprecipitate dose.
   - Institute frequent neurochecks and therapy of acutely elevated ICP, as needed.
   - Additional options or considerations.
   - If platelet dysfunction suspected, give platelets 4 U.
   - If heparin has been administered in the past 3 hours:
   - Discontinue the heparin infusion and order protamine sulfate. Calculate total amount of heparin received over the preceding 3 hours.
   - If initiated within 30 minutes of last heparin dose: Give 1 mg protamine per 100 U heparin.
   - If initiated within 30-60 minutes: Give 0.5-0.75 mg protamine per 100 U heparin.
   - If initiated within 60-120 minutes: Give 0.375-0.5 mg protamine per 100 U heparin.
   - If heparin stopped greater than 120 minutes ago: Give 0.25-0.375 mg protamine per 100 U heparin.
   - Give by slow IV injection, not to exceed 5 mg/min, with total dose not to exceed 50 mg.
   - Monitor for signs of anaphylaxis; the risk is higher in diabetics who have received insulin.
   - Follow-up with STAT a-PTT q1 hour for the next 4 hours, then q4 hours through 12 hours of hospitalization.
   - Serious systemic hemorrhage should be treated in a similar manner. Manually compress and compressible sites of bleeding, and consult appropriate additional services to consider mechanically occluding arterial or venous sources of medically uncontrollable bleeding.

Appendix – 3

Bedside swallowing assessment

Name	Registration No.	
Date	Day	
Conscious level	(Alert =1, drowsy but arousable = 2, response but no Eye opening to speech = 3, response to pain = 4)	[ ]
Head and trunk control	(Normal sitting balance = 1, sitting balance Not maintained = 2, head control only = 3, No head control = 4	[ ]
Breathing pattern	(Normal 1, abnormal =2)	[ ]
Lip closure	(Normal = 1, abnormal = 2)	[ ]
Palate movement	(Symmetrical =1, asymmetrical =2, minimal/ absent =3)	[ ]
Laryngeal function	(Aah/ee) (Normal = 1, weak = 2, absent =3	[ ]
Voluntary cough	(Normal = 1, weak = 2, absent = 3)	[ ]
Stage 1: Give a teaspoon (5 mL) of water three times		
Dribbles water	(None /once = 1, > once = 2)	[ ]
Laryngeal movement on attempted swallow	(Yes = 1, no = 2)	[ ]
"Repeated movements" felt ?	(None/once = 1, > once = 2)	[ ]
Cough on swallowing	(None/once = 1, > once = 2)	[ ]
Stridulous on swallowing	(No = 1, yes = 2)	[ ]
Laryngeal function after Swallowing	(Normal = 1, weak/wet =2, absent =3)	[ ]
Stage 2: If the swallow is normal in stage 1 (two of three attempts), try 60 mL of water in a glass or beaker.		
Able to finish in seconds		[ ]
No of sips		[ ]
Cough during or after swallowing	(No = 1, yes = 2)	[ ]
Stridor during or after swallowing	(No = 1, yes = 2)	[ ]
Laryngeal function after swallowing	(Normal = 1, weak/wet = 2,	[ ]
Do you feel aspiration is present?	(No = 1, possible =2, yes =3)	[ ]

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