QUICK REFERENCE

CLINICAL PRACTICE GUIDELINES

Management of Ischaemic Stroke

3rd Edition
2020

STROKE COUNCIL
Malaysian Society of Neurosciences (Persatuan Neurosains Malaysia)

Academy of Medicine Malaysia

MINISTRY OF HEALTH MALAYSIA

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STROKE COUNCIL

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This Quick Reference provides key recommendations and and a summary of the main recommendations in the Clinical Practice Guidelines (CPG) Management of Ischaemic Stroke 3rd Edition 2020.

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

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

Also available as an app for Android and IOS platform: MyMaHTAS

KEY RECOMMENDATIONS OF STROKE CPG 2020

Chapter 1: Epidemiology, Definition and Classification Of Stroke

1. Stroke is a major cause of mortality and morbidity, and in Malaysia, stroke is the third leading cause of mortality.
2. Ischaemic stroke is the most common stroke, and hypertension was the most common risk factor followed by diabetes mellitus.
3. The new definition of stroke and transient ischaemic attack (TIA) involved either pathological imaging or clinical evidence of ischaemia and can be timed based on the presentation of symptoms.
4. Ischaemic stroke can be classified according to clinical, phenotypic or aetiologic classification.

Chapter 2: Causes and Pathophysiology

1. Three main causes of ischaemic stroke include atherothrombosis of large vessels, intracranial small vessel disease, and embolism, which may contribute to up to 80% of the cases.
2. Cryptogenic infarction or stroke of undetermined aetiology may be responsible for around 20 to 40% of the cases despite extensive workout and usually would be a diagnosis of exclusion.

Chapter 3: Diagnosis and Initial Assessment

1. The diagnosis of stroke is made by evaluating and analysing information derived from a good history, physical examination and selected diagnostic tests.
2. The symptoms and signs of stroke depend on the type, location, and the extent of the affected brain tissues.
3. A full neurological examination, including the patient's conscious level and tests of higher mental function is mandatory.
4. Stroke mimics commonly confound the clinical diagnosis of stroke.

Chapter 4: Prognosis

1. Haemorrhagic stroke has a higher mortality than ischaemic stroke.
2. There is a decline in stroke mortality in both men and women suffering from ischaemic or haemorrhagic stroke due to the introduction of dedicated stroke units and improved control of stroke risk factors.
3. The recurrence rates are 3-4% in the first month and 12% in the first year.
4. Progress of time is an independent covariate which reflects the spontaneous recovery of bodily functions.

Chapter 5: Prevention of Stroke

1. Stroke is a preventable disease and may be attributed to modifiable and non-modifiable risk factors.

2. Modifiable risk factors are the focus of primary prevention and can be clustered into three main groups i.e.
   a) Lifestyle risk factors, i.e., smoking, physical inactivity, and unhealthy eating
   b) Metabolic risk factors, i.e., high systolic BP, high cholesterol, high fasting blood glucose, low eGFR and high BMI.
   c) Environmental factors, i.e., air pollution and lead exposure.

3. Secondary prevention of stroke involves the prevention of recurrent stroke, and this may involve medical interventions includes antiplatelet therapy, anti-hypertensive treatment, lipid-lowering agents, glycaemic control, prevention of cardio-embolism and re-vascularisation procedures in selected cases.

Chapter 6: Investigations

1. Investigations carried out for stroke are aimed to confirm the diagnosis, determine the mechanism of stroke, stratify risk and to identify potential treatable vascular lesions.

2. Computed tomography (CT) brain is mandatory and preferred imaging in the emergency setting to differentiate haemorrhage from ischaemia, determine the site(s), cause, and extent of the lesion.

3. Advance imaging may be required in selected cases in the emergency settings, e.g., ruling out stroke mimics, reperfusion therapy in extended hours and determining potential re-vascularisation procedure.

4. Selected blood investigations and imaging will be required in certain patients to determine the aetiology of stroke.

Chapter 7: Emergency Medicine Services

1. The public should be encouraged to call 999 if they suspect a person is having a stroke.

2. Emergency medical dispatcher and prehospital care providers should be trained to recognize and identify stroke and are able to provide rapid transportation of suspected acute stroke patient to nearest stroke ready hospital.

3. Assessment of patients with suspected acute stroke in emergency department should be prioritized in order to expediate the diagnosis of stroke and to determine the appropriate acute stroke interventions.

4. Audit of acute stroke care and training of emergency department personnel should be conducted to improve quality of care in acute stroke cases.

Chapter 8: Acute General Management

1. Acute general management in stroke includes supportive care and treatment of acute complications in order to improve the mortality rate and functional disability.

2. General management includes management of blood pressure, glucose control, nutritional support, prevention of infection and DVT, and also to treat potential sequelae, e.g. raised intracranial pressure and seizure.

Chapter 9: Reperfusion of Ischaemic Brain

1. Intravenous alteplase (0.9 mg/kg; maximum dose of 90mg) is recommended for the definite onset stroke for up to 4.5 hours from the onset. The treatment window can also be extended via CT perfusion with clinical evidence of penumbra-core mismatch up to 9 hours from the time of the last known to be well/midpoint of sleep or via MRI (DWI-FLAIR mismatch) done to identify possible stroke onset within the last 4.5 hours.

2. Intravenous tenecteplase (0.25 mg/kg;maximum dose of 25mg) is a possible treatment agent in acute stroke that presented within 4.5 hours with evidence of large vessel occlusion on imaging.

Chapter 10: Endovascular Thrombectomy

1. Hyperacute endovascular thrombectomy is recommended for the definite onset of stroke with evidence of large vessel occlusion which is within 6 hours from the onset. The treatment window can be extended via CT/MR perfusion (penumbra-core mismatch) or MRI (clinical-imaging mismatch) with current evidence showed significant benefit up to 24 hours from the onset/time of last known to be well. However, treatment pathway should not be delayed, as the treatment outcome can be influence by the imaging-to-recanalization time.

2. Drip & Ship (IVT prior to EVT) as per Chapter 9 is recommended for eligible patients.

Chapter 11: Stroke Unit

1. The use of comprehensive specialized stroke care centres (stroke units) that incorporates rehabilitation services are able to reduce mortality and disabilities among stroke patients.

