CLINICAL PRACTICE GUIDELINES

MANAGEMENT OF ISCHAEMIC STROKE

2nd EDITION
2012

QUICK REFERENCE FOR HEALTH CARE PROVIDERS

Malaysian Society of Neurosciences
Academy of Medicine Malaysia
MINISTRY OF HEALTH MALAYSIA

MH/P/PAK/235.12(GU)

This Quick Reference provides key messages and a summary of the main recommendations in the Clinical Practice Guidelines (CPG) Management of Ischaemic Stroke, August 2011.

Details of the evidence supporting these recommendations can be found in the above CPG, available on the following website:

Ministry of Health Malaysia	: http://www.moh.gov.my
Academy of Medicine	: http://www.acadmed.org.my
Malaysia Society of Neurosciences	: http://www.neuro.org.my

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 130-139mmHg 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	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 < 220mmHg systolic or < 120mmHg diastolic. Mild hypertension is desirable at 160-180/90-100mmHg.	III	C
	Blood pressure reduction should not be drastic.	III	C
	Proposed substances: Labetolol 10-20mg boluses at 10 minute intervals up to 150-300mg or 1mg/ml infusion, rate of infusion for labetolol as 1-3mg/min or Captopril 6.25-12.5mg orally.		
Blood Glucose	Treat hyperglycaemia (Random blood glucose >11mmol/l) with insulin.	II-3	C
	Treat hypoglycaemia (Random blood glucose <3mmol/l) with glucose infusion.	III	C
Nutrition	Perform a water swallow test. (Refer appendix F)	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 0.5g/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

Acute Stroke therapy

Treatment	Recommendations	Level of evidence	Grade
rt-Pa	Intravenous rt-PA (0.9mg/kg, maximum 90mg), with 10% of the dose given as a bolus followed by a 60-minute infusion, is recommended within 4.5 hours of onset of ischaemic stroke. (new recommendation)	I	A
Intra-arterial thrombolysis	Reasonable to consider intra-arterial thrombolysis in selected patients with major stroke syndrome of <6 hours' duration and ineligible for intravenous thrombolysis. (new recommendation)	II-2	C
Endovascular mechanical thrombectomy	May be reasonable to perform mechanical disruption to restore cerebral blood flow in selected patients with major stroke syndrome of <8 hours' duration and ineligible for or failing intravenous thrombolysis. (new recommendation)	III	C
	Concentric Merci or other endovascular device can be useful for extraction of intra-arterial thrombi in appropriately selected patients, but the utility of the device in improving outcomes is still unclear. (new recommendation)	III	C
Aspirin	Start aspirin within 48 hours of stroke onset.	I	A
	Use of aspirin within 24 hours of rt-PA is not recommended.	II-1	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.	I	A
	To date, no agent with neuroprotective effects can be recommended for the treatment of patient with acute ischaemic stroke at this time.	I	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 multidisplinary stroke team.	I	A
	An efficient referral and rehabilitation network should be established to ensure the success of stroke units.	III	C

Cardiac conditions predisposing to Ischaemic stroke

<table>
<tr><th>Major Risk Conditions</th><th>Additional risk factors</th><th>Recommendation</th><th>Level of evidence</th><th>Grade</th></tr>
<tr><td>Atrial Fibrillation</td><td>Risk factors to be access by CHA_2DS_2-VASc Score.
(Refer Appendix E)
(new recommendation)</td><td>
<table>
<tr><th>CHA_2DS_2-VASc score</th><th>Recommended antithrombotic therapy</th></tr>
<tr><td>≥2</td><td>OAC[a]</td></tr>
<tr><td>1</td><td>Either OAC[a] or aspirin 75-325mg daily. Preferred: OAC rather than aspirin.</td></tr>
<tr><td>0</td><td>Either aspirin 75-325mg daily or no antithrobotic therapy. Preferred: no antithrombotic therapy rather than aspirin.</td></tr>
</table>
[a] Oral Anticoagulant

Aspirin 75-325mg daily is sufficient for patients < 65 years old with ‘lone’ AF and no additional risk factors. (new recommendation)

Dabigatran etexilate is superior (150mg bid) and as effective (110mg bid) compared to warfarin, in preventing stroke and systemic embolism in non-valvular atrial fibrillation. (new recommendation)

Bleeding rates are similar with warfarin for 150mg bid but lower bleeding rates for 110mg bid.
* Dabigatran etexilate does not require routine INR monitoring. (new recommendation)

Oral factor Xa inhibitors have also been shown to be at least as effective as VKA in their latest trials. However, at the time of writing, these agents are not yet licensed for stroke prevention in atrial fibrillation in Malaysia. (new recommendation)</td><td>I

I

I</td><td>A

A

A</td></tr>
<tr><td>Prosthetic Heart Valves (Mechanical)</td><td>Moderate risk:
Bileaflet or tilting disk aortic valves in NSR

High risk:
Bileaflet or tilting disk aortic valves in AF; Bileaflet or tilting disk mitral valve in AF or NSR.

