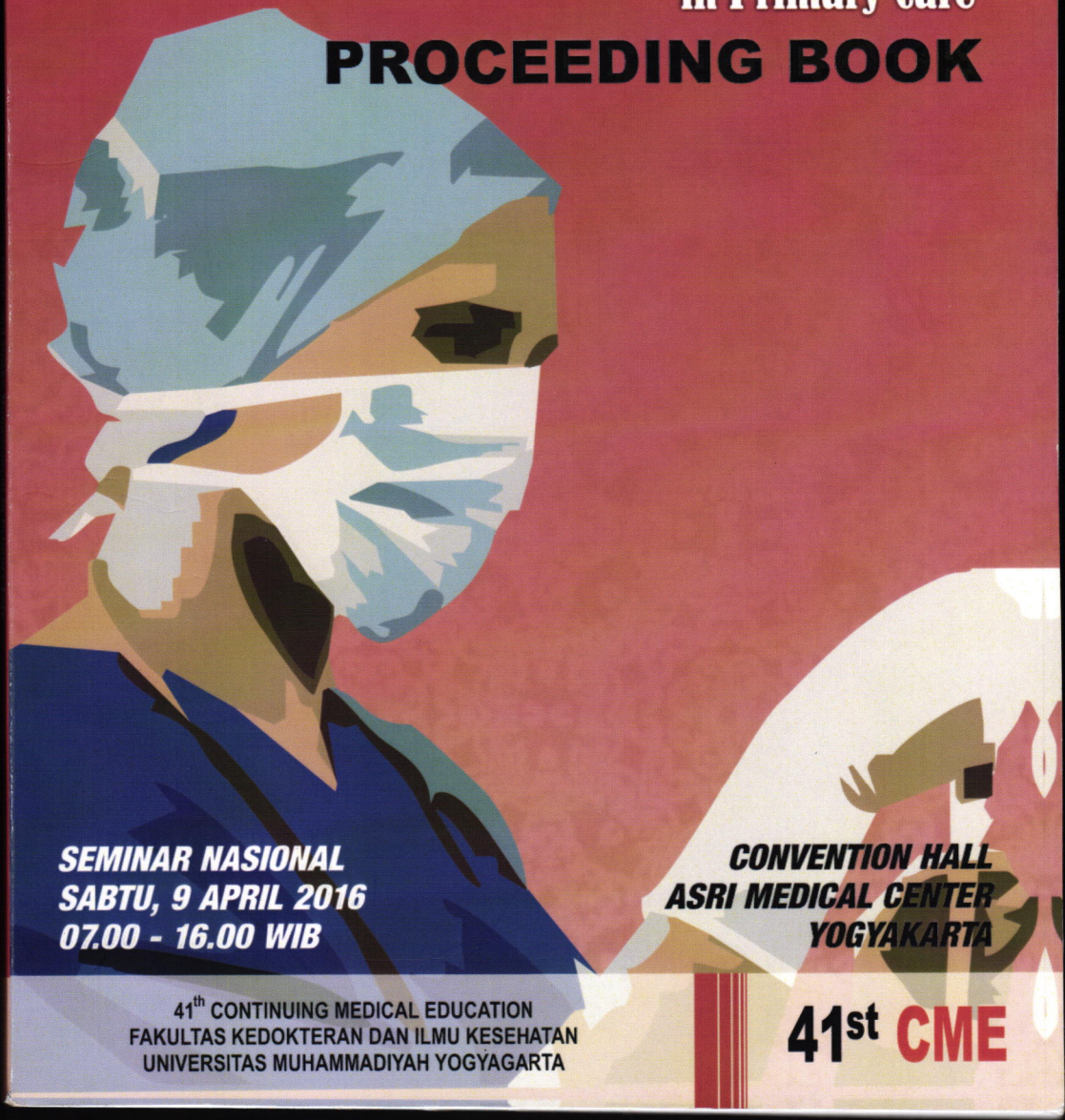
Current Updates of

Initial Shock and Stroke Management in Primary Care

PROCEEDING BOOK



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DAFTAR ISI

Recent Therapy of Acute Stroke / TIA in Prime Time at Primary Care

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Abstract

TIA, or transient ischemic attack; is a "mini stroke" that occurs when a blood clot blocks an artery for a short time. The only difference between a stroke and TIA is that with TIA the blockage is transient (temporary). TIA symptoms occur rapidly and last a relatively short time. Unlike a stroke, when a TIA is over, there's no permanent injury to the brain. There's no way to tell if symptoms of a stroke will lead to a TIA or a major stroke. It's important to manage immediately for any TIA symptoms. Because, in people who have a TIA, the incidence of subsequent stroke

is as high as 11% over the next 7 days and 24-29% over the following 5 years.