Chapter 12: Stroke in The Older Person

1. All older persons with acute stroke should be assessed for fitness/frailty level using a validated instrument to facilitate a tailored and individualised treatment plan.

2. An older person can benefit from acute treatment for stroke including stroke thrombolysis and endovascular thrombectomy, providing the inclusion and exclusion criteria of the treatment are met.

3. An older person can benefit from and should receive treatment for stroke prevention with management of polypharmacy issues, individualised medication dosages and treatment targets as is tolerated, for stroke risk factors.

4. All older persons with stroke should be:

   - screened for delirium using a validated tool, and receive a tailored multicomponent intervention and management plan for delirium, when admitted with an acute stroke

   - offered falls and fragility fracture risk assessment and management during the rehabilitation period

   - assessed by a multidisciplinary team with an appropriate discharge plan

   - able to receive end-of-life care and recommendations when the prognosis is poor either from the stroke itself, complications, or other serious comorbid conditions

Chapter 13: Stroke and Cardioembolism

1. Cardioemboli is a common cause of stroke. Stroke patient must have cardiac assessment to look for the presence of cardioemboli.
2. It causes more severe stroke and carry a higher morbidity and mortality rates.
3. Effective treatment to prevent cardioembolism is available and should be offered to patients at risk.
4. NOAC is preferred over VKA for NVAF.
5. Patient on VKA should have regular INR monitoring and aimed for time in therapeutic range (TTR) > 70%.
6. Antiplatelet is not recommended in NVAF for the prevention of stroke.

Chapter 14: Stroke in Special Circumstances

1. Young onset stroke requires more comprehensive investigation to determine the stroke aetiology.
2. Diagnosis of cryptogenic stroke and embolic stroke of undertermined source (ESUS) is made after standard evaluation to rule out possible cause of stroke.
3. Further specialized investigations needed in the cryptogenic or ESUS stroke for example prolonged Holter monitoring to look for atrial fibrillation or to look for evidence of patent foramen ovale (PFO).
4. Cerebral venous thrombosis is one of the major cause of venous infarct and would require investigations to determine the cause of thrombosis. Treatment mainly directed at anticoagulation with adjunctive therapy to prevent associated complications.

Chapter 15: Management of Stroke in Pregnancy

1. MRI of the brain (without gadolinium contrast) is the radiological modality of choice for investigating strokes in pregnancy.
2. Aspirin is the only choice of antiplatelet for pregnant patients with a well-defined low risk profile.

Chapter 16: Stroke Therapies with Limited Evidence

1. There are a variety of stroke medications and treatment modalities, but the evidence is very limited.

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 the absence of directly applicable clinical studies of good quality

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

RECOMMENDATIONS SUMMARY OF STROKE CPG 2020

Chapter 5: Primary Prevention of Stroke

Table 5.2: Primary Prevention and Management of Risk Factors

Factors	Recommendations	Level of Evidence	Grade
Hypertension	Self-BP monitoring is recommended for all hypertensive patients. *New recommendation*	I	A
	Risk stratification for hypertension based on CVD risk, target organ damage and complications are recommended for optimizing therapy. *New recommendation*		
	Lifestyle changes if systolic BP is between 130-139mmHg and/or diastolic BP is between 80-89mmHg, with three to six-monthly review. *New recommendation*	I	A
	Treat medically if systolic BP is >140mmHg and/or diastolic BP is >90mmHg.	I	A
	Hypertension should be treated in the very elderly (age >80years) to reduce the risk of stroke. *New recommendation*	I	B
Diabetes Mellitus	Strict blood pressure control is important in patients with diabetes.	I	A
	More intensive HbA1c glycaemic control targets (<6.5%) may be required for optimal ischemic stroke prevention.	I	A
	Target BP for diabetics is systolic BP <130mmHg and diastolic BP <80mmHg, preferably <120mmHg if tolerated. *New recommendation*	I	A
Hyperlipidaemia	Treatment of dyslipidaemia / LDL-C is stratified based on risk.	I	B
	High-risk group: lowering LDL to <1.8 mmol/l is recommended. *New recommendation*		
	Intermediate and low risk: keep LDL <3.4mmol/l.		
	Low-risk group may benefit from cholesterol-lowering therapy with a statin. *New recommendation*		
	No risk – keep LDL <4.2 mmol/L.		
Smoking	Cessation of smoking.	III	C
Aspirin therapy	Aspirin therapy is not recommended for primary prevention of stroke in the elderly, diabetics, or other high-risk groups. *New recommendation*	I	A
Post-menopausal Hormone Replacement Therapy	Oestrogen-based HRT is not recommended for primary stroke prevention.	II	B
Alcohol	Avoid heavy alcohol consumption or limit to < 1 drink per day. *New recommendation*	II-2	B

Physical Activity	Physical activity (occupational and leisure time) is recommended for all groups of patients. *New recommendation*	I	A
	Physical activity > 30mins/day or >150mins/week as part of a healthy lifestyle is recommended *New recommendation*	I	A
Diet	DASH diet is recommended to reduce BP. *New recommendation*	I	A
	Mediterranean diet (low glycaemic content with high intake of vegetables) supplemented with nuts and olive oil is beneficial. *New recommendation*	II	B
	Diet high in fruits and leafy green vegetables is beneficial. *New recommendation*	II	B

Table 5.3: Secondary Prevention of Stroke

Factors/Treatment	Recommendations	Level of Evidence	Grade
Antiplatelet (Single agent)			
Aspirin	The recommended dose of aspirin is 75mg to 325mg daily.	I	A
	Alternatives:		
Clopidogrel	The recommended dose is 75mg daily.	I	A
Ticlopidine	The recommended dose is 250mg twice a day.	I	A
Triflusal	The recommended dose is 600mg daily	I	A
Cilostazol	The recommended dose is 100mg twice a day.	I	A
Double therapy	Combination therapy of Clopidogrel and Aspirin is recommended in patient with minor ischaemic stroke and high-risk TIA for 21 days. *New recommendation*	I	A
Antihypertensive 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 patients with previous ischaemic strokes.	I	A
	LDL target < 1.8 is recommended in all patients with previous ischaemic stroke. *New recommendation*	I	A
Diabetic control	All diabetic patients with a previous stroke should have good glycaemic control.	III	C
Cigarette smoking	All smokers should stop smoking.	III	C

