

CLINICAL PRACTICE GUIDELINES

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MANAGEMENT OF STROKE



Malaysian Society of Neurosciences



Academy of Medicine Malaysia



MINISTRY OF HEALTH MALAYSIA

STATEMENT OF INTENT

These guidelines are meant to be a guide for clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not necessarily ensure the best outcome in every case. Every health care provider is responsible for the management of his/her unique patient based on the clinical picture presented by the patient and the management options available locally.

REVIEW OF THE GUIDELINES

These guidelines were issued in 2006 and will be reviewed in 2011 or sooner if new evidence becomes available.

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Available on the following websites:

www.moh.gov.my/medical/htm

www.acadmed.org.my

www.neuro.org.my

FOREWORD

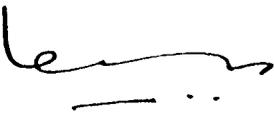
Stroke is a global health problem and is the second commonest cause of death worldwide. It is also a leading cause of adult disability (WHO report 2003). Stroke also caused 3% of the world's disability burden in 1990. By 2020, stroke mortality would have almost doubled, mainly as a result of an increase in the proportion of older people and inadequate control of major risk factors for stroke especially in less developed countries. Two thirds of strokes occur in low income and middle income countries, where the average age of patients with stroke is 15 years below that in high income countries.

In Malaysia, stroke was consistently the 3rd commonest cause of death in the 1990s (SEAMIC data). In 2002 stroke was the 4th highest cause of death, following septicaemia, heart disease and cancer. Population-based studies on the incidence of stroke have been carried out almost exclusively in Caucasians in Europe, Australasia and the USA. There is a steep rise in incidence with age, with three-quarters of all first strokes occurring after the age of 85 years, at least in white populations. There are virtually no comparable data from less developed countries such as Africa, South America and Asia.

Stroke shares major risk factors – tobacco use, unhealthy diet, physical inactivity, obesity, high blood pressure – with other chronic diseases such as coronary heart disease and some cancers. Most conventional vascular risk factors - age, cigarette smoking, diabetes, and obesity-age broadly similar for ischaemic stroke and for vascular disease in other parts of the arterial tree.

The clinical practice guideline (CPG) on Ischaemic Stroke will assist healthcare professionals in recognizing the symptoms of a stroke, understanding the spectrum of underlying causes, performing appropriate investigations and most importantly, providing comprehensive treatment for stroke patients. There have been many advances in the management of acute stroke and rehabilitation. Information on evidence-based approaches to primary and secondary stroke prevention are important to disseminate to health care professionals who will then be able to improve awareness amongst the general population. The importance of a multidisciplinary approach cannot be underestimated in all aspects of stroke.

Stroke is one of the illnesses included as a Research Priority in the Health Sector for the 9th Malaysia Plan. This CPG is just one of the efforts of the Ministry of Health to provide improved stroke care in the country.



(TAN SRI DATUK DR. HJ. MOHD ISMAIL MERICAN)

The Director General of Health Malaysia

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RATIONALE AND PROCESS OF GUIDELINE DEVELOPMENT

Rationale

The Clinical Practice Guidelines in the Management of Ischaemic Stroke was developed to provide a clear and concise approach to all clinicians on the current concepts in the management of stroke patients. In Malaysia, a significant number of ischaemic stroke patients are managed by non-neurologists. We therefore felt that it was important for stroke experts in the country to summarise and adapt relevant clinical trial data and current treatment strategies to the local context.

A previous effort resulted in the 'Consensus Statement on the Management of Ischaemic Stroke', 2000 prepared by a panel of eight neurologists representing the Ministry of Health, Universities and private sector.

However, since 2000, there have been many more studies in stroke and numerous guidelines and updates from other countries and stroke organizations. A new updated CPG was therefore required.

Process

This current CPG is the initiative of the Stroke Council of the Malaysian Society of Neurosciences. A working group of eight neurologists and one cardiologist met in 2003 and proposed an update of the previous Consensus of Stroke Management. Members of the working group were consultant neurologists from the Ministry of Health, Universities, Academy of Medicine and private sector, and a consultant cardiologist from the Ministry of Health. Five senior neurologists were enlisted as reviewers to advise and comment on the chapter topics.

The principles and layout follows methodology as stated in the Guidelines for Clinical Practice Guidelines booklet 2003 published by the Medical Development division of Ministry of Health. A standard methodology based on a systematic review of current evidence was used to look at the literature.

These guidelines have been presented to the Chairman of the Health Technology Assessment and Clinical Practice Guidelines Council of the Ministry of Health Malaysia for review and approval.

OBJECTIVES, QUESTION AND TARGETS

Objectives

These guidelines are intended to provide awareness and education in

- identifying symptoms and signs of stroke
- scope of various types and causes of ischaemic stroke

These guidelines are intended to provide evidence in

- management of acute ischaemic stroke
- primary and secondary prevention of ischaemic stroke

These guidelines however do not cover

- management of cerebral haemorrhage
- stroke rehabilitation (already outlined in Stroke Rehabilitation Guidelines 2000)

Clinical Questions

The clinical questions to be addressed by these guidelines include:

- i) What is the current best practice for the management of acute ischaemic stroke?
- ii) What are the strategies in stroke prevention?

Target Population

These guidelines are to be applied to adults with ischaemic stroke as well as those at risk of developing stroke.

Target Group

These guidelines are developed for all healthcare providers involved in the management and prevention of ischaemic stroke in adults.

KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS

LEVELS OF EVIDENCE SCALE

| | |
|--------|---|
| I | Evidence obtained from at least one properly randomized controlled trial |
| II – 1 | Evidence obtained from well-designed controlled trials without randomization |
| II – 2 | Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group |
| II – 3 | Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence |
| III | Opinions of respected authorities, based on clinical experience, descriptive studies and case reports; or reports of expert committees |

Source : U.S./ CANADIAN PREVENTIVE SERVICES TASK FORCE

GRADES OF RECOMMENDATIONS

| | |
|---|---|
| A | At least one meta analysis, systematic review, or randomized controlled trial (RCT), or evidence rated as good and directly applicable to the target population |
| B | Evidence from well conducted clinical trials, directly applicable to the target population, and demonstrating overall consistency of results; or evidence extrapolated from meta analysis, systematic review or RCT |
| C | Evidence from expert committee reports, or opinions and/or clinical experiences of respected authorities; indicates absence of directly applicable clinical studies of good quality |

Source : Guidelines for CLINICAL PRACTICE GUIDELINES, Ministry of Health Malaysia 2003

SUMMARY OF RECOMMENDATIONS

The following are management steps in which levels of evidence have been established.

Primary Prevention

| Factors | Recommendation | Level of evidence | Grade |
|---|--|--------------------------|--------------|
| Hypertension | Treat medically if BP>140mmHg systolic and/or >90mmHg diastolic. | I | A |
| | Lifestyle changes if BP between 130-139 mmHg systolic and/or 80-89mmHg diastolic. | I | A |
| | Target BP for diabetics is <130mmHg systolic and <80mmHg diastolic. | I | A |
| | Hypertension should be treated in the very elderly (age > 70 yrs) to reduce risk of stroke. | I | A |
| Diabetes mellitus | Strict blood pressure control is important in diabetics. Maintain tight glycaemic control. | I | A |
| Hyperlipidaemia | High risk group: keep LDL < 2.6mmol/l. 1 or more risk factors: keep LDL < 3.4mmol/l. No risk factor: keep LDL < 4.2mmol/l. | I | B |
| Smoking | Cessation of smoking. | III | C |
| Aspirin therapy | 100mg aspirin every other day may be useful in women above the age of 65. | II-1 | B |
| Post menopausal Hormone Replacement therapy | Oestrogen based HRT is not recommended for primary stroke prevention. | I | A |
| Alcohol | Avoid heavy alcohol consumption. | II-2 | B |

General Management of Acute Ischaemic Stroke

| Factors | Recommendation | Level of evidence | Grade |
|--------------------|--|--------------------------|--------------|
| Airway & Breathing | Ensure clear airway and adequate oxygenation. Elective intubation may help some patients with severely increased ICP. | III | C |
| Mobilization | Mobilize early to prevent complications | II-3 | C |
| Blood Pressure | Do not treat hypertension if < 220 mmHg systolic or < 120mmHg diastolic. Mild hypertension is desirable at 160-180/90-100 mmHg . | III | C |

| | | | |
|------------------------------|---|-------------------------------------|-----------------------|
| | Blood pressure reduction should not be drastic. Proposed substances: Labetolol 10-20 mg boluses at 10 minute intervals up to 150-300 mg or 1 mg/ml infusion, 1-3 mg/min or Captopril 6.25-12.5 mg orally. | III | C |
| Blood Glucose | Treat hyperglycaemia (Random blood glucose > 11 mmol/l) with insulin. Treat hypoglycaemia (Random blood glucose < 3 mmol/l) with glucose infusion. | II-3 III | C C |
| Nutrition | Perform a water swallow test. Insert a nasogastric tube if the patient fails the swallow test. PEG is superior to nasogastric feeding only if prolonged enteral feeding is required. | III III II-1 | C C B |
| Infection | Search for infection if fever appears and treat with appropriate antibiotics early. | III | C |
| Fever | Use anti-pyretics to control elevated temperatures. | II-1 | B |
| Raised Intracranial Pressure | Hyperventilate to lower intracranial pressure. Mannitol (0.25 to 0.5 g/kg) intravenously administered over 20 minutes lowers intracranial pressure and can be given every 6 hours. If hydrocephalus is present, drainage of cerebrospinal fluid via an intraventricular catheter can rapidly lower intracranial pressure. Hemicraniectomy and temporal lobe resection have been used to control intracranial pressure and prevent herniation among those patients with very large infarctions of the cerebral hemisphere. Ventriculostomy and suboccipital craniectomy is effective in relieving hydrocephalus and brain stem compression caused by large cerebellar infarctions. | II-2 II-2 III II-3 II-3 | B B C C C |

Acute Stroke therapy

| Treatment | Recommendations | Level of evidence | Grade |
|------------------|--|--------------------------|--------------|
| rt-Pa | In selected patients presenting within 3 hours: IV rt-pa (0.9mg/kg, maximum 90mg) with 10% given as a bolus followed by an infusion over one hour. | I | A |

| | | | |
|------------------------|--|------------|------------|
| Aspirin | Start aspirin within 48 hours of stroke onset. Use of aspirin within 24 hours of rt-PA is not recommended | I II-1 | A A |
| Anticoagulants | The use of heparins (unfractionated heparin, low molecular weight heparin or heparinoids) is not routinely recommended as it does not reduce the mortality in patients with acute ischaemic stroke. | I | A |
| Neuroprotective Agents | A large number of clinical trials testing a variety of neuroprotective agents have been completed. These trials have thus far produced negative results. To date, no agent with neuroprotective effects can be recommended for the treatment of patient with acute ischaemic stroke at this time. | I I | A A |