Effective treatment of stroke can prevent long-term disability and save lives. The specific treatments recommended depend on whether a stroke is caused by a blood clot obstructing the flow of blood to the brain (ischaemic stroke) or by bleeding in or around the brain (haemorrhagic stroke). It is very important to determaine a diagnosis of an ischaemic stroke or haemorrhagic stroke because the false medication can make the bleeding that occurs in haemorrhagic strokes worse.

Key word : TIA, stroke, acute, therapy

Introduction

A transient ischaemic attack (TIA) or "mini stroke" is caused by a temporary disruption in the blood supply to part of the brain. The disruption in blood supply results in a lack of oxygen to the brain. This can cause sudden symptoms similar to those of a stroke, such as speech and visual disturbance, and numbness or weakness in the face, arms and legs. However, a TIA does not last as long

as a stroke. The effects often only last for a few minutes or hours and fully resolve within 24 hours. But, in people who have a TIA, the incidence of subsequent stroke is as high as 11% over the next 7 days and 24-29% over the following 5 years.

The incidence of TIAs increases with age, from 1-3 cases per 100,000 in those younger than 35 years to as many as 1500 cases per 100,000 in those older than 85 years. The incidence of TIAs in men (101 cases per 100,000 population) is significantly higher than that in women (70 per 100,000).The incidence of TIAs in blacks (98per 100,000 population) is higher than that in whites (81 per 100,000 population).

The causes TIAs

During a TIA, one of the blood vessels that supply your brain with oxygen-rich blood becomes blocked.This blockage is usually caused by a blood clot that has formed elsewhere in your body and travelled to the blood vessels supplying the brain, although it can also be caused by pieces of fatty material or air bubbles.Certain things can increase

your chances of having a TIA, including:smoking, hypertension, obese, high cholesterol levels, alcohol, atrial fibrillation, diabetes, over 60 years of age, ras (people of Asian, African or Caribbean are also at a higher risk of having a TIA).

Preventing TIAs

A TIA is often a sign that another one may follow and you are at a high risk of having a full, life-threatening stroke in the near future.Regardless of whether or not you have had a TIA or stroke in the past, there are a number of ways you can lower your risk of having either in the future. These include Lifestyle changes:

- maintaining a healthy weight
- **eating a healthy diet** – a low-fat, reduced salt, high-fibre diet is usually recommended, including plenty of fresh fruit and vegetables
- **exercising regularly** – for most people, at least 150 minutes of moderate-intensity aerobic activity, such as cycling or fast walking, every week is recommended

- **stopping smoking** – if you smoke, stopping may significantly reduce your risk of having a stroke in the future
- **cutting down on alcohol** – you should aim not to exceed the recommended alcohol limits of three to four units a day for men and two to three units a day for women

In addition to lifestyle changes, most people who have had a TIA will need to take one or more daily medications indefinitely to help reduce their chances of having a stroke or another TIA.

Diagnosis

Ruling out metabolic or drug-induced causes of symptoms consistent with a transient ischemic attack (TIA) is important. Initial assessment is aimed at excluding emergency conditions that can mimic a TIA (eg, hypoglycemia, seizure, or intracranial hemorrhage). A fingerstick blood glucose test should be performed and blood drawn for a complete blood count (CBC), coagulation

studies, and serum electrolyte levels. Obtain a 12-lead electrocardiogram (ECG) with rhythm strip, and evaluate for symptomatic arrhythmias or evidence of ischemia.Brain imaging is recommended within 24 hours of symptom onset.Brain imaging can identify an area of ischemia in as many as 25% of patients, and TIA mimics may be identified as well. Vessel imaging can identify a stenosis or occlusion that may warrant early intervention.Electroencephalography (EEG) may be indicated to evaluate for seizure activity.

Signs and symptoms

The main symptoms of a TIA can be remembered with the word FAST: Face-Arms-Speech-Time.

- **Face**– dropped on one side (not be able to smile, mouth or eye may have dropped)
- **Arms** – weakness or numbness in one arm
- **Speech**– slurred, garbled, not be able to talk at all
- **Time**– it is time to take care immediately if you see any of these signs or symptoms

Initial vital signs should include the following:Temperature, Blood pressure , Heart rate and rhythm, Respiratory rate and pattern, and Oxygen saturation. The examiner should assess the patient's overall health and appearance, making an assessment of the following: attentiveness, ability to interact with the examiner, language and memory skills, hydration status, development.