Table 5.4: Cardiac Conditions Predisposing to Ischaemic stroke				
Major Risk Conditions	**Additional Risk Factors**	**Recommendations**	**Level of Evidence**	**Grade**
Atrial Fibrillation	Risk factors to be assessed by CHA_2DS_2-VASc Score.	OAC to prevent cardioembolic stroke is recommended for all NVAF male patients with CHA_2DS_2-VASc score of 2 or more and female patients with a CHA_2DS_2-VASc score of 3 or more. *New recommendation*	I	A
		Direct Oral Anticoagulant (DOAC) vs. Warfarin		
		Dabigatran is superior (150mg bid) to and as effective (110mg bid) as compared to Warfarin, in preventing stroke and systemic embolism. Bleeding rates are similar with Warfarin at 150mg bid but with a lower bleeding rates at 110mg bid.	I	A
		Rivaroxaban was compared with adjusted-dose warfarin and was found to be non-inferior with regard to the primary composite end point of stroke or non-central nervous systemic embolism. *New recommendation*	I	A
		Apixaban was compared with adjusted-dose warfarin and was found to be superior to warfarin in preventing stroke or systemic embolism. Apixaban also caused less major bleeding events as compared with warfarin and resulted in lower overall mortality. *New recommendation*	I	A
		Edoxaban* as compared to warfarin was found to be noninferior with regard to the primary efficacy end point and caused less bleeding. *New recommendation* *Currently not available in Malaysia.	I	A
Prosthetic Heart Valves (Mechanical)	*Moderate risk:* Bi-leaflet or tilting disk aortic valves in NSR	Lifelong Warfarin	II-2	B
	High risk: Bileaflet or tilting disk aortic valves in AF; Bileaflet or tilting disk mitral valve in AF or NSR.	Lifelong Warfarin (target INR 3.0; range 2.5-3.5)	II-3	B
	Caged-ball and caged-disk designs; Documented stroke/TIA despite adequate therapy with Warfarin.	Lifelong Warfarin (target INR 3.0; range 2.5-3.5) plus Aspirin 75-150mg daily	II-1	B
Bioprosthetic heart valves	*High risk:* AF; left atrial thrombus at surgery; previous stroke/TIA or systemic embolism.	If major risk factors are 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	*High risk:* AF; previous stroke/TIA; left atrial thrombus; left atrial diameter > 55mm on Echo.	If major risk factors are present, consider lifelong Warfarin.	II-3	B
		For all other patients start Aspirin 75-150mg daily.	II-2	B
MI and LV dysfunction	*High risk:* Acute/recent MI (<6 months); 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 are present without LV thrombus: consider Warfarin for 3-6 months followed by Aspirin 75-150mg daily.	III	C
		If LV thrombus is present, consider Warfarin for 6-12 months	III	C
		For dilated cardiomyopathies including peripartum, consider lifelong Warfarin	III	C
Recommended Warfarin dose INR target 2.5 [range 2.0 to 3.0] unless stated otherwise				

Table 5.5: Anticoagulation for the Patient with Acute Cardioembolic Stroke

Treatment	Recommendations	Level of Evidence	Grade
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 a very high risk of embolism.	III	C
Anticoagulant	Anticoagulant 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 the high risk of intracranial bleeding.	I	A

Table 5.6: Revascularisation Procedures			
Treatment	**Recommendations**	**Level of Evidence**	**Grade**
Carotid Endarterectomy (CEA)	*Primary Prevention* May be considered in patients with a high grade asymptomatic carotid stenosis (70-99%) when performed by surgeons with less than 3% morbidity/mortality rate.	I	A
	Secondary Prevention Indicated for most patients with a 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 a stenosis of 50-69% after a recent ischaemic event in centres with complication rates of less than 6%.	III	C
	Not recommended for patients with a stenosis of less than 50%.	I	A
	Patients should remain on antiplatelet therapy before and after surgery.	II-2	B
Carotid angioplasty and 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 protective devices should be used during the procedure.	I	A
	Use of dual antiplatelet for at least 4 weeks after CAS.	I	A
	The long-term safety (for 4 years) for CAS is as good as CEA.	I	A
	Complex configuration of the aortic arch and internal carotid artery tortuosity increase the risk of cerebral ischemia in CAS.	II-2	B
Intracranial angioplasty & stenting (IAS)	Role of IAS in intra-cranial stenoses, asymptomatic stenoses and acute stroke is unclear and may not be recommended.	II-2	C

Chapter 7: Emergency Medicine Services

Table 7.1: Emergency Medicine Services			
Management	**Recommendations**	**Level of Evidence**	**Grade**
	Pre-Hospital Management		
Public education	Educational programmes - should be designed to create awareness and knowledge of stroke warning signs. - should include the timely recognition and need to seek emergency care by calling 999 promptly. *New recommendation*	II-1 II-1	A A
Emergency dispatch system	ADC - should be familiar with common descriptors used by the public for stroke. Whenever the descriptors are used, EMD are trained to use the stroke protocols to identify suspected stroke patients - should have a protocol or tools that allow Emergency Medical Dispatchers (EMD) to identify suspected stroke patients. e.g. MDPS Stroke Diagnostic Tool, FAST stroke assessment. - should have a system to priorities suspected stroke calls to facilitate early arrival of patients to the ED. *New recommendation*	II-1 II-1 II-1	A A A
Initial on-scene management	PHC responders - should rapidly evaluate airway, breathing and circulation to identify life threatening situation, and manage them accordingly. - should use a validated and standardized stroke identification assessment tool such as FAST or BE-FAST stroke assessment - should be trained to identify hypoglycaemia as a stroke-mimic and apply appropriate management protocols - should ascertain the time of onset of stroke symptoms from the patient or witness(es). PHC Service Providers should ensure its responders are made aware of the nearest hospital capable of providing thrombolysis and hospital capable of performing endovascular stroke treatment, within their service area. A written protocol that ensures the ambulance diversion of the patient to such hospitals should be made available for use. All stroke patients from PHC with positive signs of stroke within the 4.5-hour time window for medical thrombolytic therapy should be transported immediately to an acute stroke ready hospital. Titrated dose of oxygen should be delivered to stroke patients with an oxygen saturation level of below 95%. *New recommendation*	II-1 II-1 I I I II-1 II-3	A A A A A A B
Pre-arrival communication	PHC Responders should be trained to provide pre-arrival notification of stroke patients to receiving hospitals. MECC and associated stroke ready hospital(s) are recommended to have local regional stroke referral system/ network and agreement with the ED to facilitate the transport decision from PHC to ensure the treatment window of 4.5 hours is achieved. *New recommendation*	II-1 I	A A