AntiCoagulation following Acute Cardioembolic Stroke

| Treatment | Recommendations | Level of Evidence | Grade |
|--------------------------|--|--------------------------|--------------|
| Aspirin | All patients should be commenced on aspirin within 48 hours of ischaemic stroke. | I | A |
| Warfarin | Adjusted-dose warfarin may be commenced within 2-4 days after the patient is both neurologically and medically stable. | II-2 | C |
| Heparin (unfractionated) | Adjusted-dose unfractionated heparin may be started concurrently for patients at very high risk of embolism. | III | C |
| Anticoagulation | Anticoagulation may be delayed for 1-2 weeks if there has been substantial haemorrhage. | III | C |
| | Urgent routine anticoagulation with the goal of improving neurological outcomes or preventing early recurrent stroke is not recommended. | I | A |
| | Urgent anticoagulation is not recommended for treatment of patients with moderate-to-large cerebral infarcts because of a high risk of intracranial bleeding complications | I | A |

Stroke Unit

| Treatment | Recommendations | Level of evidence | Grade |
|------------------|---|--------------------------|--------------|
| Stroke unit | Every hospital should be encouraged to set up a stroke unit. | I | A |
| | Stroke units significantly reduce death, dependency, institutionalisation and length of hospital stay | I | A |

| | | | |
|--|---|-----|---|
| | A stroke unit should be managed by a multidisciplinary stroke team | III | C |
| | An efficient referral and rehabilitation network should be established to ensure the success of stroke units. | III | C |

Cardiac conditions predisposing to Ischaemic stroke

| Major Risk Conditions | Additional risk factors | Recommendation | Level of evidence | Grade |
|--------------------------------------|--|---|-------------------|-------|
| Atrial Fibrillation | <i>High risk:</i> Age >75 years; previous stroke/TIA; mitral valve disease; congestive heart failure; hypertension. | Long-term warfarin for patients with 1 or more high-risk factors | I | A |
| | | Long term warfarin for patients with 2 or more moderate-risk factors | III | C |
| | <i>Moderate risk:</i> Age 65-75 years; coronary artery disease, peripheral artery disease; | Warfarin or aspirin for patients with 1 moderate risk factor | I | A |
| | diabetes; active thyroid disease. | Aspirin 75-325mg daily is sufficient for patients < 65 years of age with 'lone' AF and no additional risk factors present | I | A |
| Prosthetic Heart Valves (Mechanical) | <i>Moderate risk:</i> Bileaflet or tilting disk aortic valves in NSR | Life-long warfarin | II-2 | B |
| | <i>High risk:</i> Bileaflet or tilting disk aortic valves in AF; Bileaflet or tilting disk mitral valve in AF or NSR. | Life-long warfarin (target INR 3.0; range 2.5-3.5) | II-3 | B |
| | <i>Very high risk:</i> Caged-ball and caged-disk designs; documented stroke/TIA despite adequate therapy with warfarin. | Life-long warfarin (target INR 3.0; range 2.5-3.5) plus aspirin 75-150mg daily | II-1 | B |
| Bioprosthetic heart valves | <i>High risk:</i> AF; left atrial thrombus at surgery; previous CVA/TIA or systemic embolism | If high risk factors present, consider warfarin for 3-12 months or longer For all other patients, give | III | C |

| | | | | |
|--|--|--|-------------------|-------------|
| | | warfarin for 3 months post-op, then aspirin 75-150mg daily | III | C |
| Mitral Stenosis | <i>High risk:</i> AF; previous stroke/TIA; left atrial thrombus; left atrial diameter > 55mm on echo. | If high risk factors present, consider long-term warfarin For all other patients start aspirin 75-150mg daily | II-3 II-2 | B B |
| MI and LV dysfunction | <i>High risk:</i> Acute/recent MI (<6 mos); extensive infarct with anterior wall involvement; previous stroke/TIA. <i>Very high risk:</i> Severe LV dysfunction (EF < 28%); LV aneurysm; spontaneous echo contrast; LV thrombus; dilated non-ischaeamic cardiomyopathies. | If risk factors present without LV thrombus: consider warfarin for 3-6 months followed by aspirin 75-150mg daily If LV thrombus is present, consider warfarin for 6-12 months For dilated cardiomyopathies including peripartum, consider long-term warfarin | III III III | C C C |
| <i>Recommended warfarin dose INR target 2.5 [range 2.0 to 3.0] unless stated otherwise</i> | | | | |

Secondary Prevention

| Factors Treatment | Recommendations | Level of evidence | Grade |
|---|---|--------------------------|--------------|
| Antiplatelets <u>Single agent</u> | | | |
| Aspirin <i>Alternatives:</i> | The recommended dose of aspirin is 75mg to 325mg daily. | I | A |
| Clopidogrel | The recommended dose is 75 mg daily. or | I | A |
| Ticlopidine <u>Double therapy</u> | The recommended dose of ticlopidine is 250mg twice a day. | I | A |
| Addition of clopidogrel to aspirin | In selected high risk patients only when benefit outweighs risk | I | B |

| | | | |
|------------------------------------|---|-----------|--------|
| Aspirin + clopidogrel | In selected high risk patients only when benefit outweighs risk | I | B |
| <i>Anti-hypertensive treatment</i> | ACE-inhibitor based therapy should be used to reduce recurrent stroke in normotensive and hypertensive patients. ARB-based therapy may benefit selected high risk populations. | I II-1 | A B |
| <i>Lipid lowering</i> | Lipid reduction should be considered in all subjects with previous ischaemic strokes. | I | A |
| <i>Diabetic control</i> | All diabetic patients with a previous stroke should improve glycaemic control. | III | C |
| <i>Cigarette smoking</i> | All smokers should stop smoking | III | C |

Endarterectomy, Angioplasty & Stenting

| Treatment | Recommendations | Level of evidence | Grade |
|--------------------------------------|---|--------------------------|--------------|
| Carotid Endarterectomy (CEA) | Indicated for most patients with stenosis of 70-99% after a recent ischaemic event in centres with complication rates of less than 6% | I | A |
| | Earlier intervention (within 2 weeks) is more beneficial. | II-1 | B |
| | May be indicated for patients with stenosis of 50-69% after a recent ischaemic event in centres with complication rates of less than 6% | III | C |
| | CEA is not recommended for patients with stenosis of less than 50% | I | A |
| | Patients should remain on antithrombotic therapy before and after surgery | II-2 | B |
| Carotid angioplasty & stenting (CAS) | CAS represents a feasible alternative to carotid endarterectomy for secondary stroke prevention when surgery is undesirable, technically difficult or inaccessible. | II-2 | B |
| | Distal protection devices should be used during the procedure and anti-platelet agents such as clopidogrel be initiated. | I III | A C |
| | The long-term safety and efficacy of CAS is not known | | |
| Intracranial | Role of AS in intra-cranial stenoses, asymptomatic | II-2 | C |

| | | | |
|------------------------------|--|--|--|
| angioplasty & stenting (IAS) | stenoses and acute stroke is unclear and not recommended | | |
|------------------------------|--|--|--|

Stroke in Special Circumstances

| Treatment | Recommendations | Level of evidence | Grade |
|---------------------------|--|--------------------------|--------------|
| Aspirin | Young Ischaemic stroke If the cause is not identified, aspirin is usually given. There are currently no guidelines on the appropriate duration of treatment. | III | C |
| Heparin | Cerebral Venous thrombosis Anticoagulation appears to be safe, and cerebral haemorrhage is not a contra-indication for anticoagulation. | II-I | B |
| Warfarin | Simultaneous oral warfarin should be commenced. The appropriate length of treatment is unknown. | III | C |
| Endovascular thrombolysis | It is currently considered for patients with extensive disease and clinical deterioration | III | C |

ABBREVIATIONS

- AF: atrial fibrillation
 ASA: atrial septal aneurysm
 CAS: carotid angioplasty and stenting
 CEA: carotid endarterectomy
 CVA: cerebrovascular accident
 EF: ejection fraction
 IAS: intracranial angioplasty and stenting
 ICP: intracranial pressure
 LV: left ventricle
 NSR: normal sinus rhythm
 MI: myocardial infarction
 PEG: percutaneous endoscopic gastrostomy
 PFO: patent foramen ovale
 TIA: transient ischaemic attack

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1 – INTRODUCTION & EPIDEMIOLOGY

Stroke is a global health problem and is the second commonest cause of death and a leading cause of adult disability worldwide .¹ Annually, 15 million people worldwide suffer a stroke. Of these, 5 million die and another 5 million are left permanently disabled.² It is presently among the top four leading causes of death in ASEAN countries, with the crude death rate ranging from 10.9/100 000 (Thailand) to 54.2 per 100 000 (Singapore).³

Ministry of Health statistics show stroke consistently as the third leading cause of death in the 1990s, surpassed only by coronary heart disease and cancer (SEAMIC). Data in 2002 show cerebrovascular disease causing a mortality of 11.9 per 100 000 population (see table 1).⁴ There is no incidence or prevalence data available for the country.

Table 1: Top 5 Mortality rate in MOH hospitals 2002⁴

| Mortality (rate per 100 000 population) | |
|--|-------|
| Septicaemia | 22.60 |
| Heart diseases and diseases of pulmonary circulation | 21.24 |
| Malignant neoplasms | 13.51 |
| Cerebrovascular diseases | 11.97 |
| Accident | 9.25 |

Stroke is a clinical syndrome with many different subtypes and a large variety of causes. Atherothromboembolism is the major cause of ischaemic stroke worldwide but there are interethnic differences in stroke mortality and subtype. Small vessel infarction (lacunar infarcts) were more commonly seen when compared to Caucasians in one study.⁵ There is also possible variation in stroke types among Chinese with a higher proportion of haemorrhagic strokes as well as studies highlighting the importance of intracranial arterial stenosis as a cause of stroke among Chinese.⁶ There is a greater predominance of intracranial atherosclerotic vascular disease compared to extracranial or carotid artery disease in Asians.⁷ Studies have also shown poorer outcome and recurrent strokes in patients who have both intracranial and extracranial atherosclerotic large vessel disease.⁸

2 – DEFINITION & CLASSIFICATION OF STROKE

Definition of Stroke

“Stroke is a clinical syndrome characterized by rapidly developing clinical symptoms and/or signs of focal, and at times global, loss of cerebral function, with symptoms lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin”.

Definition of Transient Ischaemic Attack (TIA)

“A Clinical syndrome characterized by an acute loss of focal cerebral or monocular function with symptoms lasting less than 24 hours and which is thought to be due to inadequate cerebral or ocular blood supply as a result of arterial thrombosis or embolism”.

Why classify stroke?

Classification of stroke has numerous implications during immediate stroke supportive care and rehabilitation, for prognostic purposes, guides cost effective investigations for underlying cause

as well as aids decisions for therapy and secondary stroke prevention strategies. Furthermore, classifications are useful in setting up stroke registries and data banks as well as for epidemiological studies.

Oxfordshire Community Stroke Project (OCSP) is a handy clinical classification to use (refer to appendix).

3 – DIAGNOSIS

In general, the diagnosis of stroke is made by evaluating and analysing information derived from a good history, physical examination and supplemented with selected diagnostic tests. Because of the nature of the illness and the dramatic manner of the neurological deficits, history is of utmost importance. Every effort must be made to obtain information from the patient, family members, friends, or witnesses.

The diagnosis should provide answers to the following questions:

1. What is the neurological deficit?
2. Where is the lesion?
3. What is the lesion?
4. Why has the lesion occurred?
5. What are the potential complications and prognosis?