Very high risk:
Caged-ball and caged-disk designs; documented stroke/TIA despite adequate therapy with warfarin.</td><td>Life-long warfarin

Life-long warfarin (target INR 3.0; range 2.5-3.5)

Life-long warfarin (target INR 3.0; range 2.5-3.5) plus aspirin 75-150mg daily</td><td>II-2

II-3

II-1</td><td>B

B

B</td></tr>
</table>

Bioprosthetic heart valves	*High risk:* 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 warfarin for 3 months post-op, then aspirin 75-150mg daily.	III III	C C
Mitral Stenosis	*High risk:* 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	*High risk:* Acute/recent MI (<6 mos); extensive infarct with anterior wall involvement; previous stroke/TIA. *Very high risk:* Severe LV dysfunction (EF < 28%); LV aneurysm; spontaneous echo contrast; LV thrombus; dilated non-ischaemic 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
Recommended warfarin dose INR target 2.5 [range 2.0 to 3.0] unless stated otherwise				

Secondary Prevention

Factors Treatment	Recommendations	Level of evidence	Grade
Antiplatelets **Single agent**			
Aspirin *Alternatives:*	The recommended dose of aspirin is 75mg to 325mg daily.	I	A
Clopidogrel	The recommended dose is 75mg daily. or	I	A
Ticlopidine	The recommended dose is 250mg twice a day.	I	A
Trifusal	The recommended dose is 600mg daily. (new recommendation)	I	A
Cilostazol	The recommended dose is 100mg twice a day. (Not licensed yet for ischaemic stroke in Malaysia.) (new recommendation)	I	A
Double Therapy	Combination therapy of clopidogrel and aspirin is not superior to clopidogrel or aspirin alone; but with higher bleeding complication. (new recommendation)	I	A
Anti-hypertensive treatment	ACE-inhibitor based therapy should be used to reduce recurrent stroke in normotensive and hypertensive patients.	I	A
	ARB-based therapy may benefit selected high risk populations.	II-1	B
Lipid lowering	Lipid reduction should be considered in all subjects with previous ischaemic strokes.	I	A
Glycaemic control	All diabetic patients with a previous stroke should have good glycaemic control.	III	C
Cigarette smoking	All smokers should stop smoking.	III	C