Emergency Department Management			
ED Evaluation	All patients presenting to an ED with suspected acute stroke must have immediate clinical evaluation and investigations to establish the diagnosis and to determine the eligibility for intravenous thrombolytic therapy and/or EVT The use of clinical screening tools such as FAST or BE-FAST to identify stroke by ED staff can be beneficial *New recommendation*	I II-2	A B
Initial Assessment in ED	ED staff should rapidly evaluate airway, breathing and circulation in patients with suspected acute stroke and manage accordingly All patients with suspected acute stroke should have their blood glucose level checked upon arrival at the ED A standardized stroke severity scale should be used such as the National Institutes of Health Stroke Scale (NIHSS) to assess stroke severity in the ED *New recommendation*	I II-1 II-1	A A A
Imaging	All patients with suspected stroke who are candidates for intravenous thrombolysis and/ or EVT should undergo at least CT scan immediately. All other suspected stroke patients should have an urgent CT brain. Interpretation of acute stroke imaging for thrombolysis decisions should only be made by healthcare professionals who have received appropriate training. *New recommendation*	II-1 III	A C
Other Considerations	Patients with acute stroke should only receive supplemental oxygen only if their oxygen saturation is below 95%. Hypotension and hypertension in patients with acute stroke should be identified and managed accordingly. Patients with acute stroke should have their swallowing ability screened as early as possible after arrival at the hospital and before being given any oral food, fluid, or medication *New recommendation*	II-3 III II-2	B C B
Quality Improvement	Joint multidisciplinary audit to review and monitor stroke care quality benchmarks, indicators, evidence-based practices, and outcomes should be performed periodically. ED personnel should undergo a standardized training in acute stroke management. *New recommendation*	II-1 III	A C

Chapter 8: Acute General Management

Table 8.1: Acute General Management			
Factors	**Recommendations**	**Level of Evidence**	**Grade**
Oxygen and Airway support	Patients with acute stroke should only receive supplemental oxygen if their oxygen saturation is below 95% and be titrated to achieve above 95%. *New recommendation*	II-3	B
Observation	Regular observation is mandatory to recognise impaired pulmonary function (pulse oxymeter), circulatory function (pulse rate, blood pressure), NIHSS score, head chart, GCS, and complications from mass effect.	III	C
Mobilisation	Mobilise early to prevent complications.	II-3	C
	High-dose, very early mobilisation within 24 hours of stroke onset should not be performed because it can reduce the odds of a favourable outcome at 3 months. *New recommendation*	I	-
Blood Pressure	Lowering BP initially by 15% is probably safe. Blood pressure reduction should not be drastic. *New recommendation*	III	C
	Do not treat hypertension if systolic BP is <220mmHg or diastolic BP is <120mmHg. Mild hypertension is desirable at 160-180/90-100 mmHg.	III	C
	Recommended therapy: Labetalol 10-20mg boluses at 10-minute intervals up to 150-300mg or 1mg/ml infusion, rate of infusion for Labetalol as 1-3mg/min or Captopril 6.25-12.5mg orally.	III	C
Blood Glucose	After an acute stroke, treat hyperglycaemia to keep the blood glucose levels between 6.0-10.0 mmol/L and ensure that hypoglycaemia is avoided. *New recommendation*	III	C
	Avoid very tight target of glucose control (4.0-7.5 mmol/L) in the first hours of acute ischaemic stroke. *New recommendation*	I	A
Nutrition	Perform a water swallowing test.	III	C
	Insert a nasogastric tube if the patient fails the swallowing test.	III	C
	PEG is superior to nasogastric feeding only if prolonged enteral feeding is required	II-1	B
	Enteral feeding should be started within 7 days of admission (oral or tube feeding). *New recommendation*	I	A
Infection	Search for the presence of infection if fever appears and treat it early with appropriate antibiotics.	III	C
Fever	Use anti-pyretics to control elevated temperatures.	II-1	B
Continence	The application of indwelling catheter should be used cautiously and should be removed as soon as possible. *New recommendation*	I	A
	All stroke patients should be assessed for urinary retention or incontinence, faecal incontinence, and constipation. *New recommendation*	III	C
Raised Intracranial Pressure	Hyperventilate to lower the intracranial pressure.	II-2	B
	Mannitol (0.25 to 0.5g/kg) intravenously administered over 20 minutes lowers the 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 surgical decompressive therapy within 48 hours after symptom onset is recommended to control intracranial pressure and prevent herniation among those patients with very large infarcts of the cerebral hemisphere.	I	A
	Patients >60 years of age may be considered for decompressive craniectomy in selected cases. *New recommendation*	I	A
	Ventriculostomy and sub-occipital craniectomy are effective in relieving hydrocephalus and brain stem compression caused by large cerebellar infarctions.	II-2	B
Deep Vein Thrombosis Prophylaxis	For immobile stroke patients without contraindications, intermittent pneumatic compression (IPC) in addition to routine care (aspirin and hydration) is recommended over routine care alone to reduce the risk of deep vein thrombosis (DVT). *New recommendation*	I	A
	The benefit of prophylactic-dose subcutaneous heparin (unfractionated heparin [UFH] or LMWH) in immobile patients with AIS is not well established. *New recommendation*	III	C
	In ischaemic stroke, elastic compression stockings should not be used. *New recommendation*	I	A
Seizure	New-onset seizures in admitted patients with acute stroke should be treated using appropriate short-acting medications if they are not self-limiting. *New recommendation*	III	C
	A single, self-limiting seizure occurring at the onset, or within 24 hours after an ischemic stroke (considered an ‘‘immediate’’ post-stroke seizure) should not be treated with long-term anticonvulsant medications. The use of prophylactic anti-seizure medications is not recommended. *New recommendation*	III	C
	Patients that have an immediate post-stroke seizure should be monitored for recurrent seizure activity and should be treated as per treatment recommendations for seizures in as in other neurological conditions and treatment should be individualised. *New recommendation*	III	C