The signs and symptoms of a stroke depend on the type, location and the extent of the affected brain tissue. Stroke patients usually have a sudden or rapid onset of focal neurological symptoms, within minutes to an hour. Some patients may, however, have a stepwise or gradual worsening or waxing and waning symptoms. A third of all strokes occur during night sleep, therefore, the weakness is first noted on waking up in the morning.

A full neurological examination, including the patient's conscious level and tests of higher mental function (such as the mini-mental state examination) is mandatory. Every positive and negative finding should point to the site of the lesion. These can be divided into 2 broad groups: a) clinical features that are caused by anterior circulation stroke (carotid artery), and b) those caused by posterior circulation stroke (vertebrobasilar system) (see table 1).

Table 1. Clinical Features of Stroke

Anterior (carotid) artery circulation

Middle cerebral artery

- Aphasia (dominant hemisphere)
- Hemiparesis / plegia
- Hemisensory loss/disturbance
- Homonymous hemianopia
- Parietal lobe dysfunction, e.g. astereognosis, agraphesthesia, impaired two-point discrimination, sensory and visual inattention, left-right dissociation and acalculia

Anterior cerebral artery

- Weakness of lower limb more than upper limb

Posterior (vertebrobasilar) artery circulation

- Homonymous hemianopia
- Cortical blindness
- Ataxia
- Dizziness or vertigo
- Dysarthria
- Diplopia
- Dysphagia
- Horner's syndrome
- Hemiparesis or hemisensory loss contralateral to the cranial nerves palsy
- Cerebellar signs

Table 2. Differential diagnosis of stroke

| Differential diagnosis of stroke ¹ |
|--|
| <ul style="list-style-type: none">• Metabolic/toxic encephalopathy (hypoglycaemia, non-ketotic hyperglycaemia, Wernicke-Korsakoff syndrome, drug intoxication)• Epileptic seizures (postictal Todd's paresis)• Hemiplegic migraine• Structural intracranial lesions (e.g. subdural haematoma, brain tumour, arteriovenous malformation)• Encephalitis (e.g. herpes simplex virus), brain abscess, tuberculoma• Head injury• Hypertensive encephalopathy• Relapsing Multiple Sclerosis• Conversion disorders• Hyperviscosity syndrome• Peripheral nerve lesions (e.g. Guillain-Barre Syndrome) |

4 – PROGNOSIS

Prognosis of stroke depends on the stroke type, size and location. Haemorrhagic stroke has a higher mortality than ischaemic stroke.¹⁻⁴ However patients with haemorrhagic stroke show a better neurological and functional recovery.⁵ Brainstem infarct, large hemispheric infarct and cardio embolic stroke also carry a poor prognosis.⁶ Lacunar infarct has the lowest mortality rate.⁷

Survival after stroke

There is a decline in stroke mortality in both men and women suffering from ischaemic or haemorrhagic stroke at all ages in many countries over the past few decades.^{8,9} This can be attributed to the introduction of stroke units which provide organized stroke care and a better control of stroke risk factors resulting in milder stroke.¹⁰⁻¹⁵

A patient who survives the first 30 days after a first-ever stroke has an annual death risk of 9-10 %.^{16,17} Studies in recent years showed that case fatality rates after a first-ever stroke (all types combined) were 10% at one week, 20% at one month, 30% at one year, 60% at 5 years^{16,17} and

76% at 10 years.¹⁸

In a local study published in 2003, the in-hospital mortality in ischaemic stroke was 11% while for haemorrhagic stroke is much higher, at 27.3%.¹⁹

Death occurring within the first 30 days after stroke is commonly due to the direct effect of brain damage.⁴ Thereafter, mortality is usually caused by complications of immobilisation (bronchopneumonia, deep vein thrombosis), recurrent stroke and coronary heart disease.¹⁶

Risk factors for stroke mortality

Previous use of antiplatelet drugs nearly halves the risk of early death in patient with ischaemic stroke while old age, atrial fibrillation, ischaemic disease and diabetes mellitus increase the risk of early death.⁶

Diabetes mellitus, both diastolic and systolic hypertension, smoking, cardiothoracic ratio, pre-existing coronary heart disease are risk factors for long term stroke mortality.²⁰

Recurrent stroke

The recurrent rates are 4% in the first month and 12% in the first year. Thereafter the risk falls to about 4-5% per year, so that by 5 years, 30% will have suffered a recurrent stroke.^{21, 22}

Disability

After a first-ever stroke, about 60% of the patients are alive at 5 years.¹⁸ Of these survivors, 1 in 7 would be living in a nursing home at 5 years and a third becomes disabled at 5 years.²⁴ Predictors of disability are older age, a very low premorbid level of activities before the stroke and subsequent recurrent stroke.²⁴

5 – CAUSE & PATHOPHYSIOLOGY

Three main causes of ischaemic stroke are:

1. Atherothromboembolism (50%)
2. Intracranial small vessel disease (penetrating artery disease) (25%)
3. Cardiogenic embolism (20%)

Other causes include arterial dissection, trauma, vasculitis (primary/secondary), metabolic disorders, congenital disorders and other less common causes such as migraine, pregnancy, oral contraceptives, etc.

Atheroma affects mainly the large and medium sized arteries at places of confluence, branching or tortuosity of vessels. The process begins in childhood as fatty streaks and progresses over years with gradual buildup of fibrolipid plaque and infiltration of inflammatory cells, eventually narrowing the vessel lumen. The final step occurs with ulceration and platelet-fibrin thrombus formation on the plaque surface.

The atherothrombotic plaque can grow to obstruct a vessel, with intraluminal propagation of the thrombus proximally or distally to cause occlusion, or embolism occurs from the plaque surface to occlude smaller distant vessel(s).

Intracranial small vessel disease is thought to be due to lipohyalinosis but other causes may include microatheroma and angionecrosis, or thromboembolism from a larger artery. The clinical syndrome caused by this is lacunar infarction due to occlusion of small perforating arteries.

Vascular risk factors associated with increased risk of stroke:

| NON-MODIFIABLE | MODIFIABLE |
|--------------------------|--|
| Age | High Blood Pressure (systolic and diastolic) |
| Sex | Cigarette smoking |
| Ethnicity / Race | Diabetes mellitus |
| Family history of stroke | Atrial Fibrillation |
| | Coronary heart disease |
| | Hyperlipidaemia |
| | Obesity & physical inactivity |
| | Raised Homocysteine levels |
| | High dietary salt intake |
| | Heavy alcohol consumption |
| | Previous stroke |

Embolism from the heart causes approximately 20% of all ischaemic strokes. The most common causes are atrial fibrillation and valvular heart disease. Not all cardiac sources pose similar threat in causing stroke.

The algorithm in appendix b outlines the steps to a diagnosis of ischaemic stroke and the various causes which need investigation to identify the underlying cause for the stroke. Despite thorough investigations, in up to 40% of strokes no definite cause can be found, especially in young stroke patients.

6 - INVESTIGATIONS

The following investigations for patients with ischaemic stroke are recommended in order to achieve the following objectives:-

1. Confirm the diagnosis
2. Determine the stroke mechanism
3. Risk stratification and prognostication
4. Identify potentially treatable large obstructive lesions of the cerebrovascular circulation

Blood investigations

| ON ADMISSION | |
|--|--|
| Full blood count | Exclude anaemia, polycythaemia, thrombocytosis, thrombocytopenia, etc |
| Random blood glucose | Exclude hypoglycemia, new diagnosis of diabetes mellitus |
| Urea & electrolytes | Hydration status, excludes electrolyte imbalances |
| Clotting profile* | Baseline |
| NEXT DAY | |
| Lipid profile (fasting) | |
| Glucose (fasting) | |
| OPTIONAL TESTS (in selected patients) | |
| VDRL | |
| autoimmune screen | ESR, antinuclear Factor, Rheumatoid Factor, anti double stranded DNA antibodies, C3 C4 levels, etc |
| Thrombophilia screen & lupus anticoagulant | Serum fibrinogen, Anti-thrombin III, Protein C, Protein S, Factor V-Leyden, anti-phospholipid antibodies |
| Homocysteine (fasting) | |
| C reactive protein | |

*if thrombolysis is considered

Other investigations

| | |
|----------------|--|
| 12 lead ECG | Mandatory |
| Ambulatory ECG | For suspected arrhythmias or sinoatrial node disease |

Imaging

| | |
|-------------------------------------|--|
| For all suspected stroke | |
| Chest x-ray | Mandatory |
| CT brain | The emergency neuroimaging scan of choice for all patients Differentiates haemorrhage from infarction Confirms site of lesion, cause of lesion, extent of brain affected |
| In selected patients | |
| ECHO cardiography | For suspected cardioembolism, assess cardiac function |
| MRI (magnetic resonance imaging) | Sensitive Not available in emergency setting, limited by expense Useful tool to select patients for thrombolysis where available |
| Carotid duplex Ultrasound | Allows identification of extracranial vessel disease |
| Transcranial Doppler Ultrasound | Identifies intracranial vessel disease with prognostic and therapeutic implications |
| MR angiography (MRA) | Non invasive tool to assess intra- and extra-cerebral circulation Objective assessment of vessel stenosis |
| CT angiography (multislice CT scan) | Non invasive tool to assess intra- and extra-cerebral circulation. Involves intravenous contrast injection |
| MR venography | In suspected cerebral venous thrombosis |
| Contrast angiogram | Gold standard assessment of cerebral vasculature Reserved for patients planned for intervention |

7 –ACUTE TREATMENT

REPERFUSION OF ISCHAEMIC BRAIN

In cerebral infarcts, restoration of perfusion to the ischaemic brain tissue is a key therapeutic strategy. The concept of the existence of an ischaemic penumbra is fundamental to the current approach to treatment of ischaemic stroke: although a core of infarct tissue might not be salvageable, adjacent dysfunctional tissue might be saved if the circulation is restored and metabolism is normalized.

Intravenous Thrombolysis With rt-PA

The use of intravenous rt-PA (0.9mg/kg, maximum 90mg) with 10% given as a bolus followed by an infusion over one hour is recommended for carefully selected patients within three hours of the acute onset of ischaemic stroke.^{1,2,3,4} Recent publications have raised the question of effectiveness of rt-PA outside of clinical trials. More data is needed for routine use of rt-PA outside of specialist centres.⁵ (Level 1, Grade A)

The use of streptokinase is contraindicated in acute ischaemic stroke due to poor clinical outcome.⁶ (Level 1, Grade A)

Intravenous rt-PA can be given only if the following is available:

1. A physician with expertise in the diagnosis and management of stroke.
2. Appropriate neuroimaging tests are available 24 hours a day
3. Capability to manage the complications of thrombolysis, particularly intracranial haemorrhage.