Risk Stratification Scores

In people who have a TIA, the incidence of subsequent stroke is as high as 11% over the next 7 days and 24-29% over the following 5 years.Appropriate risk stratification must be employed to ensure that diagnostic and therapeutic interventions are targeted to the highest-risk patients.A number of risk stratification scores are available to assist in this task, but the most widely validated is the $ABCD^2$ score.(See Table 1 below.)

Table 1. $ABCD^2$ Score

A: Age ≥60 years	1 point
B : Blood pressure: Systolic ≥140 mm Hg *or* diastolic ≥90 mm Hg	1 point
C: Clinical features : - Unilateral weakness with or without speech impairment	2 points
- Speech impairment without unilateral weakness	1 point
D: Duration : - ≥60 min	2 points
- 10-59 min	1 point
D: Diabetes	1 point

Individuals with an $ABCD^2$ score of 6 or 7 have an 8% risk of stroke within 2 days, whereas those with an $ABCD^2$ score lower than 4 have a 1% risk of stroke within 2 days.Some of these patients with lower scores may well have non-TIA events rather than true TIAs.It has been proposed that this scoring system can be used to risk-stratifyand to predict the severity of recurrent stroke after TIA.

Physical Examination

The goals of the physical examination are to uncover any neurologic deficits, to evaluate for underlying cardiovascular risk factors, and to seek any potential thrombotic or embolic source of the event. Global CNS depression and airway or cardiac compromise are not typically features of a TIA. In fact, the level of consciousness and neurologic examination findings are expected to be at the patient's baseline.

Ideally, any neurologic deficits should be recorded with the aid of a formal and reproducible stroke scale, such as the National Institutes of Health Stroke Scale (NIHSS). A stroke scale prompts the examiner to be thorough and allows different examiners to repeat the examination reliably during subsequent phases of the evaluation. Any neurologic abnormalities should suggest the diagnosis of stroke (or ongoing neurologic event) rather than TIA.

Neurologic Examination

A neurologic examination is the foundation of the TIA evaluation and should focus in particular on the neurovascular distribution suggested by the patient's symptoms. Subsets of the neurologic examination include the following:Cranial nerve testing, Determination of somatic motor strength, Somatic sensory testing, Speech and language testing, Assessment of the cerebellar system (be sure to watch the patient walk)

For somatic motor testing, test muscle stretch reflexes of the biceps, triceps, brachioradialis, patellar, and Achilles. In addition, inspect posture and look for tremors. Test the strength of the shoulder girdle, upper extremities, abdominal muscles, and lower extremities. Test passive movement of major joints to look for spasticity, clonus, and rigidity.

Stroke Scale

The National Institutes of Health Stroke Scale (NIHSS) (see Table 2 below) is used mostly by stroke teams for quantifying neurologic impairment. It enables rapid determination of the severity and possible location of the stroke. A patient's score on the NIHSS is strongly associated with outcome, and it can help identify those patients who are likely to benefit from thrombolytic therapy and those who are at higher risk for developing hemorrhagic complications of thrombolytic use.The NIHSS is easily used and focuses on the following 6 major areas of the neurologicexamination:level of consciousness, Visual function, Motor function, Sensation and neglect, Cerebellar function and Language.

Table 2. National Institutes of Health Stroke Scale (NIHSS)

	Category	Score - Description
1a	level of consciousness (LOC)	0 Alert 1 Drowsy 2 Stuporous 3 Coma
1b	LOC questions (month, age)	0 Answers both correctly 1 Answers 1 correctly 2 Incorrect on both
1c	LOC commands (open and close eyes, grip and release nonparetic hand)	0 Obeys both correctly 1 Obeys 1 correctly 2 Incorrect on both
2	Best gaze (follow finger)	0 Normal 1 Partial gaze palsy 2 Forced deviation
3	Best visual (visual fields)	0 No visual loss 1 Partial hemianopia 2 Complete

		hemianopia 3 Bilateral hemianopia
4	Facial palsy (show teeth, raise brows, squeeze eyes shut)	0 Normal 1 Minor 2 Partial 3 Complete
5	Motor arm left* (raise 90°, hold 10 seconds)	0 No drift 1 Drift 2 Cannot resist gravity 3 No effort against gravity 4 No movement
6	Motor arm right* (raise 90°, hold 10 seconds)	0 No drift 1 Drift 2 Cannot resist gravity 3 No effort against gravity 4 No movement
7	Motor leg left* (raise 30°, hold 5 seconds)	0 No drift 1 Drift 2 Cannot resist gravity 3 No effort against gravity