Chapter 9: Reperfusion of Ischaemic Brain

Table 9.1: Treatment of Acute Ischaemic Stroke with Intravenous Thrombolysis			
Treatment	**Recommendations**	**Level of Evidence**	**Grade**
Alteplase	Onset within 4.5 hours Dose: 0.9 mg/kg, max 90 mg, 10% bolus and remaining dose given as infusion over 1 hour.	I	A
	Onset >4.5 up to 9 hours if known onset or wake-up stroke guided by CT perfusion, with the presence of a significant penumbra core mismatch. *New recommendation*	II	B
	Uncertain onset and wake up stroke guided by MRI (DWI-FLAIR mismatch) *New recommendation*	II	B
Tenecteplase	Onset within 4.5 hours and eligible for thrombolytic treatment can be considered for intravenous Tenecteplase prior to EVT. Dose: 0.25mg/kg; maximum dose of 25mg *New recommendation*	II	B

Chapter 10: Endovascular Thrombectomy

Table 10.1: Acute Endovascular Thrombectomy Treatment			
Treatment	**Recommendations**	**Level of Evidence**	**Grade**
Acute Endovascular Thrombectomy (EVT)	EVT is indicated for AIS with large vessel occlusion; proximal middle cerebral artery segment 1 (M1)/proximal M2 occlusion/internal carotid artery (ICA), and presenting within 6 hours from onset. *New recommendation*	I	A
	EVT is indicated in selected patients who arrive after 6 hours and up to 24 hours of stroke onset with evidence of large vessel occlusion. *New recommendation*	I	A
EVT bridging with Alteplase (Drip & Ship)	AIS patients who arrive within 4.5 hours of stroke onset and are eligible for rtPA treatment should be considered for thrombolytic treatment prior to EVT. *New recommendation*	I	A
	For patients undergoing “Drip & Ship” (EVT following administration of IVT), there should be no delay in proceeding to EVT to determine the clinical effectiveness of Alteplase. *New recommendation*	I	A
EVT bridging with Tenecteplase	AIS patients who arrive within 4.5 hours of stroke onset and are eligible for thrombolytic treatment can be considered for intravenous Tenecteplase prior to EVT. *New recommendation*	II	B

Chapter 11: Stroke Unit

Table 11.1: Stroke Unit			
Factor	**Recommendations**	**Level of Evidence**	**Grade**
Stroke Unit	Every hospital should set up a stroke unit as it can significantly reduce deaths, dependency, institutionalisation, and length of hospital stay.	I	A
	The use of comprehensive specialized stroke care (stroke units) that incorporates rehabilitation is recommended.	I	A
	A stroke unit should be managed by a multidisciplinary stroke team.	I	A

Chapter 12: Stroke in the Older Person

Table 12.1: Stroke in the Older Person			
Management	**Recommendations**	**Level of Evidence**	**Grade**
Screening for Frailty	All older adults should be screened for frailty using a validated instrument suitable for the specific setting or context with a tailored management plan thereafter. *New recommendation*	III	C
Stroke Thrombolysis	An older person should receive and can benefit from intravenous thrombolysis. *New recommendation*	I	A
Endovascular thrombectomy	An older person can benefit from endovascular thrombectomy for anterior circulatory large vessel occlusion. *New recommendation*	I	A
Management of glucose level in the acute phase of stroke	After an acute stroke, treat hyperglycaemia to keep the blood glucose levels between 6.0-10.0 mmol/L (110-180 mg/dL) and ensure that hypoglycaemia is avoided. *New recommendation*	III	C
	Avoid very tight targets of glucose control (4.0-7.5 mmol/L) in the first hours of acute ischaemic stroke. *New recommendation*	I	A
Hypertension	Older persons who have one or more of the following: frailty, multiple comorbidities and/or cognitive impairment, require an individualised approach for blood pressure management. *New recommendation*	I	A
Diabetes Mellitus	Targets of blood glucose control in older persons with diabetes should be individualised taking into account their functional status, medical comorbidities, and likelihood of developing adverse events. *New recommendation*	III	C
Dyslipidaemia	Statins are recommended for stroke prevention in older persons with a less direct evidence of benefit for stroke prevention and primary prevention of vascular events in those aged over 75 years. *New recommendation*	I	A
Atrial Fibrillation	Older persons with atrial fibrillation can benefit from oral anticoagulant for stroke prevention with an individualised treatment plan taking into account medical co-morbidities, functional status, and social factors. *New recommendation*	I	A

Medication management in the older person with stroke	A comprehensive care plan for a frail older person should include management of polypharmacy. *New recommendation*	III	C
Delirium post-acute stroke	All post-stroke patients should be screened for delirium throughout hospitalization. *New recommendation*	II-2	B
	Screening for post-stroke delirium using the 4AT tool is recommended. *New recommendation*	II-2	B
	A multi-component intervention for post-stroke delirium prevention and management should be implemented to decrease the incidence and severity of delirium as well as to reduce the length of stay. *New recommendation*	II-2	B
Falls prevention post-stroke	All people with stroke should be offered falls and fragility fracture risk assessment and management during their rehabilitation period. *New recommendation*	III	C
Discharge planning and early supported discharge post stroke	Discharge planning for older persons with stroke should occur at the appropriate time following a multidisciplinary recommendation in where any decisions about care is made in the person's best interests. *New recommendation*	II-3	B
	Hospital in-patients with stroke who have mild to moderate disability should be offered early supported discharge, with treatment at home beginning within 24 hours of discharge. *New recommendation*	II-3	B
	An early stroke supported discharge team should be organised as a single multi-disciplinary team comprising of: ● Doctors ● Nurses ● Physiotherapists ● Occupational therapists ● Speech and language therapists ● Clinical psychologists ● Social workers *New recommendation*	II-1	A
	Older persons with stroke and their family members/carers should be involved in decisions about the discharge and are prepared to be involved in their care. *New recommendation*	III	C
	Discharge planning should include providing necessary equipment and support services including identification of follow-up treatment. *New recommendation*	III	C
	Evaluation of home environment by an occupational therapist should be carried out, by doing a home visit or conducting an interview about the home environment, including taking photographs or videos with the consent of the family members/carers. *New recommendation*	III	C
End-of-life care	The multidisciplinary stroke team should be trained in principles and practice of end-of-life care. *New recommendation*	II-3	C
	Burdensome treatment should be avoided at the end-of-life care and this should include decisions to continue oral feeding and hydration despite potential risk of aspiration. *New recommendation*	II-3	C