Characteristics of Patients With Ischaemic Stroke Who Could Be Treated With rt-PA

1. Diagnosis of ischaemic stroke causing measurable neurological deficit
2. The neurological signs should not be clearing spontaneously
3. The neurological signs should not be minor and isolated
4. Caution should be exercised in treating a patient with major deficits
5. Onset of symptoms <3 hours before beginning treatment
6. No contraindication for thrombolytic therapy
7. Blood pressure less than 185mm Hg systolic and/or less than 110mm Hg diastolic
8. Brain CT is normal
9. The patient or family understand the potential risks and benefits from treatment

Contraindications for intravenous thrombolytic therapy

1. Current use of oral anticoagulant or a prothrombin time (PT) > 15 seconds (INR > 1.7)
2. Use of heparin in the previous 48 hours and a prolonged partial thromboplastin time (PTT)
3. A platelet count < 100,000/mm³
4. Another stroke or any serious head injury in the previous 3 months
5. Major surgery within the preceding 14 days
6. Arterial puncture at noncompressible site within the last 21 days
7. Pre-treatment systolic blood pressure > 185mmHg or diastolic blood pressure > 110mmHg
8. Neurological signs that are improving rapidly
9. Isolated mild neurological deficits, such as ataxia alone, sensory loss alone, dysarthria alone or minimal weakness
10. Prior intracranial haemorrhage
11. A blood glucose < 2.7mmol/l or > 22.2mmol/l
12. Seizure at the onset of stroke
13. Gastrointestinal or urinary bleeding within the preceding 24 days
14. Recent myocardial infarction

Old age is not a contraindication but it is not wise to use it in patients above 75 years old. Caution is advised before giving intravenous rt-PA to persons with severe stroke.

Regimen for Treatment of Acute Ischaemic Stroke with Intravenous rtPA

1. Infuse 0.9mg/kg maximum of 90 mg over 60 minutes with 10% of the dose given as a bolus dose over 1 minute.
2. Admit the patient to an intensive care unit or a stroke unit for monitoring.
3. Perform neurological assessments every 15 minutes during the infusion of rt-PA and every 30 minutes for the next 6 hours and then every hour until 24 hours from treatment.
4. If the patient develops severe headache, acute hypertension, nausea or vomiting discontinue the infusion if agent is still being administered and obtain a CT scan of brain.
5. Measure blood pressure every 15 minutes for the first 2 hours, every 30 minutes for the next 6 hours and then every hour until 24 hours from treatment.
6. Increase blood pressure measurements if a systolic blood pressure > 180mm Hg or diastolic blood pressure >105mm Hg is recorded. Administer anti-hypertensive medications to maintain blood pressure at or below these levels.
7. Delay placement of nasogastric tubes, indwelling bladder catheters or intra-arterial pressure catheters.
8. Avoid antiplatelet drugs for the first 24 hours after administration of rt-PA.

Management of Bleeding Complications

Haemorrhagic transformation should be considered as a cause of neurological deterioration following the use of a thrombolytic agent. If an urgent brain CT confirms a haemorrhage, stop the rt-Pa infusion. Obtain blood samples for coagulation tests, infuse fresh frozen plasma and cryoprecipitate, and seek immediate neurosurgical opinion.

Recommendations

| Treatment | Recommendations | Level of evidence | Grade |
|------------------------|--|-------------------|--------|
| rt-Pa | In selected patients presenting within 3 hours: IV rt-pa (0.9mg/kg, maximum 90mg) with 10% given as a bolus followed by an infusion over one hour. | I | A |
| Aspirin | Start aspirin within 48 hours of stroke onset. Use of aspirin within 24 hours of rt-PA is not recommended | I II-1 | A A |
| Anticoagulants | The use of heparins (unfractionated heparin, low molecular weight heparin or heparinoids) is not routinely recommended as it does not reduce the mortality in patients with acute ischaemic stroke. | I | A |
| Neuroprotective Agents | A large number of clinical trials testing a variety of neuroprotective agents have been completed. These trials have thus far produced negative results. To date, no agent with neuroprotective effects can be recommended for the treatment of patient with acute ischaemic stroke at this time. | I I | A A |

STROKE UNIT

All patients with acute stroke should ideally have access to stroke units. There is clear evidence that treatment of patients with stroke in stroke units significantly reduces death, dependency, institutionalisation and length of hospital stay compared to treatment in a general medical ward.¹⁻⁷ (Level I)

This benefit is independent of patients' age, sex, co morbidity and stroke severity.^{1,8} (Level I)

A stroke unit is a dedicated unit in the hospital exclusively managing stroke patients. A team of specially trained staff provides co-coordinated multidisciplinary care throughout 24 hours to patients on a stroke unit. The core disciplines of the stroke team are: medical (neurologist, geriatrician or general physicians with interest in stroke), nursing, physiotherapy, occupational therapy and speech therapy. In bigger centres, it may include neurosurgeon, social worker and dietitian. Effectiveness of a stroke unit is not necessarily related to a certain medical specialty. A stroke unit runs by general physician, geriatrician, neurologist or specialist in rehabilitation medicine may be equally effective.¹ (Level I)

Stroke units are available in several categories:

- (1) The acute stroke unit which accepts patients acutely but discharged patients early, usually within 1 week
- (2) the combined acute and rehabilitation stroke unit admitting patients acutely but also provide rehabilitation for several weeks,
- (3) the rehabilitation stroke unit which accepts patients after a delay of 1 or 2 weeks and focuses on rehabilitation for several weeks or months if necessary

Of these, only the combined acute and rehabilitation stroke unit, and the rehabilitation stroke unit have proven effectiveness in terms of reduced mortality and handicap.¹ (Level I)

Possible reasons for stroke unit benefits include early acute treatment, reduced incidence of infection and systemic complications as well as early and more intense rehabilitation.⁹ (Level I)

Stroke unit can only work optimally if a well-established referral and rehabilitation network is available. This also includes co-operation with primary care physician in primary and secondary stroke prevention.

Recommendation:

| Treatment | Recommendations | Level of evidence | Grade |
|-------------|---|-------------------|-------|
| Stroke unit | Every hospital should set up a stroke unit. | I | A |
| | Stroke units significantly reduces death, dependency, institutionalisation and length of hospital stay | I | A |
| | A stroke unit should be managed by a multidisciplinary stroke team | III | C |
| | An efficient referral and rehabilitation network should be established to ensure the success of stroke units. | III | C |

GENERAL MANAGEMENT

The general management of acute stroke includes supportive care and treatment of acute complications. This is important to improve mortality and functional disability.

Oxygen and Airway Support

Adequate tissue oxygenation is imperative to prevent hypoxia and potential worsening of the neurological injury.¹⁻⁵ (Level II-3 to III)

Observation

Regular observation is mandatory to recognise impaired pulmonary function (pulse oxymeter), circulatory function (pulse rate, blood pressure) and to recognise complications from mass effect.¹ (Level III)

Mobilisation

Most patients are first treated with bed rest, but mobilisation should begin as soon as the patient's condition is judged to be stable.⁶⁻⁹ This involves passive and full-range-of-motion exercises, frequent turning, the use of alternating pressure mattresses (ripple mattress), and close surveillance of the skin. Measures to avoid falls are an important part of mobilisation.^{8,9} (Level II-3)

Blood Pressure

Hypertension following stroke is quite common. However, its optimal management has not been established.^{1,10-12} (Level II-3 to III)

Very high blood pressure should be reduced gradually.

Proposed drugs: Labetolol 10-20 mg boluses at 10 minute intervals up to 150-300 mg or 1 mg/ml infusion, 1-3 mg/min or Captopril 6.25-12.5 mg orally. Sublingual use of a calcium antagonist, such as nifedipine, should be avoided because of rapid decline in blood pressure.¹²

(Level II-3)

Blood Glucose

Hyperglycaemia following acute stroke is strongly associated with subsequent mortality and impaired neurological recovery. This applies to diabetics and non-diabetics.^{13,14} (Level II-3)

Nutrition

Sustaining nutrition is important as malnutrition after a stroke might interfere with recovery.¹⁵ Persons with infarctions of the brain stem, multiple strokes, large hemispheric lesions, or depressed consciousness are at the greatest risk for aspiration. Swallowing impairments are associated with an increased mortality. Early initiation of PEG feeding has not been shown to improve long-term outcome.¹⁶

A water swallow test should be performed before the patient is allowed to eat or drink. A wet voice after swallowing, incomplete oral-labial closure, or coughing reflex on swallowing indicates high risk of developing aspiration. A videofluoroscopic modified barium swallow examination can be performed later if indicated.^{1,17} (Level III)

If the patient fails the swallowing test, a nasogastric tube should be inserted to prevent aspiration. Percutaneous placement of an endogastric (PEG) tube is superior to nasogastric tube feeding if a prolonged need for devices is anticipated.¹⁸ (level II-1)

Infection

Infection is the commonest complication after an acute stroke especially pneumonia and urinary tract infection.¹⁹

The appearance of fever should prompt a search for infection and appropriate antibiotic therapy should be administered early. ¹⁹ Bladder catheters should be avoided if possible ¹ (Level III)

Fever

A meta-analysis suggested that fever after stroke onset is associated with marked increase in mortality and morbidity.²⁰ Anti-pyretics should be used to control elevated temperatures in acute stroke patients. ^{20, 21} (Level II-1)

Raised Intracranial Pressure

Cerebral oedema and increased intracranial pressure largely occur with large cerebral infarctions. The head of the bed can be elevated by 20 to 30 degrees in an attempt to help venous drainage. Hyperventilation is an emergency measure that acts almost immediately; a reduction of the PCO₂ by 5 to 10 mm Hg can lower intracranial pressure by 25% to 30%.^{1,22} (Level II-2)

Mannitol (0.25 to 0.5 g/kg) intravenously administered over 20 minutes lowers intracranial pressure and can be given every 6 hours.²³ The usual maximum daily dose is 2 g/kg. (Level II-2)

If hydrocephalus is present, drainage of cerebrospinal fluid via an intraventricular catheter can rapidly lower intracranial pressure.¹ (Level III)

Hemicraniectomy and temporal lobe resection have been used to control intracranial pressure and prevent herniation among those patients with very large infarctions of the cerebral hemisphere ²⁴⁻²⁶ (Level II-2)

Ventriculostomy and suboccipital craniectomy is effective in relieving hydrocephalus and brain stem compression caused by large cerebellar infarctions.^{27,28} (Level II-2)

Recommendation:

| Factors | Recommendation | Level of evidence | Grade |
|--------------------|--|-------------------|-------|
| Airway & Breathing | Ensure clear airway and adequate oxygenation Elective intubation may help some patients with severely increased ICP | III | C |
| Mobilization | Mobilize early to prevent complications | II-3 | C |
| Blood Pressure | Do not treat hypertension if < 220 mmHg systolic or < 120mmHg diastolic. Mild hypertension is desirable at 160-180/90-100 mmHg | III | C |
| | Blood pressure reduction should not be drastic. Proposed substances: Labetolol 10-20 mg boluses at 10 minute intervals up to 150-300 mg or 1 mg/ml infusion, 1-3 mg/min or Captopril 6.25-12.5 mg orally. | III | C |

| | | | |
|------------------------------|--|------|---|
| Blood Glucose | Treat hyperglycaemia (Random blood glucose > 11 mmol/l) with insulin | II-3 | C |
| | Treat hypoglycaemia (Random blood glucose < 3 mmol/l) with glucose infusion | III | C |
| Nutrition | Perform a water swallow test | III | C |
| | Insert a nasogastric tube if the patient fails the swallow test | III | C |
| | PEG is superior to nasogastric feeding only if prolonged enteral feeding is required | II-1 | B |
| Infection | Search for infection if fever appears and treat with appropriate antibiotics early | III | C |
| Fever | Use anti-pyretics to control elevated temperatures | II-1 | B |
| Raised Intracranial Pressure | Hyperventilate to lower intracranial pressure | II-2 | B |
| | Mannitol (0.25 to 0.5 g/kg) intravenously administered over 20 minutes lowers intracranial pressure and can be given every 6 hours | II-2 | B |
| | If hydrocephalus is present, drainage of cerebrospinal fluid via an intraventricular catheter can rapidly lower intracranial pressure. | III | C |
| | Hemicraniectomy and temporal lobe resection have been used to control intracranial pressure and prevent herniation among those patients with very large infarctions of the cerebral hemisphere | II-3 | C |
| | Ventriculostomy and suboccipital craniectomy is effective in relieving hydrocephalus and brain stem compression caused by large cerebellar infarctions | II-3 | C |

8 –PREVENTION

PRIMARY PREVENTION

Primary prevention is the key factor in any plan to reduce the incidence of stroke. This should be targeted to the whole population as well as high-risk groups by increasing awareness and promoting healthy lifestyles to reduce risk factors for stroke. The strategies should be integrated in the overall programme of health promotion for vascular diseases.