		4 No movement
8	Motor leg right* (raise 30°, hold 5 seconds)	0 No drift 1 Drift 2 Cannot resist gravity 3 No effort against gravity 4 No movement
9	Limb ataxia (finger-nose, heel-shin)	0 Absent 1 Present in 1 limb 2 Present in 2 limbs
10	Sensory (pinprick to face, arm, leg)	0 Normal 1 Partial loss 2 Severe loss
11	Extinction/neglect (double simultaneous testing)	0 No neglect 1 Partial neglect 2 Complete neglect
12	Dysarthria (speech clarity to "mama, baseball, huckleberry, tip-top, fifty-fifty")	0 Normal articulation 1 Mild to moderate dysarthria 2 Near to unintelligibl e or worse

13	Best language** (name items, describe pictures)	0 No aphasia 1 Mild to moderate aphasia 2 Severe aphasia 3 Mute
	Total	0-42
* For limbs with amputation, joint fusion, etc, score 9 and explain. ** For intubation or other physical barriers to speech, score 9 and explain. Do not add 9 to the total score		

The NIHSS is a 42-point scale, with minor strokes usually being considered to result in a score lower than 5. An NIHSS score higher than 10 correlates with an 80% likelihood of visual flow deficits on angiography. Yet, discretion must be used in assessing the magnitude of the clinical deficit; for instance, if a patient's only deficit is being mute, the NIHSS score will be 3. Additionally, the scale does not measure some deficits associated with posterior circulation strokes (eg, vertigo and ataxia).

Management

The following should be done urgently in patients with TIA:Evaluation, Risk stratification (eg, with the California or ABCD score), Initiation of stroke prevention therapy. For patients with a recent (≤1 week) TIA, guidelines recommend a timely hospital referral with hospitalization for the following:

- Crescendo TIAs
- Duration of symptoms longer than 1 hour
- Symptomatic internal carotid stenosis greater than 50%
- Known cardiac source of embolus (eg, atrial fibrillation)
- Known hypercoagulable state
- Appropriate combination of the California score or ABCD score (category 4)

Although the symptoms of a TIA resolve in a few minutes or hours**without any specific treatment,**you will

need treatment to help prevent another TIA or a full stroke happening in the future. A TIA is a warning sign that you are at a significantly increased risk of having a full stroke in the near future, with the highest risk in the days and weeks following the attack.A stroke is a serious health condition that can cause permanent disability and can be fatal in some cases, but appropriate treatment following a TIA can help to reduce your risk of having one.Your treatment will depend on your individual circumstances, such as your age and medical history.In some cases, surgery may be needed to unblock the carotid arteries (the main blood vessels that supply the brain with blood). The healthcare team can discuss treatment options with you, and tell you about possible benefits and risks.

Pharmacologic management for transient ischemic attacks (TIAs) is aimed at reducing both short-term and long-term risk of stroke. In view of the high short-term risk of stroke after TIA, antithrombotic therapy should be initiated as soon as intracranial hemorrhage has been ruled out.In view of the high short-term risk of stroke after TIA, antithrombotic therapy should be initiated as soon as

intracranial hemorrhage has been ruled out. For noncardioembolic TIA, the following antiplatelet agents are all reasonable first-line options for initial therapy:

- Aspirin (50-325 mg/day)
- Aspirin plus extended-release dipyridamole
- Clopidogrel

Stroke prevention medication typically recommended for cardioembolic TIA is as follows:

- For patients with atrial fibrillation after TIA, long-term anticoagulation with warfarin (target international normalized ratio [INR], 2-3); aspirin 325 mg/day for those unable to take oral anticoagulants
- In acute myocardial infarction (MI) with left ventricular thrombus, oral anticoagulation with warfarin (target INR, 2-3; concurrent aspirin up to 162 mg/day for ischemic coronary artery disease [CAD])

- In dilated cardiomyopathy, oral anticoagulation with warfarin (target INR, 2-3) or antiplatelet therapy
- In rheumatic mitral valve disease, oral anticoagulation with warfarin (target INR, 2-3)

For patients with TIA due to 50-99% stenosis of a major intracranial artery, the following is recommended:

- Aspirin 50-325 mg/day rather than warfarin
- Maintenance of blood pressure below 140/90 mm Hg and total cholesterol below 200 mg/dL
- Angioplasty or stent placement is investigational and of unknown utility

Antiplatelets

Platelets are blood cells that help blood to clot (thicken). If a blood vessel is damaged, platelets stick together to form a blood clot to prevent bleeding. Antiplatelet agents inhibit platelet function by blocking cyclooxygenase and subsequent aggregation. Antiplatelet medicines work by reducing the ability of the platelets to

stick together and form clots. If you have had a TIA, it is likely that you will be offered antiplatelet medication.