	Advanced care planning should be provided for individuals who are expected to have limited life expectancy. *New recommendation*	II-2	B
	Decisions to withhold and withdraw treatment should take into account prior expressed wishes of the individual with stroke which often needs to be established from the next-of-kin and close relatives. *New recommendation*	III	C
	Stroke teams should be prepared to facilitate the transfer of care of the individual dying of stroke to their own homes supported by local hospices and palliative care services if available. *New recommendation*	III	C

Chapter 13: Stroke and Cardioembolism

Table 13.1: Prevention of Stroke in Atrial Fibrillation Patients

Treatment	Recommendations	Level of Evidence	Grade
Stroke Prevention			
Antiplatelet monotherapy	Antiplatelet monotherapy is not indicated for stroke prevention in patients with non-valvular atrial fibrillation (NVAF).	I	A
Oral anticoagulant (OAC)	OAC has been proven to be superior to no treatment or Aspirin in patients with NVAF.	I	A
	OAC is recommended to prevent cardioembolic stroke for all NVAF male patients with CHA_2DS_2-VASc score of 2 or more and female patients with a CHA_2DS_2-VASc score of 3 or more. *New recommendation*	I	A
	The OAC of choice for valvular AF (moderate-to-severe mitral stenosis) and mechanical heart valves patients is Vitamin K Antagonist (Warfarin).	I	A
Secondary Stroke Prevention			
Parenteral anticoagulant (heparin or low molecular weight heparin)	After a cardioembolic stroke, parenteral anticoagulant therapy (heparin or low molecular weight heparin) is not recommended to prevent secondary stroke.	I	A
DOACs	For secondary stroke prevention in an AF patient, the initiation of DOACs is recommended after excluding haemorrhagic transformation *New recommendation*	II	B
	DOACs are preferred over VKA and Aspirin in AF patients with a previous stroke. *New recommendation*	I	A
Aspirin	Aspirin could be considered before the initiation of OAC after an AF patient develops an ischaemic stroke.	III	C
Combination therapy of OAC and antiplatelet	The risk of bleeding is high after initiation of the combination therapy of OAC and antiplatelet for secondary stroke prevention. *New recommendation*	III	C
OAC	After an intracranial haemorrhage, OAC could be re-initiated after 4-8 weeks in a NVAF patient with high CHA_2DS_2-VASc score if the underlying cause and risk factors of bleeding have been treated. *New recommendation*	II	B

Chapter 14: Stroke in Special Circumstances

Table 14.2: Investigation of Young Stroke			
Investigation	**Recommendations**	**Level of Evidence**	**Grade**
Homocysteinaemia	Routine screening for hyperhomocysteinaemia among patients with a recent ischaemic stroke or TIA is not indicated.	III	C
Anti-phospholipid antibodies	Routine testing for anti-phospholipid antibodies is not recommended for patients with ischaemic stroke or TIA who have no other manifestations of the anti-phospholipid antibody syndrome and who have an alternative explanation for their ischaemic event, such as atherosclerosis, carotid stenosis, or AF.	III	C
Sleep study	A sleep study might be considered for patients with an ischaemic stroke or TIA.	II-2	B
Coagulation screening	The usefulness of screening for thrombophilic states in patients with ischaemic stroke or TIA is unknown.	II-2	C

Table 14.3: Treatment of Stroke in Certain Circumstances			
Treatment	**Recommendations**	**Level of Evidence**	**Grade**
Aspirin	If the cause is not identified, Aspirin is usually given while additional tests are obtained to guide the choice between long-term antiplatelet or anticoagulant therapy.	III	C
	Antiplatelet therapy is recommended in patients who are found to have abnormal findings on coagulation testing after an initial ischaemic stroke or TIA if anticoagulant therapy is not used.	I	A
	For patients with ischaemic stroke or TIA who have an anti-phospholipid antibody but who do not fulfil the criteria for anti-phospholipid antibody syndrome, antiplatelet therapy is recommended	I	B
	For patients with ischaemic stroke or TIA who meet the criteria for the anti-phospholipid antibody syndrome but in whom anticoagulation is not yet started, antiplatelet therapy is indicated	I	A
DOAC	*ESUS:* There is no role of anticoagulant in ESUS. *New recommendation*	I	A
	For patients with an ischaemic stroke or TIA and both a PFO and a venous source of embolism, anticoagulation is indicated, depending on the characteristics of the stroke. *New recommendation*	I	A
	Anticoagulation might be considered in patients who are found to have abnormal findings on coagulation testing after an initial ischaemic stroke or TIA, depending on the abnormality and the clinical circumstances. *New recommendation*	II-2	C
	For patients with ischaemic stroke or TIA who meet the criteria for APS, anticoagulant therapy might be considered depending on the perception of risk for recurrent thrombotic events and bleeding. *New recommendation*	II-2	C
Device	*PFO closure device therapy* PFO closure devices have moderate benefit in young and middle-aged patients with cryptogenic ischaemic stroke. PFO closure devices combined with antiplatelet therapy is also recommended. *New recommendation*	I	A

	Continuous positive airway pressure (CPAP) machine CPAP therapy might be considered for patients with ischaemic stroke or TIA and sleep apnoea given the emerging evidence in support of improved outcomes. *New recommendation*	II-2	B
Blood transfusion	For patients with sickle cell disease and prior ischaemic stroke or TIA, long-term blood transfusions to reduce the level of haemoglobin S to <30% of the total haemoglobin composition are recommended. *New recommendation*	I	B
Supplements	*Supplementation with folate, vitamin B6 and vitamin B1* In adults with a recent ischaemic stroke or TIA who are known to have mild to moderate hyperhomocysteinaemia, supplementation with folate, vitamin B6 and vitamin B12 safely reduces the homocysteine levels but has not been shown to prevent stroke. *New recommendation*	III	B