Although the following factors are non-modifiable, they identify individuals at highest risk of stroke and those who may benefit from rigorous prevention or treatment of modifiable risk factors.

Age: The cumulative effects of aging on the cardiovascular system and the progressive nature of stroke risk factors over a prolonged period of time age substantially increase stroke risk. The risk of stroke doubles in each successive decade after 55 years of.^{1,2}

Sex: Stroke is more prevalent in men than women.¹ Overall, men also have higher age-specific stroke incidence rates than women.³ Exceptions are in 35 to 44 year-olds and in those over 85 years of age in whom women have slightly greater age-specific incidence than men.³

Circumstances such as oral contraceptive use and pregnancy uniquely contribute to the risk of stroke in women.⁴⁻⁶

Family History: Both paternal and maternal history of stroke may be associated with increased risk. This may be mediated through genetic and shared environmental factors.^{7,8}

Medical Therapy

Aspirin

Aspirin may benefit women above the age of 65 in the primary prevention of stroke.⁹ (Level II-I)

Recommendation:

100mg aspirin every other day may be useful in women above the age of 65.

Hypertension

Hypertension is a major risk factor for both cerebral infarction and intracerebral haemorrhage.¹⁰ The incidence of stroke increases in proportion to both systolic and diastolic blood pressures. Isolated systolic hypertension is an important risk factor for stroke in the elderly (systolic blood pressure > 160 mm Hg and diastolic blood pressure < 90 mm Hg)¹¹.

Large randomized controlled trials and meta-analyses have confirmed that reduction in blood pressure reduces stroke incidence¹²⁻¹⁵ (Level I)

Lowering the systolic blood pressure by 10 mmHg is associated with a reduction in risk of stroke by about a third, irrespective of baseline blood pressure levels.²⁹ (Level I)

Combination therapy is more likely to achieve target blood pressures.

Recent published studies suggest that certain classes of anti-hypertensives may have additional benefits above and beyond lowering of blood pressure^{30,31} but no definite recommendations can be made. (Level I)

Hypertension in the very elderly should be treated to reduce the risk of stroke, with reduction of stroke risk in elderly with hypertension, isolated hypertension and previous stroke.³² (Level I)

Smoking

All forms of smoking, both active and passive is a major risk factor for stroke.¹⁸ Smokers who stopped for more than 5 years have the same risk as non-smokers.¹⁹ (Level III)

Alcohol

Heavy alcohol drinking, more than 3 units/day (1unit =1glass wine = 1 pack of hard liquor), increases the risk of stroke while light or moderate alcohol intake is protective against all strokes.²⁰ (Level II-2)

Post menopausal Hormone Replacement therapy

Stroke rates rapidly rise in women once they become menopausal. The Nurses' Health Study (6-year follow-up of 59,337 postmenopausal women) showed only a weak association between stroke and oestrogen replacement. However, the Women's Health Initiative Estrogen Plus

Progestin Study (E+P Study) showed a 31% increase in the risk of stroke due to E + P.²¹
(Level I)

Diabetes

Case-control studies of stroke patients and prospective epidemiological studies have confirmed an independent effect of diabetes on ischaemic stroke, with an increased relative risk in diabetics ranging from 1.8- to nearly 6-fold.²²
(Level II-2)

Tight control of hypertension in diabetics significantly reduced stroke incidence.²³ (Level I)

Tight glycemic control (Hb A1c < 6%) is important and supported by epidemiology and a meta-analysis.²⁴
(Level II-2)

Asymptomatic Carotid Stenosis

See Revascularization Procedures

Atrial fibrillation

See CardioEmbolism & Stroke

Hyperlipidaemia

Recent epidemiological studies have shown an association between raised serum lipids and risk of ischaemic stroke.²⁵⁻²⁶

In the high risk group, (those with cardiovascular disease, occlusive arterial disease or diabetes) statin therapy reduces the incidence of coronary events and ischaemic strokes even amongst individuals with normal cholesterol concentrations.^{27, 28}
(Level I)

Well-Documented Modifiable Risk Factors.

| Factors | Recommendation | Level of evidence | Grade |
|-------------------|---|-------------------|-------|
| Hypertension | Treat medically if BP>140mmHg systolic and/or >90mmHg diastolic. | I | A |
| | Lifestyle changes if BP between 130-139 mmHg systolic and/or 80-89mmHg diastolic. | I | A |
| | Target BP for diabetics is <130mmHg systolic and <80mmHg diastolic. | I | A |
| | Hypertension should be treated in the very elderly (age > 70 yrs) to reduce risk of stroke. | I | A |
| Diabetes mellitus | Strict blood pressure control is important in diabetics. | I | A |
| | Maintain tight glycaemic control. | | |
| Hyperlipidaemia | High risk group: keep LDL < 2.6mmol/l | I | B |
| | 1 or more risk factors: keep LDL < 3.4mmol/l | | |
| | No risk factor: keep LDL < 4.2mmol/l | | |
| Smoking | Cessation of smoking | III | C |

| | | | |
|---|--|------|---|
| Aspirin therapy | 50mg aspirin every other day may be useful in women above the age of 65. | II-1 | B |
| Post menopausal Hormone Replacement therapy | Oestrogen based HRT is not recommended for primary stroke prevention. | I | A |
| Alcohol | Avoid heavy alcohol consumption. | II-2 | B |

SECONDARY PREVENTION

Secondary Prevention of Stroke

Secondary prevention are strategies used after a stroke to prevent recurrence. This should be tailored according to individual stroke pathogenesis based on neuroimaging and investigations. (see Investigations)

The risk for recurrent vascular events after a stroke or transient ischaemic attack is approximately 5% per year for stroke, 3% per year for myocardial infarction and 7% per year for any one of stroke, myocardial infarction or vascular death.¹ This figure is even higher in certain populations especially those with high cerebrovascular atherosclerotic burden and for patients with ipsilateral high grade ($\geq 70\%$) extracranial carotid stenosis.²

Anti-platelet therapy

There is substantial evidence to support the value of aspirin. A 25% risk reduction of stroke was seen in all patients with strokes who have received aspirin.³ Aspirin given within 48 hours has also been shown to be beneficial in reducing recurrent stroke and death.³⁻⁵ Studies comparing the effects of different dosages of aspirin failed to show differences in stroke recurrences.⁶⁻⁹

Aspirin: The recommended dose of aspirin post-stroke is 75 mg to 325 mg orally daily (Level I)

Alternative antiplatelet medications can be considered for patients with aspirin allergy, aspirin failure, aspirin intolerance or aspirin contraindications based on the evidence presented below.

Previous clinical trials have demonstrated that ticlopidine is slightly superior to aspirin.¹⁰⁻¹¹ Blood monitoring is essential as neutropenia is the most significant side-effect.¹⁰ Severe neutropenia usually occurs within 3 months. Thus, baseline full blood count should be performed every 2-3 weeks within this time frame. Ticlopidine can be used if the patient has recurrent symptoms despite aspirin.

Ticlopidine: The recommended dose of ticlopidine is 250 mg orally twice a day. (Level I)

Clopidogrel is a newer thienopyridine derivative. It is slightly superior to 325 mg of aspirin.¹² It may be more beneficial than aspirin in several settings including patients with contraindications or adverse effects to aspirin and in high risk subjects with multiple risk factors (i.e. with a previous stroke, peripheral artery disease, symptomatic coronary disease and diabetes).¹³

Clopidogrel: The recommended dose is 75 mg daily (Level I)

Aspirin plus dipyridamole slow release. This combination is superior to aspirin or dipyridamole alone.¹⁴ The combination of aspirin (50 mg) plus dipyridamole (400 mg) doubles the effect of aspirin or dipyridamole alone.

Recommendation: The recommended dose of aspirin is 50 to 325 mg daily & slow release dipyridamole 400 mg orally daily* (Level I)

*Slow release dipyridamole is not available in Malaysia. Regular dipyridamole can be used with gradual titrations up to the required dosage, but may be limited by side-effects.

Aspirin and clopidogrel combination

Recent evidence from a large trial in post-stroke patients which compared clopidogrel 75 mg alone against clopidogrel 75 mg and 100 mg of aspirin over an 18 month period¹⁵ have shown an excess of gastrointestinal and major intracranial bleeding in the combination arm. The trial results do not support the addition of aspirin to clopidogrel in stroke patients for the purpose of long term secondary prevention. The use of this combination of antiplatelet drugs can only be used in selected high risk patients, who experience stroke recurrence despite monotherapy, when the benefit outweighs the risk.

Anticoagulation with warfarin

See Cardioembolism & Stroke

Long-term anticoagulation with warfarin after a stroke may reduce recurrent events in patients with atrial fibrillation.