Two common antiplatelets offered to people who have had a TIA are aspirin and clopidogrel. Aspirin may also sometimes be taken with another antiplatelet medicine called dipyridamole because this can be more effective than taking these medications separately.

The main side effects of antiplatelet medications include indigestion and an increased risk of bleeding – for example, you may bleed for longer if you cut yourself, and you may bruise easily.Antiplatelet Agents are :

- Aspirin. Aspirin blocks prostaglandin synthetase action, and this, in turn, inhibits prostaglandin synthesis and prevents formation of platelet-aggregating thromboxane A2.
- Aspirin 25 mg/dipyridamole 200 mg : Combination aspirin-dipyridamole therapy has been shown to prevent cardiovascular events following TIAs. Each capsule contains 25 mg of aspirin and 200 mg of dipyridamole,

for a daily total dose of 50 mg of aspirin and 400 mg of dipyridamole.

Aspirin irreversibly inhibits formation of cyclooxygenase, thus preventing formation of thromboxane A2, a platelet aggregator and vasoconstrictor. Platelet inhibition lasts for the life of a cell (approximately 10 days).

Dipyridamole is a platelet adhesion inhibitor that possibly inhibits red blood cell (RBC) uptake of adenosine, itself an inhibitor of platelet reactivity. In addition, it may inhibit phosphodiesterase activity, leading to increased cyclic 3′,5′-adenosine monophosphate within platelets and formation of the potent platelet activator thromboxane A2.

- Clopidogrel : Clopidogrel selectively inhibits the binding of adenosine diphosphate (ADP) to its platelet receptor and subsequent ADP-mediated activation of the glycoprotein GPIIb/IIIa complex, thereby inhibiting platelet aggregation.

- Dipyridamole : Dipyridamole is administered to complement usual warfarin therapy. It inhibits platelet adhesion, which may inhibit adenosine uptake by RBCs. It may increase cyclic 3′,5′-adenosine monophosphate (cAMP) within platelets and formation of the potent platelet activator thromboxane A2. In addition, it may reduce the risk of stroke when used as monotherapy instead of aspirin.
- Ticlopidine : Ticlopidine is a second-line antiplatelet therapy for patients who cannot tolerate or do not respond to aspirin therapy. In some circumstances, it can be an alternative to clopidogrel.

Anticoagulants

Anticoagulant medicines can help to prevent blood clots by changing the chemical composition of the blood in a way that prevents clots.They are usually offered to people who have had a TIA if the blood clot that caused your TIA originated in your heart. This is often due to a condition called atrial fibrillation, which causes your heart to beat irregularly.Anticoagulants agents are :

- Warfarin : Warfarin interferes with hepatic synthesis of vitamin K–dependent coagulation factors. It is used for prophylaxis and treatment of venous thrombosis, pulmonary embolism, and thromboembolic disorders. A side effect of all anticoagulants is the risk of bleeding caused by the reduction in the blood's ability to clot. You may need regular blood tests while taking warfarin, so doctors can ensure your dose is not too high / low.

Antihypertensives (blood pressure medication)

If you have high blood pressure (hypertension), you will be offered a type of medication called an antihypertensive to control it. This is because high blood pressure significantly increases your risk of having a TIA or stroke. There are lots of different types of medicine that can help control your blood pressure, including:

- thiazide diuretics
- angiotensin-converting enzyme (ACE) inhibitors
- calcium channel blockers
- beta-blockers

Some people may be offered a combination of two or three different medications.

Patients may be significantly hypertensive. Unless there is specific concern for end-organ damage from a hypertensive emergency, blood pressure should be managed conservatively while ischemic stroke is being ruled out.

For acute ischemic stroke, the AHA recommends initiating antihypertensive therapy only if blood pressure is higher than 220/120 mm Hg or if mean arterial pressure exceeds 130 mm Hg. Unless there is a comorbid cardiac or other condition that necessitates reduction of blood pressure, allowing the patient's blood pressure to autoregulate at a higher level (during the acute phase) may help maximize cerebral perfusion pressure.