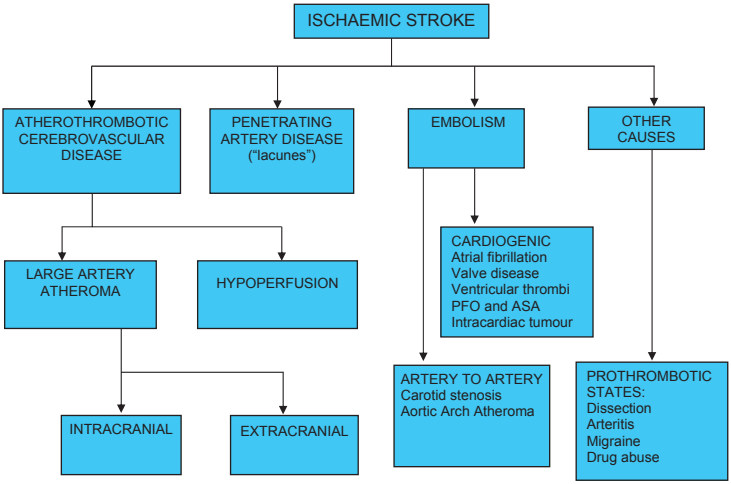
Endarterectomy, Angioplasty & Stenting

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

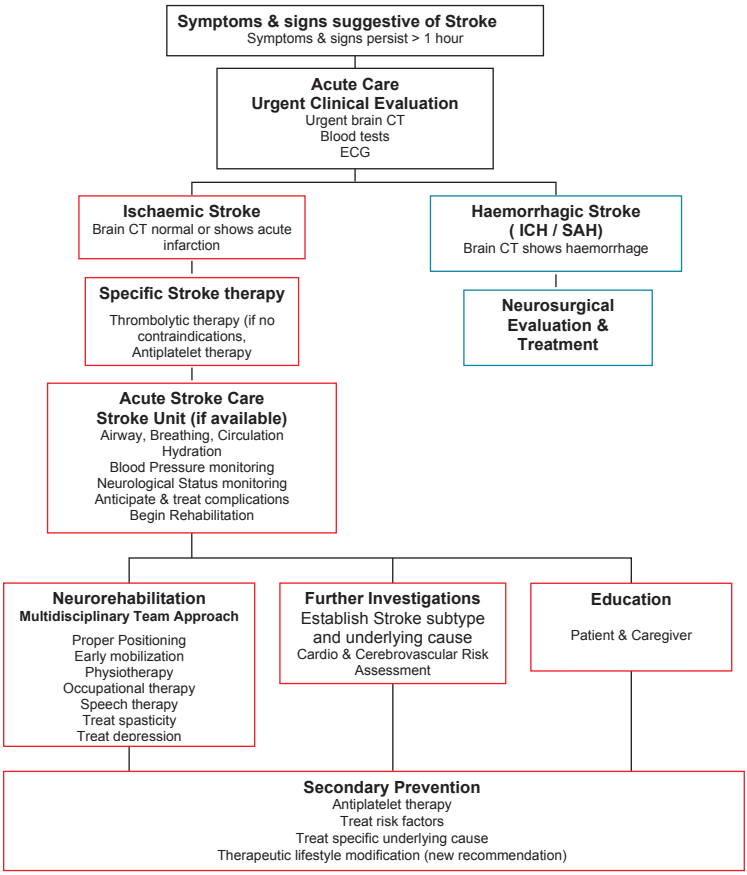
Stroke in Special Circumstances

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
	Cerebral Venous thrombosis		
Heparin	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	Refer guidelines for recommandation.	III	C

Stroke Pathophysiology Algorithm



Stroke Management Algorithm



Therapeutic Agents Available in Malaysia

Anti-platelets	**Cyclo-oxygenase inhibitors** Acetylsalicylic acid (Aspirin) Triflusal (new) **Adenosine Diphosphate Receptor Antagonists** Ticlopidine Clopidogrel **Other Antiplatelet Agents** - Dipyridamole - Cilostazol (new)
Anticoagulants IV Oral	**Unfractionated Heparin (UFH)** Heparin **Low Molecular Weight Heparin (LMWH)** Nadroparin Enoxaparin Fondaparinux Warfarin Dabigatran Etexilate (new)
Thrombolytics	**Recombinant-tissue PA (rt-PA)** Alteplase

CHA_2DS_2VASc score and stroke rate (new recommendation)

(a) Risk factor for stroke and thrombo-embolism in non-valvular AF	
'Major' risk factors	**'Clinically relevant non-major' risk factors**
Previous stroke, TIA, or systemic embolism Age ≥75 years	**Heart failure of moderate to severe LV systolic dysfunction (e.g. LV EF ≤40%) Hypertension - Diabetes mellitus Female sex - Age 65-74 years Vascular disease[a]**

(b) Risk factor-based approach expressed as a point based scoring system, with the acronym CHA_2DS_2VASc
(Note: maximum score is 9 since age may contribute 0, 1, or 2 ponits)

Risk factors	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age ≥75	2
Diabetes mellitus	1
Stroke/TIA/thrombo-embolism	2
Vascular disease[a]	1
Age 65-74	1
Sex category (i.e. female sex)	1
Maximum score	**9**

(c) Adjusted stroke rate according to CHA_2DS_2VASc score

CHA_2DS_2VASc score	Patients (n=7329)	Adjusted stroke rate (%/year[b])
0	1	0%
1	422	1.3%
2	1230	2.2%
3	1730	3.2%
4	1718	4.0%
5	1159	6.7%
6	679	9.8%
7	294	9.6%
8	82	6.7%
9	14	15.2%

See text for definitions.
[a]Prior myocardial infarction, peripheral artery disease, aortic plaque. Actual rates of stroke in contemporary cohorts may vary from these estimates.
[b]Based on Lip *et al.*[53]
AF = atrial fibrillation; EF = ejection fraction (as documented by echocardiography, radionuclide ventriculography, cardiac catheterization, cardiac magnetic resonance imaging, etc.); LV = left ventricular; TIA = transient ischaemic attack.