For patients without atrial fibrillation, modern clinical trials such as the WARSS study suggest that warfarin was not more effective compared to aspirin alone.²⁴ In the latest study (WASID) comparing warfarin with high-dose aspirin (1300mg daily) in patients with intra-cranial stenosis, patients on warfarin had an excess of major haemorrhage and deaths.²⁵

Recommendations: Warfarin is indicated for secondary stroke prevention for patients with atrial fibrillation. (Level I)

Warfarin is not indicated for secondary stroke prevention for patients in sinus rhythm in absence of other conditions predisposing to cardio-embolic risk. (Level I)

Anti-hypertensive treatment

Reduction of blood pressure after the acute phase of the cerebrovascular event results in a further reduction of vascular events. This benefit has been noted in both ischaemic and haemorrhagic stroke with hypertensive and normotensive subjects.¹⁸ Meta-analyses of randomized controlled trials confirm approximately 30 – 40% reduction in stroke risk with blood pressure lowering.²⁶

In one study, the combination of an ACE-inhibitor and thiazide diuretic has been beneficial in both hypertensive and normotensive stroke patients when started two weeks after the event.¹⁹ Other studies have proven the superiority of an angiotensin receptor blocker, losartan (ARBs) over a beta-blocker (atenolol) in a specific group of high risk patients with left ventricular hypertrophy including subjects with previous stroke.²⁰

In the post-stroke situation (2 weeks or more after a stroke), ACE-inhibitor based therapy has been shown to reduce recurrent stroke in normotensive and hypertensive patients. (Level I)

Other classes of anti-hypertensives (ARB-based) therapy appear to be effective in selected high risk populations. (Level I)

Target blood pressure of absolute levels are not certain but targets based on hypertension guidelines (local or international) can be followed but should be individualized.²⁷ (Level II-1)

The choice of antihypertensive drug therapy (single or combination) should also be individualized based on current evidence and specific patient characteristics.²⁷ (Level II-1)

Carotid Endarterectomy (CEA)

See Revascularization Procedures

Lipid lowering

Statins have been proven to reduce vascular events among high risk patients including subjects with previous strokes.²¹⁻²² (Level I)

Other risk factors

The control of risk factors such as better glycaemic control in diabetes and smoking cessation have not been the subject of major randomized secondary prevention clinical trials. Although diabetes is recognized as an independent risk factor for ischaemic stroke, better diabetes control results only in a reduction of microvascular but not macrovascular complications.²³ Inferences can also be drawn from the positive results of primary prevention trials.(see primary prevention section). Nevertheless, better control of these risk factors should be advocated for better overall health after an ischaemic stroke. (Level III)

Recommendation:

| Factors Treatment | Recommendations | Level of evidence | Grade |
|---|---|-------------------|-------|
| Antiplatelets <u>Single agent</u> | | | |
| Aspirin | The recommended dose of aspirin is 75mg to 325mg daily. | I | A |
| <i>Alternatives:</i> | | | |
| Clopidogrel | The recommended dose is 75 mg daily. | I | A |
| | or | | |
| Ticlopidine | The recommended dose of ticlopidine is 250mg twice a day. | I | A |
| <u>Double therapy</u> | | | |
| Addition of clopidogrel to aspirin | In selected high risk patients only when benefit outweighs risk | I | B |

| | | | |
|------------------------------------|---|-----------|--------|
| Aspirin + clopidogrel | In selected high risk patients only when benefit outweighs risk | I | B |
| <i>Anti-hypertensive treatment</i> | ACE-inhibitor based therapy should be used to reduce recurrent stroke in normotensive and hypertensive patients. ARB-based therapy may benefit selected high risk populations. | I II-1 | A B |
| <i>Lipid lowering</i> | Lipid reduction should be considered in all subjects with previous ischaemic strokes. | I | A |
| <i>Diabetic control</i> | All diabetic patients with a previous stroke should improve glycaemic control. | III | C |
| <i>Cigarette smoking</i> | All smokers should stop smoking | III | C |

9 – CARDIOEMBOLISM

Cardioembolic stroke accounts for about 20% of all ischaemic strokes¹⁻³. They are in general severe, prone to early recurrence, more likely when there is documented source of embolism, and involvement of different cerebrovascular territories or multiple infarctions. The predominant pathogenic process for stroke associated with cardiac disease is embolism due to formation of intra-atrial and intra-ventricular thrombus.

Atrial fibrillation (AF) whether chronic or paroxysmal, is the most common cause of cardioembolism and accounts for 50% of all cardiogenic emboli. Other high risk conditions are prosthetic heart valves, rheumatic mitral valvular disease, acute myocardial infarction and severe left ventricular dysfunction. Non-thrombotic embolism may result from atrial myxoma and endocarditis.

Investigations are directed at demonstrating cardiac sources of embolism in the absence of significant atherosclerosis or other vascular disease. All patients with CVA/TIA require a 12-lead electrocardiograph. A 24-hour or 48-hour Holter monitor may be required for diagnosis of paroxysmal AF. In addition, all patients under 45 years of age and those in whom baseline investigations did not reveal an apparent cause for CVA will require a transthoracic echocardiogram (TTE). Patients in whom there is high suspicion of cardioembolism not found on TTE may undergo a trans-esophageal echocardiogram (TEE). Conditions in which this method is superior to TTE include identifying thrombi in left atrium and left atrial appendage, patent foramen ovale, atrial septal aneurysm and aortic arch atheroma^{3,4}.

Oral anticoagulation may reduce the risk of first and subsequent strokes for selected high-risk cardiac conditions but must be weighed against the risk of haemorrhagic complications^{1,2,5,6}. (see table b)

Patients with minor risk cardiac conditions (such as mitral valve prolapse, mitral regurgitation,

atrial septal aneurysm and patent foramen ovale) without additional risk factors may be offered aspirin 75-325mg/day for primary prevention of stroke . (Level III)

If patients were aspirin intolerant then consider: clopidogrel 75mg daily, ticlopidine 250mg bd or dipyridamole 400mg daily ¹. (Level III)

Anticoagulation is not indicated for non-thrombotic causes of cardiac emboli and may cause substantial intracranial haemorrhage in infective endocarditis of native valves ¹.

Anticoagulation is not proven to reduce recurrent stroke in the first 14 days following an acute cardioembolic event [I, A] with the possible exception of prosthetic heart valves, recent MI, presence of intra-cardiac thrombus, AF with additional risk factors and previous CVA. ³ (see table a) (Level III)

Table a. Anticoagulation for the patient with acute cardioembolic stroke

| Treatment | Recommendations | Level of Evidence | Grade |
|--------------------------|--|-------------------|-------|
| Aspirin | All patients should be commenced on aspirin within 48 hours of ischaemic stroke. | I | A |
| Warfarin | Adjusted-dose warfarin may be commenced within 2-4 days after the patient is both neurologically and medically stable. | II-2 | C |
| Heparin (unfractionated) | Adjusted-dose unfractionated heparin may be started concurrently for patients at very high risk of embolism. | III | C |
| Anticoagulation | Anticoagulation may be delayed for 1-2 weeks if there has been substantial haemorrhage. | III | C |
| | Urgent routine anticoagulation with the goal of improving neurological outcomes or preventing early recurrent stroke is not recommended. | I | A |
| | Urgent anticoagulation is not recommended for treatment of patients with moderate-to-large cerebral infarcts because of a high risk of intracranial bleeding complications | I | A |

Table b. Cardiac conditions predisposing to Ischaemic stroke

| Major Risk Conditions | Additional risk factors | Recommendation | Level of evidence | Grade |
|-----------------------|-------------------------|----------------|-------------------|-------|
| Atrial | <i>High risk:</i> | | | |

| | | | | |
|--------------------------------------|--|---|------|---|
| Fibrillation | Age >75 years; previous stroke/TIA; mitral valve disease; congestive heart failure; hypertension. | Long-term warfarin for patients with 1 or more high-risk factors | I | A |
| | <i>Moderate risk:</i> | Long term warfarin patients with 2 or more moderate-risk factors | III | C |
| | Age 65-75 years; coronary artery disease, peripheral artery disease; diabetes; active thyroid disease. | Warfarin or aspirin for patients with 1 moderate risk factor | I | A |
| | | Aspirin 75-325mg daily is sufficient for patients < 65 years of age with 'lone' AF and no additional risk factors present | I | A |
| Prosthetic Heart Valves (Mechanical) | <i>Moderate risk:</i> Bileaflet or tilting disk aortic valves in NSR | Life-long warfarin | II-2 | B |
| | <i>High risk:</i> Bileaflet or tilting disk aortic valves in AF; Bileaflet or tilting disk mitral valve in AF or NSR. | Life-long warfarin (target INR 3.0; range 2.5-3.5) | II-3 | B |
| | <i>Very high risk:</i> Caged-ball and caged-disk designs; documented stroke/TIA despite adequate therapy with warfarin. | Life-long warfarin (target INR 3.0; range 2.5-3.5) plus aspirin 75-150mg daily | II-1 | B |
| Bioprosthetic heart valves | <i>High risk:</i> AF; left atrial thrombus at surgery; previous CVA/TIA or systemic embolism | If high risk factors present, consider warfarin for 3-12 months or longer | III | C |
| | | For all other patients, give warfarin for 3 months post-op, then aspirin 75-150mg daily | III | C |
| Mitral Stenosis | <i>High risk:</i> AF; previous stroke/TIA; left atrial thrombus; left atrial diameter > 55mm on echo. | If high risk factors present, consider long-term warfarin | II-3 | B |
| | | For all other patients start aspirin 75-150mg daily | II-2 | B |
| MI and LV dysfunction | <i>High risk:</i> Acute/recent MI (<6 mos); extensive infarct | If risk factors present without LV thrombus: consider warfarin for | III | C |

| | | | | |
|--|--|--|-----|---|
| | with anterior wall involvement; previous stroke/TIA. <i>Very high risk:</i> | 3-6 months followed by aspirin 75-150mg daily | III | C |
| | Severe LV dysfunction (EF < 28%); LV aneurysm; spontaneous echo contrast; LV thrombus; dilated non-ischaemic cardiomyopathies. | If LV thrombus is present, consider warfarin for 6-12 months For dilated cardiomyopathies including peripartum, consider long-term warfarin | | |

Recommended warfarin dose INR target 2.5 [range 2.0 to 3.0] unless stated otherwise

10– REVASCULARISATION PROCEDURES

Surgical procedures in stroke management may be classified to procedures performed to prevent first stroke occurrence (primary prevention in asymptomatic patients) or following a stroke event (secondary prevention).

PRIMARY PREVENTION

Carotid endarterectomy (CEA) has been compared to conservative medical therapy for asymptomatic patients without prior history of TIA or stroke but for whom imaging of the carotid arteries has revealed a definite stenosis. There have been 5 published randomized studies but only 2 are sufficiently powered to detect outcomes between surgery and conservative approach. The absolute 5-year risk reduction for patients with 70-99% carotid artery stenosis (by ultrasound) was 5.4% in the recent follow-up of the ACST trial,¹ which was consistent with the ACAS study² from North America (5.9% absolute 5-year risk reduction). This translates into 1% annual stroke rate reduction. Patients who are asymptomatic and receiving appropriate medical therapy face only a 2% annual stroke rate without CEA. Surgical morbidity and mortality often exceed this beneficial risk reduction. In the ACST and ACAS trials, surgery-related events was 3.1% and 2.3% respectively.¹⁻² In an unselected patient group undergoing CEA in a centre without proper auditing of the surgeon's or centre's operative records, the complications are likely to outweigh the benefits of CEA. Furthermore asymptomatic patients should not be offered CEA if their 5-year probability of dying from unrelated causes are high. Finally, in the NASCET study, nearly 45% of all strokes occurring in patients with asymptomatic stenosis may be attributable to lacunar infarcts or cardioembolism.⁵

Recommendation:

Endarterectomy may be considered in patients with high-grade asymptomatic carotid stenosis (70-99%) when performed by a surgeon with less than 3% morbidity / mortality rate. (Level I)

Careful patient selection, guided by comorbid conditions, life expectancy, and patient preference, followed by a thorough discussion of the risks and benefits of the procedure is required. It is important that asymptomatic patients receive appropriate medical treatment and be fully evaluated for other treatable causes of stroke.