Table 14.4: Investigation of Cerebral Venous Thrombosis

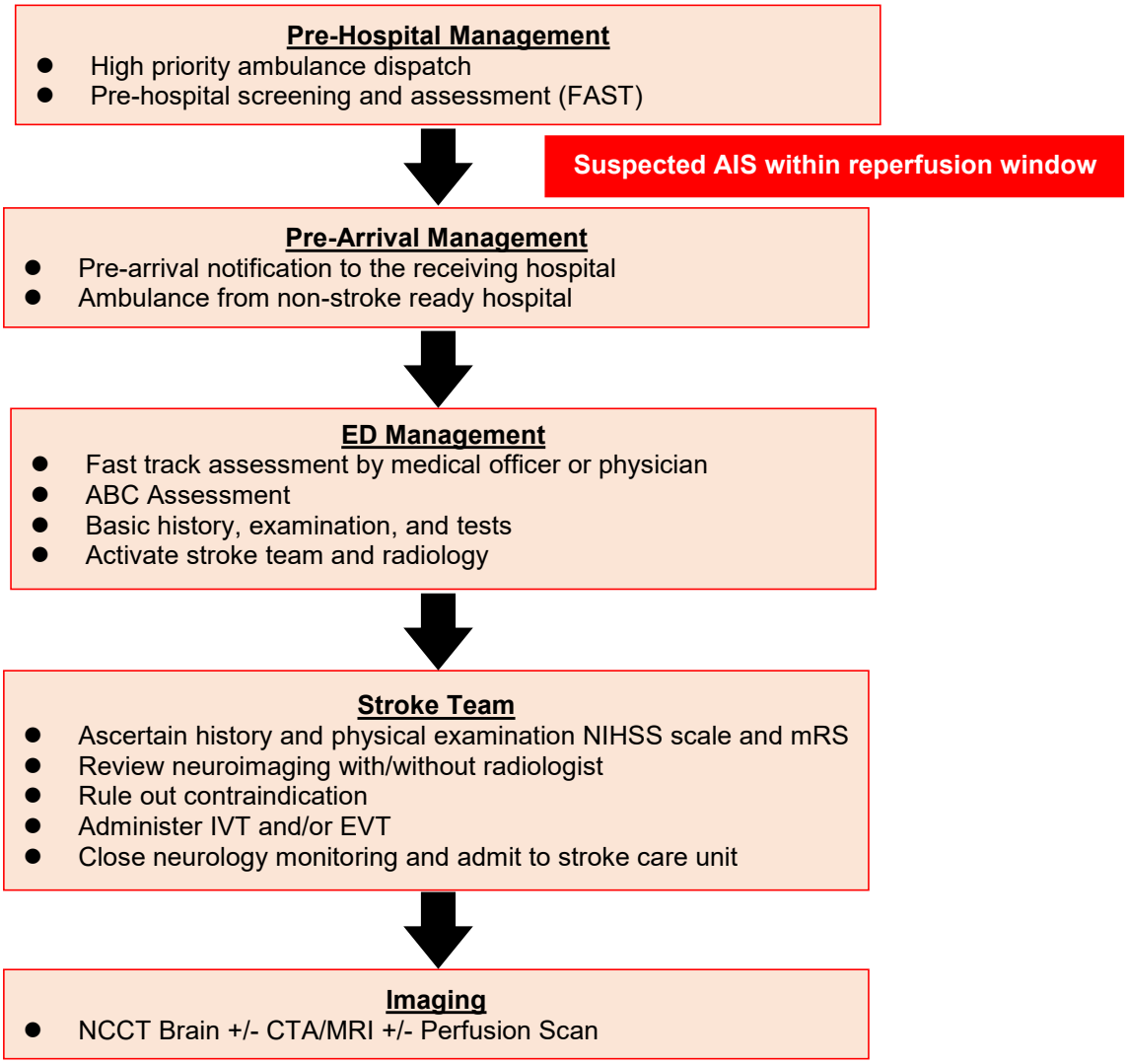
Investigation	Recommendations	Level of Evidence	Grade
CTV/ MRV	Either CT or MR venography can be used as a reliable alternative to DSA for the diagnosis of CVT in patients with suspected CVT	II-3	B
Digital Subtraction Angiography (DSA)	DSA as a diagnostic modality is indicated in cases of suspected CVT when the diagnosis of CVT is doubtful with non-invasive imaging alone.	II-1	C
D-Dimer	Measurement of the D-dimer level before neuroimaging is recommended in patients with suspected CVT, except in those with isolated headache or prolonged duration of symptoms (high false negative rates).	II-2	B
Thrombophilia screening	Thrombophilia screening may be performed in patients with high pre-test probabilityof having severe thrombophilia (i.e. a personal and/or family history of venous thrombosis, a young age at CVT and/or CVT without a transient or a permanent risk factor) to prevent recurrent venous thrombotic events. However, routine thrombophilia screening is not recommended to reduce deaths, improve functional outcome, or prevent recurrent venous thrombosis in patients with CVT.	II-3	B
Occult malignancy screening	Routine screening for occult malignancy in patients with CVT is not recommended to improve outcomes	II-3	B

Table 14.5: Treatment of Central Venous Thrombosis			
Treatment	**Recommendations**	**Level of Evidence**	**Grade**
Acute anticoagulant treatment	Treatment of acute CVT adult patients with heparin in therapeutic dosage is recommended, including in those with intracerebral haemorrhage at baseline.	I	B
Type of heparin	Treatment of acute CVT patients with LMWH instead of UFH is recommended (unless fast reversal of the anticoagulant effect is required, or the patient has contraindications to LMWH).	I	B
Thrombolysis in acute CVT	Thrombolysis in acute CVT patients with a pre-treatment low risk of poor outcome is not recommended.	III	C
Endovascular therapy or Thrombectomy	Endovascular therapy or Thrombectomy may be considered in patients with clinical deterioration despite anticoagulation, with severe neurological deficits or in coma.	II-2	C
Warfarin	Using oral anticoagulants (vitamin K antagonists) for a variable period (3-12 months) after CVT is recommended to prevent recurrent CVT and other venous thromboembolic events. Patients with recurrent venous thrombosis or with an associated prothrombotic condition with a high thrombotic risk may need permanent anticoagulation. We suggest following specific recommendations for the prevention of recurrent venous thromboembolic events in such conditions.	III	C
DOACs	Treatment of CVT with DOACs is not recommended especially during the acute phase.	III	C
Therapeutic LP	Therapeutic LP is not recommended. However, it may be considered in patients with cerebral venous thrombosis and signs of intracranial hypertension, because of a potential beneficial effect on visual loss and/or headache, whenever its safety profile is acceptable.	III	C
Acetazolamide	Acetazolamide is not recommended in patients with acute CVT to prevent death or to improve the functional outcome. However, in isolated intracranial hypertension secondary to CVT, causing severe headaches or is threatening the vision, Acetazolamide may be considered if its safety profile is acceptable	III	C
Steroids	Steroids in patients with acute CVT without any co-existing inflammatory disease are not recommended to prevent death or to improve the functional outcome	III	C
Shunt	Routine shunting (without other surgical treatment) in patients with acute CVT and impending brain herniation due to parenchymal lesions is not recommended to prevent death	II-3	C
Decompressive surgery	Decompressive surgery for patients with acute CVT and parenchymal lesion(s) with impending herniation is recommended to prevent death.	II-1	B
Antiepileptic drugs (AEDs)	Antiepileptic drugs usage in patients with acute CVT with supratentorial lesions and seizures are recommended to prevent early recurrent seizures.	II-3	C