9 KPI Recommended by Stroke Council Malaysian Society of Neurosciences (MSN) 2011 (Used in Malaysian National Stroke Registry)

(new recommendation)

1. **Deep Vein Thrombosis (DVT) Prophylaxis**
2. **Discharged on Antithrombotic Therapy**
3. **Patients with Atrial Fibrillation Receiving Anticoagulation Therapy**
4. **Thrombolytic Therapy Administered**
5. **Antithrombotic Therapy by End of Hospital Day Two**
6. **Discharged on Cholesterol Reducing Medication**
7. **Dysphagia Screening**
8. **Stroke Education**
9. **Assessed for Rehabilitation**

National Institutes of Health Stroke Scale (NIHSS)
(new recommendation)

1a. LOC	0=alert and responsive 1=arousable to minor stimulation 2=arousable only to painful stimulation 3=reflex responses or unarousable	
1b. LOC Questions – Ask patient's age and month. Must be exact.	0=Both correct. 1=One correct (or 2=Neither correct	
1c. Commands – Open/close eyes, grip and release non-paretic hand.	0=Both correct (ok if impaired by weakness) 1=One correct. 2=Neither correct	
2. Best Gaze – Horizontal EOM by voluntary or Doll's.	0=Normal. 1=Partial gaze palsy; abnormal gaze in 1 or both eyes 2=Forced eye deviation or total paresis which cannot be overcome by Doll's.	
3. Visual Field – Use visual threat if necessary. If monocular, score field of good eye.	0=No visual loss 1=Partial hemianopia, quadrantanopia, extinction 2=Complete hemianopia 3=Bilateral hemianopia or blindness	
4. Facial Palsy – If stuporous, check symmetry of grimace to pain.	0=Normal. 1=Minor paralysis, flat nasolabial fold, asymmetrical smile 2=Partial paralysis (lower face = UMN) 3=Complete paralysis (upper & lower face)	
5. Motor Arm – Arms outstretched 90 degrees (sitting) or 45 degrees (supine) for 10 sec. Encourage best effort. Circle paretic arm in score box.	0=No drift. 1=Drift but does not hit bed 2=Some antigravity effort, but cannot sustain 3=No antigravity effort, but even minimal movement counts 4=No movement at all X=Unable to assess due to amputation, fusion, fractures, etc.	L / R
6. Motor Leg – Raise leg to 30 degrees supine x 5 sec.	0=No drift . 1=Drift but does not hit bed 2=Some antigravity effort, but cannot sustain 3=No antigravity effort, but even minimal movement counts 4=No movement at all X=Unable to assess due to amputation, fusion, fractures, etc.	L / R
7. Limb Ataxia – Check finger-nose-finger; heel-shin; and score only if out of proportion to paralysis	No ataxia. 1=Ataxia in upper or lower extremity. 2=Ataxia in upper AND lower extremity X=Unable to assess due to amputation, fusion, fractures, etc.	L / R
8. Sensory – Use safety pin. Check grimace or withdrawal if stuporous. Score only stroke-related losses.	0=Normal. 1=Mild-mod unilateral loss but patient aware of touch (or aphasic, confused) 2=Total loss, patient unaware of touch. Coma, bilateral loss	
9. Best Language – Describe cookie jar picture, name objects, read sentences. May use repeating, writing, stereognosis	0=Normal 1=Mild-mod aphasia; (difficult but partly comprehensible) 2=Severe aphasia; (almost no info exchanged) 3=Mute, global aphasia, coma. No 1 step commands	
10. Dysarthria – Read list of words	0=Normal; 1=Mild-mod, slurred but intelligible 2=Severe; unintelligible or mute X=Intubation or mechanical barrier	
11.Extinction/Neglect – Simultaneously touch patient on both hands, show fingers in both visual fields, ask about deficit, left hand.	0=Normal, none detected. (visual loss alone) 2=Profound neglect in more than one modality	

Modified Rankin Scale (new recommendation)

0 = No symtoms at all.

1 = **No significant disability** despite symtoms;
Able to carry out all usual duties and activities.

2 = **Slight** disability;
Unable to carry out all previous activities, but able to look after own affairs without assistance.

3 = **Moderate** disability requiring some help, but able to walk without assistance.

4 = **Moderate severe** disability;
Unable to walk without assistance and unable to attend to own bolidy needs without assistance.

5 = **Severe disability**;
Bedridden, incontinent, and requiring constant nursing care and attention.

6 = **Dead**.

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

Note