SECONDARY PREVENTION

2 large randomized trials (NASCET and ECST) have compared the outcomes of patients with recent cerebrovascular symptoms treated conservatively or with carotid endarterectomy.¹⁰⁻¹¹ Long term follow-up and a meta-analysis is available for these trials.¹² Standardizing for the same measurements and definitions yielded highly consistent results among all 3 trials. In general, CEA is highly beneficial for patients with carotid stenosis 70-99% producing a 16% absolute 5-year risk reduction (ARR). For patients with 50-69% stenosis, the 5-year ARR was 4.6%. No benefit was observed for patients with milder degrees of stenosis. Subgroup analyses revealed that benefit in surgery was greatest in men, aged 75 years or older, and those randomized within 2 weeks of their stroke event. The studies excluded patients with medical co-morbidities, previous neck irradiation, recurrent stenosis following previous endarterectomy.

Extracranial-intracranial anastomosis between the superficial temporal and middle cerebral arteries (EC-IC Bypass) has not been shown to be beneficial for secondary stroke prevention by the EC/IC Bypass Study Group.

Recommendations:

CEA is indicated for patients with carotid stenosis of 70-99% without a severe neurological deficit with recent ischaemic events (less than 180 days) in centres with a perioperative complications rate for all strokes and deaths of less than 6%. (Level I)

Early CEA is indicated for patients with carotid stenosis of 70-99% without a severe neurological deficit within 2 weeks of recent ischaemic events in centres with a perioperative complications rate for all strokes and deaths of less than 6%. (Level II-1)

CEA may be indicated for patients with carotid stenosis of 50-69% without a severe neurological deficit with recent ischaemic events (less than 180 days) in centres with a perioperative complications rate for all strokes and deaths of less than 6%. (Level III)

CEA is not recommended for patients with carotid stenosis less than 50%. (Level I)

CEA should not be performed in centres not exhibiting low complications rates similar to those seen with NASCET or ECST. (Level I)

Patients should remain on antithrombotic therapy before and after surgery. (Level II-2)

EC/IC Bypass is not recommended for secondary stroke prevention. (Level I)

ANGIOPLASTY OR STENTING

This is a rapidly evolving field in stroke treatment and prevention. Several randomized trials have compared extra-cranial carotid angioplasty and stenting (CAS) to carotid endarterectomy (CEA).¹⁻⁵ CAS represents a feasible alternative to carotid endarterectomy for secondary stroke

prevention when surgery is undesirable, technically difficult or inaccessible.⁶⁻⁸ (Level II-2)

However, compared to carotid endarterectomy, percutaneous transluminal carotid angioplasty and stenting is a new mode of intervention currently under evaluation.¹⁴⁻¹⁵ It is not a standard treatment until further clinical data is available. In particular, The long-term safety and efficacy of CAS is unknown.⁷⁻⁹ Patients should be made aware that carotid angioplasty is to date, not a routine treatment modality for stroke prevention. The procedure should be performed by experienced operators with high technical success and low complication rates and the patient jointly managed with a neurologist.^{5,8}

Intracranial artery stenting (IAS) is also technically feasible but has also not been proven as an established treatment modality. Re-stenosis rate up to 30% have been reported.¹⁶ The clinical data has much less evidence with more controversy compared to carotid angioplasty.¹⁷⁻¹⁸ The role of CAS in intra-cranial stenoses, asymptomatic stenoses and acute stroke is unclear and not recommended.⁹⁻¹¹ (Level II-2)

Recommendations:

Careful selection of patients by centers experienced in cerebrovascular disease is recommended. As angioplasty with or without stenting is still an investigational procedure, it should be carried out under appropriate clinical trial protocols.

| Treatment | Recommendations | Level of Evidence | Grade |
|--------------------------------------|---|-------------------|--------|
| Carotid Endarterectomy (CEA) | Indicated for most patients with stenosis of 70-99% after a recent ischaemic event in centres with complication rates of less than 6% | I | A |
| | Earlier intervention (within 2 weeks) is more beneficial. | II-1 | B |
| | May be indicated for patients with stenosis of 50-69% after a recent ischaemic event in centres with complication rates of less than 6% | III | C |
| | CEA is not recommended for patients with stenosis of less than 50% | I | A |
| | Patients should remain on antithrombotic therapy before and after surgery | II-2 | B |
| Carotid angioplasty & stenting (CAS) | CAS represents a feasible alternative to carotid endarterectomy for secondary stroke prevention when surgery is undesirable, technically difficult or inaccessible. | II-2 | B |
| | Distal protection devices should be used during the procedure and anti-platelet agents such as clopidogrel be initiated. | I III | A C |

| | | | |
|---|---|------|---|
| | The long-term safety and efficacy of CAS is not known | | |
| Intracranial angioplasty & stenting (IAS) | Role of AS in intra-cranial stenoses, asymptomatic stenoses and acute stroke is unclear and not recommended | II-2 | C |

11 – STROKE IN SPECIAL CIRCUMSTANCES

STROKE IN THE YOUNG

Stroke is a rare occurrence before the age of 45. Young stroke is usually caused by a variety of conditions which are distinct from degenerative arterial disease. Across a broad range of causes, stroke in the young is associated with better prognosis than in the elderly. Nevertheless, the socioeconomic impact is often substantial. This discussion will cover ischaemic infarction; stroke in childhood will be excluded.

Young stroke may be broadly classified into two groups: (i) atherothrombotic disease caused by accelerated atherosclerosis and (ii) non-atherothrombotic stroke. The cause can be identified in approximately half the cases.

The list below is not exhaustive.

| Atherothrombotic | |
|-----------------------------|--|
| Atherothrombotic | Uncommon before age 45, incidence increases with age Classic vascular risk factors present |
| Non atherothrombotic | |
| Pro-thrombotic states | Abnormal blood rheology – dehydration, polycythaemia, thrombocythaemia, paraproteinaemia, etc Hypercoaguable states – malignancy, pregnancy, oestrogens, hyperhomocysteinaemia, anti-phospholipid antibodies, deficiency protein c, protein s, carrier state of Factor V-Leyden, etc Abnormal cellular components – sickle cell disease, leukaemia, etc |
| Cardiogenic embolism | Atrial fibrillation Valvular lesions PFO (patent foramen ovale), ASA (atrial septal aneurysm), etc see Cardioembolism |
| Arterial diseases | Trauma, vascular dissection, cystic medial necrosis, fibromuscular dysplasia, hereditary haemorrhagic telangiectasia Vasculitis – primary / secondary to infection / drug-related - Primary – SLE, PAN, Takayasu’s (primary) arteritis, granulomatous angiitis - Complication of infection – meningitis, syphilis, chicken pox, HIV/AIDS - Drug-related – heroin, LSD, cocaine, amphetamines, ephedrine, phenylpropanolamine |
| Miscellaneous | Migraine |

| | |
|----------------------------|---|
| | Moya-moya's disease Metabolic disorders – mitochondrial cytopathies , leukodystrophy (CADASIL),etc |
| Cerebral venous thrombosis | This condition is associated with a significant mortality ranging from 5 to 30 percent from retrospective studies. Notable for its occurrence in young children and the peri-partum state. Headache, seizures and imaging appearance should alert to this possibility. An increased thrombotic tendency occurs in low-flow states (including dehydration), hypercoagulable states (primary and secondary) as well as abnormalities of the vessel wall caused by infection, inflammation, trauma or cancer. Often, more than one risk factor is necessary for the development of CVT. Hence, even in the presence of a known risk factor such as pregnancy and dehydration, an underlying cause should be excluded. |

Investigation of the Young Stroke

- I. Identify the cause / predisposing factor
 - A) Search for classical vascular risk factors
 - B) Special diagnostic tests (see section on Investigations)
 - i. Fasting homocysteine
 - ii. Auto-antibody screen, including antiphospholipid antibodies
 - iii. Coagulation screen if indicated:
 - Serum fibrinogen
 - Anti-thrombin III
 - Protein C and Protein S
 - Factor V-Leyden
 - C) Radiological investigations (see chapter Investigations)

Recommendations:

| Treatment | Recommendations | Level of evidence | Grade |
|---------------------------|--|--------------------------|--------------|
| Aspirin | Young Ischaemic stroke If the cause is not identified, aspirin is usually given. There are currently no guidelines on the appropriate duration of treatment. | III | C |
| Heparin | Cerebral Venous thrombosis Anticoagulation appears to be safe, and cerebral haemorrhage is not a contra-indication for anticoagulation. | II-I | B |
| Warfarin | Simultaneous oral warfarin should be commenced. The appropriate length of treatment is unknown. | III | C |
| Endovascular thrombolysis | It is currently considered for patients with extensive disease and clinical deterioration | III | C |

STROKE AND PREGNANCY

Introduction

Stroke risk increases in pregnancy by 3 to 13-fold. Although uncommon, stroke is a leading cause of maternal death. The naturally increased risk is compounded by any hypercoagulable state (inherited or acquired), intracranial vascular lesion or arterial hypertension. Pregnancy also imposes additional haemodynamic demands, more so when there is a concomitant cardiac disorder.

I. Ischaemic stroke in pregnancy and the puerperium

Any of the causes of ischaemic stroke in the young, including cerebral venous thrombosis (see previous section) may present during pregnancy and the puerperium.

In addition, the following causes of ischaemic stroke are peculiar to the pregnant state:

- a) peripartum cardiomyopathy
- b) amniotic fluid embolism
- c) disseminated intravascular coagulation
- d) hypotensive emergency – borderzone infarction, Sheehan's syndrome

II. Haemorrhagic stroke in pregnancy

- a) eclampsia
- b) hypertension in pregnancy
- c) choriocarcinoma
- d) rupture of berry aneurysm, arteriovenous or other vascular malformation

Treatment of ischaemic stroke in pregnancy

Issues to be considered

Risks to both the mother and foetus have to be considered. When there is conflict, the welfare of the mother must take precedence.

- a) **Teratogenicity**
Aspirin may be used throughout pregnancy. Safety of the other anti-platelet agents has not been established. Warfarin is contraindicated in the first trimester and needs to be substituted with heparin (either unfractionated or low molecular weight heparin, depending on the condition under treatment). [Level III, Grade C]
- b) **Risk of bleeding**
Use of anti-thrombotic treatment needs to be closely coordinated with the obstetrician.
- c) **Foetal loss**
Drugs associated with risk of spontaneous abortion and premature labour are to be avoided.
- d) **Haemorrhagic risk to the newborn**
Any potential impact on the newborn must be assessed. This is most crucial for anticoagulants.

e) Excretion in breast milk

The following drugs may not be used when breast-feeding:

- Warfarin, Ticlopidine, Clopidogrel, Dipyridamole

12 – CONCLUSION

Over the last decade, major advances have been made in acute management of ischaemic stroke. These advances have occurred along with advances in imaging methods as well as treatments for primary and secondary prevention. Some of the recommendations may be adopted for general use while there are others that may only be used in controlled settings with highly experienced and dedicated teams.

Further ongoing studies and clinical trials will better define the usage of agents in terms of identifying particular subgroups of patients who are best suited for certain kinds of therapy based on underlying pathophysiology and cause of stroke.

The general care of stroke patients in the ward still plays a vital role in the quest to achieve better outcomes. Many complications can be anticipated and avoided in the acute stroke setting as well as in the rehabilitation period. Basic infrastructure for acute stroke care is already available but reorganization and strengthening of various components such as manpower, training and networking are necessary to enable multidisciplinary inputs to avail early for the patients' benefit. Ideally this would be done in the setting of stroke units. There is also urgent need to strengthen all the components of in-hospital and after-discharge care.