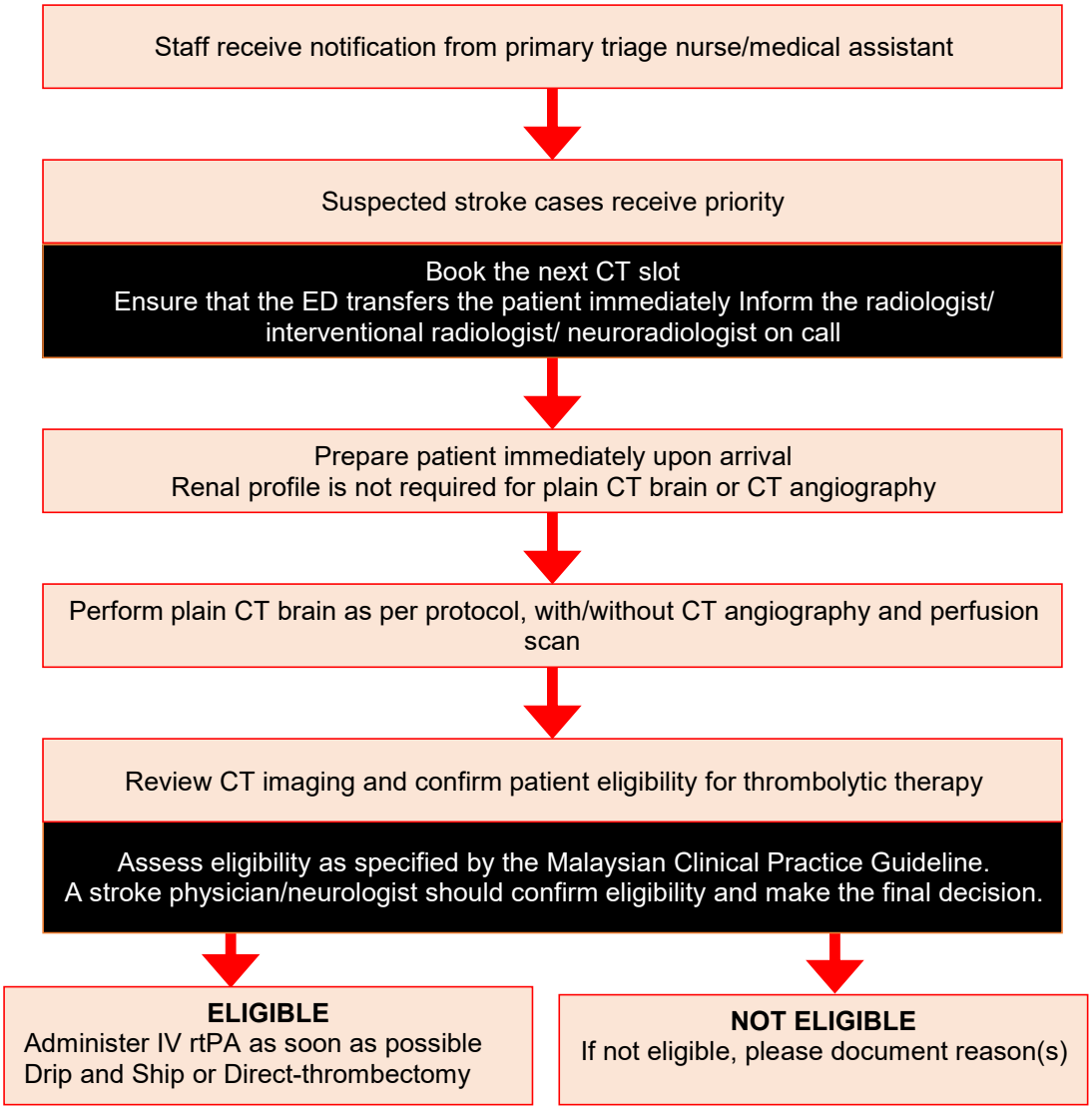
Chapter 15: Management of Stroke in Pregnancy

Table 15.1: Management of Stroke in Pregnancy			
Management	**Recommendations**	**Level of Evidence**	**Grade**
During pregnancy	In AIS, Aspirin up to 150 mg daily is well tolerated during pregnancy. Pregnant patients with well-defined low risk conditions may be given UFH or LMWH in the first trimester, followed by a low dose aspirin in the second and third trimesters.	III	C
	In pregnant patients with well-defined low risk conditions, no antiplatelet other than Aspirin can be prescribed.	III	C
	In pregnant women with well-defined high-risk conditions, Vitamin K antagonists need to be avoided between the 6th and 12th weeks of pregnancy and also near to term. During this period, UFH or LMWH can be used.	II	B
	In addition, pregnant patients with well-defined high-risk conditions currently on direct oral anticoagulants (DOACs) should be given UFH or LMWH between the 6th and 12th weeks of pregnancy. *New recommendation*	III	C
	At other weeks of gestation, Warfarin can be given.	III	C
Labour induction	When the labour process is pharmacologically induced, Aspirin can be continued.	III	C
	UFH and LMWH need to be stopped 24 hours before the induction of labour.	III	C
	UFH and LMWH should be restarted within 24 hours of delivery if there are no contraindications.	III	C
	Vitamin K antagonists (without loading dose) may be restarted after 24 hours of delivery if there are no contraindications.	III	C

Acute Ischaemic Stroke Pathway



Endovascular Thrombectomy Work Flow



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