Research, audit and epidemiological studies are needed to be carried out to know the pattern of illness in our own community, what happens to patients and what kind of support systems are available to them outside the hospital.

There are reports of ethnic differences in stroke prevalence as well as risk factor prevalence although the reasons are not fully understood. Clearly there must be impetus to gain information on ethnic and racial differences in stroke incidence, prevalence and vascular risk factors in Malaysia which can have major impact on clinical and public health services on a population level.

Finally, of importance is the management of stroke to be recognized as an acute medical emergency and for therapeutic nihilism to be abolished as standard practice. Although not available everywhere, therapeutic options are available in the first few hours after stroke onset. Education of the general population on symptoms of stroke and the urgency to arrive at a hospital for treatment will fundamentally change the outlook for many stroke survivors.

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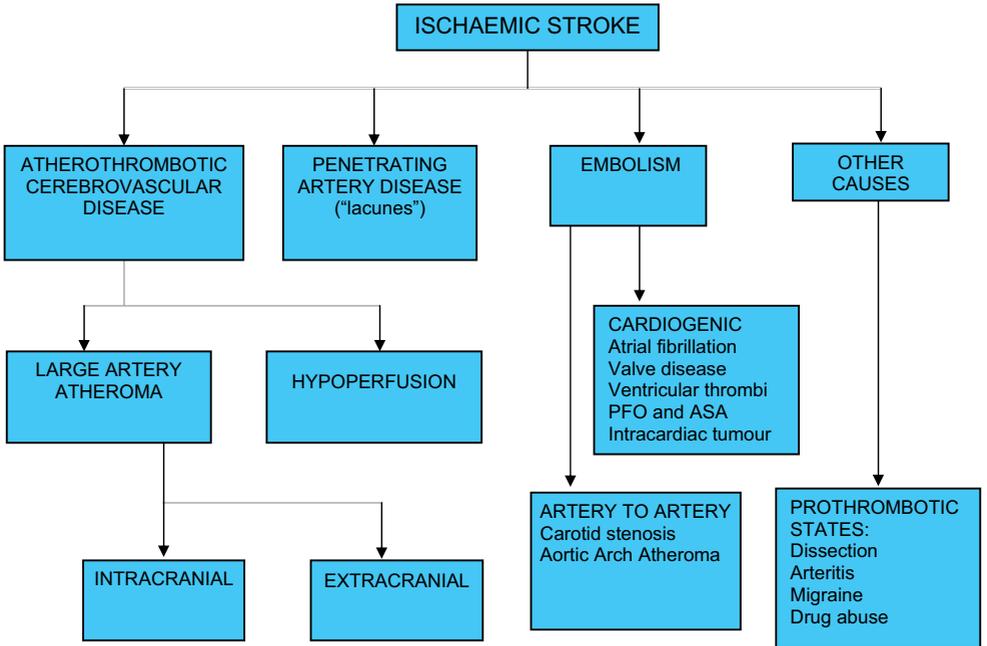
APPENDIX A

Oxfordshire Community Stroke Project Classification (OCSP)

| | |
|---|---|
| Total Anterior Circulation Stroke (TAC) | <p>All of</p> <ul style="list-style-type: none"> • Hemiplegia contralateral to the cerebral lesion, usually with ipsilateral hemisensory loss • Hemianopia contralateral to cerebral lesion • New disturbance of higher cerebral function (dysphasia, visuospatial) |
| Lacunar Stroke (LAC) | <ul style="list-style-type: none"> • Pathological definition • Occlusion of a single deep (LS) perforating artery • 5% can be due to haemorrhage • Occurs at strategic sites • More likely seen on MRI than CT scan • Classical lacunar syndromes correlated with relevant lacunes at autopsy |
| Partial Anterior Circulation Stroke (PAC) | <p>Any of</p> <ul style="list-style-type: none"> • Motor / sensory deficit + hemianopia • Motor/sensory deficit + new higher cerebral dysfunction • New higher cerebral dysfunction + hemianopia • New higher cerebral dysfunction alone • A pure motor/sensory deficit less extensive than for LAC (eg. confined to one limb, or to face and hand but not to whole arm) |
| Posterior Circulation Stroke (POC) | <p>Any of</p> <ul style="list-style-type: none"> • Ipsilateral cranial nerve palsy (single / multiple) with contralateral motor and/or sensory deficit • Bilateral motor and/or sensory deficit • Disorder of conjugate eye movement (horizontal/vertical) • Cerebellar dysfunction without ipsilateral long tract sign • Isolated hemianopia or cortical blindness <p>Other signs include Horner's sign, nystagmus, dysarthria, hearing loss, etc</p> |
| Code last letter as follows: | |
| (S) | Syndrome: Indeterminate pathogenesis, prior to imaging (e.g. TACS) |
| (I) | Infarct (e.g., TACI) |
| (H) | Haemorrhage (e.g., TACH) |

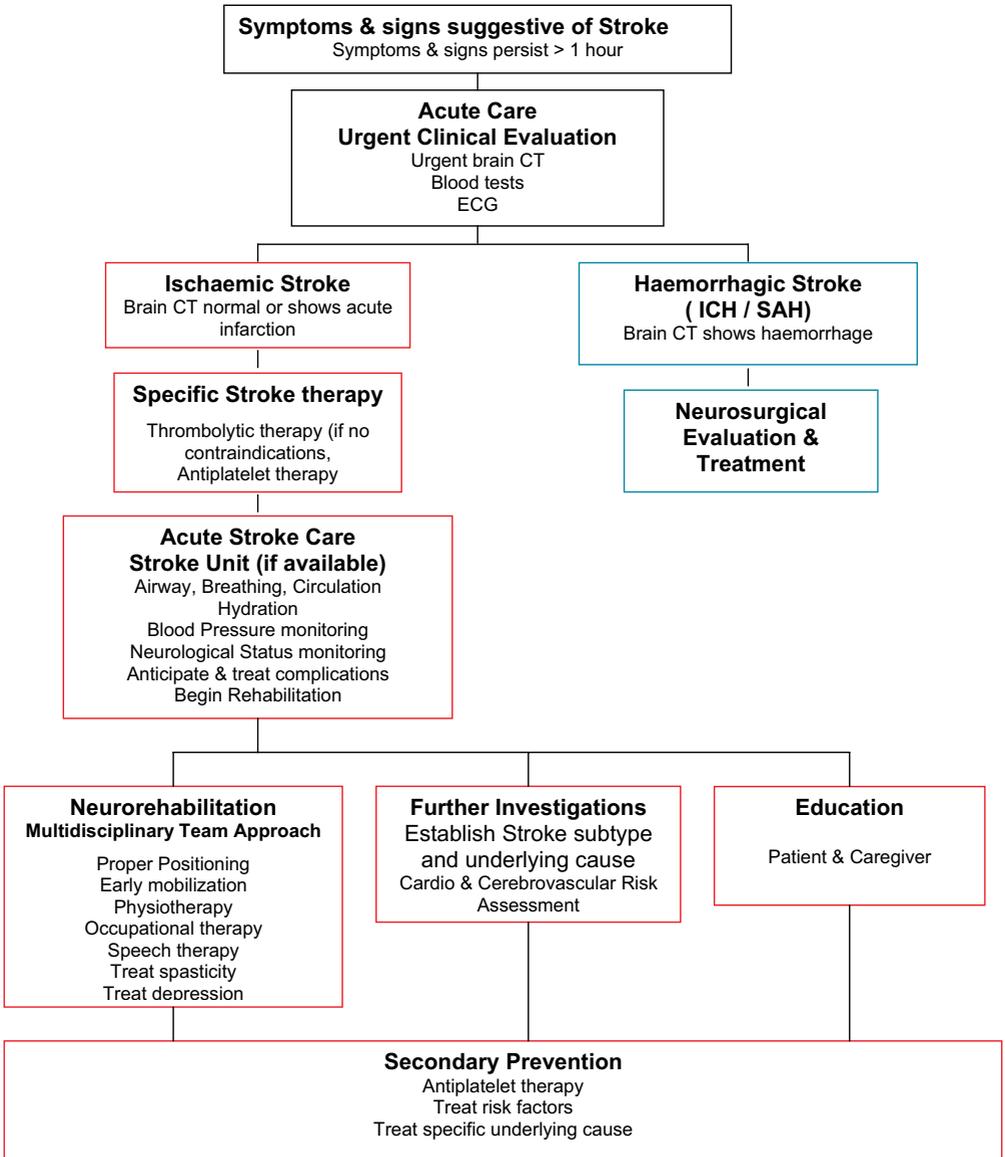
APPENDIX B

Stroke Pathophysiology Algorithm



APPENDIX C

Stroke Management Algorithm



APPENDIX E

Resources – Societies & Associations

Malaysian Society of Neuroscience

Mailing address:

Lot 9, Jalan 26/1, Seksyen 26,

Kawasan Perindustrian Hicom

40400 Shah Alam

Selangor Darul Ehsan

Website: www.neuro.org.my

NASAM (National Stroke Association of Malaysia)

1. NASAM Centre
12, Jalan 7/2
46050 Petaling Jaya
Selangor Darul Ehsan
Open : Monday-Friday 10am -4pm
Tel: 03-7956 4840 / 7956 1876
Fax: 03-7956 2275
Email : nasampj@nasam.org
2. NASAM Ampang
9, Lorong Awan 1,
68000 Ampang
Selangor Darul Ehsan
Open : Monday-Friday: 9am-1pm
Tel: 03-4256 1234
Fax: 03-4256 5360
Email : nasamampang@nasam.org
3. NASAM Penang
No. 19, Codrington Avenue
10350 Pulau Pinang
Registration and group therapy:
Mon, Wed, Fri: 10-12 noon, Sat-Sun:
3.30pm-5.30pm
Tel / Fax : 04-229 8050
Email : nasampenang@nasam.org
4. NASAM Perak
No. 9, Lorong Pinji
Off Jalan Pasir Puteh
31560 Ipoh, Perak
Open : Mon-Fri : 10am-12pm,
2pm-4pm, Sat : 2pm-4pm
Tel : 05-321 1089
Fax : 05-322 4759
Email : nasamperak@nasam.org
5. NASAM Malacca
C5458, Jalan Melor
Off Jalan Penghulu Abbas
Bukit Baru, Melaka
Open : Mon-Fri : 10am-12pm,
2pm-4pm, Sat : 2pm-4pm
Tel/Fax : 06-288 1641
Email : nasammalacca@nasam.org
6. NASAM Sabah
Kompleks Badan-Badan Sukarela
Wisma Pandu Puteri
KM4 Jalan Tuaran
88801 Kota Kinabalu
Open : Tue, Thur & Sat :
10am-12.30pm

Stroke Resources on World-wide Web

1. National Stroke Foundation
www.strokefoundation.com.au
2. Stroke Centre at Washington University
www.strokecenter.org
3. American Heart Association
www.americanheart.org
4. American Academy of Neurology
www.aan.com
5. American Stroke Association
www.strokeassociation.org
6. European Stroke Initiative (EUSI)
www.eusi-stroke.com
7. Royal College of Physician
www.rcplondon.cu.uk/pubs/books/stroke
8. Stroke Association
www.stroke.org.uk

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Dr Lam Khai Huat, Consultant Cardiologist, IJN.