Statins

If you have high cholesterol, you will be advised to take a medicine known as a statin. Statins reduce the level of cholesterol in your blood by blocking an enzyme in the liver that produces cholesterol. Statins may also help to reduce

your risk of a stroke whatever your cholesterol level is, so you may be offered a statin even if your cholesterol level is not particularly high.Examples of statins often offered to people who have had a TIA include atorvastatin, simvastatin and rosuvastatin.

Surgery

In some cases, a surgical procedure called a carotid endarterectomy may be recommended after having a TIA.A carotid endarterectomy is an operation that involves removing part of the lining of the carotid artery, plus any blockage that has built up in the artery. The carotid arteries deliver blood to your brain. When fatty deposits build up inside the carotid arteries, they become hard and narrow, making it more difficult for blood to flow through them. This is known as atherosclerosis and it can lead to TIAs and strokes if the blood supply to the brain becomes disrupted.By unblocking the carotid arteries in people whose arteries are moderately or severely narrowed, a carotid endarterectomy can significantly reduce the risk of having a stroke or another TIA.

Driving after a TIA

Although a TIA shouldn't have any long-term impact on your daily activities, you must stop driving immediately.If your doctor is happy that you have made a good recovery and there are no lasting effects after one month, you can start driving again.

Prognosis

With passive reporting, the early risk of stroke after TIA is approximately 4% at 2 days, 8% at 30 days, and 9% at 90 days.When patients with TIA are followed prospectively, however, the incidence of stroke is as high as 11% at 7 days.The probability of stroke in the 5 years following a TIA is reported to be 24-29%. In addition, patients with TIAs or stroke have an increased risk of coronary artery disease.

Patient Education

Before being discharged from the hospital, patients who have been diagnosed with TIA must receive clear

instruction to ensure that they understand the need for a complete and rapid workup through close follow-up care. Also essential for patients is education on stroke symptoms, the need to call emergency services immediately if any of these symptoms occur, and the contact number for emergency services (911 in the United States and Canada).

Despite program efforts in public education, many patients still do not seek medical attention after experiencing TIA symptoms. A 2010 population-based study found that 31% of all patients who experienced a recurrent stroke within 90 days of their first TIA or minor stroke had not sought medical attention after the initial event.

Public health professionals and physicians need to do more, such as promoting and participating in medical screening fairs and public outreach programs. In addition, patients need to be educated about lifestyle modification and cardiovascular risk factors

Noncardioembolic transient ischemic attack

Antiplatelet agents, rather than oral anticoagulants, are recommended as initial therapy. Aspirin 50-325 mg/day, a combination of aspirin and extended-release dipyridamole, and clopidogrel are all reasonable first-line options (class I recommendation).

The AHA/ASA guidelines state that the combination of aspirin and clopidogrel might be considered for initiation within 24 hours of a minor ischemic stroke or TIA and for continuation for 21 days. However, the combination of aspirin and clopidogrel, when initiated days to years after a minor stroke or TIA and continued 2 to 3 years, increases the risk of hemorrhage relative to either agent alone and is not recommended for routine long-term secondary prevention after ischemic stroke or TIA.

Cardioembolic transient ischemic attack

In patients who have atrial fibrillation in association with a TIA, long-term anticoagulation with warfarin to a

target international normalized ratio (INR) of 2-3 is typically recommended. Aspirin 325 mg/day is recommended for patients unable to take oral anticoagulants. However, the addition of clopidogrel to aspirin therapy, compared with aspirin therapy alone, might be reasonable. For most patients with a stroke or TIA in the setting of AF, it is reasonable to initiate oral anticoagulation within 14 days after the onset of neurological symptoms. Anticoagulation can be delayed beyond 14 days in the presence of high risk for hemorrhagic conversion.

The 2014 AHA/ASA guidelines also state that bridging therapy with subcutaneous low-molecular-weight heparin (LMWH) is reasonable for patients with atrial fibrillation who require temporary interruption of oral anticoagulation but are at high risk for stroke.

In acute myocardial infarction (MI) with left ventricular thrombus, oral anticoagulation with warfarin (target INR, 2-3) is reasonable.

In dilated cardiomyopathy, either oral anticoagulation with warfarin (target INR, 2-3) or antiplatelet therapy may be considered. In rheumatic mitral

valve disease, oral anticoagulation with warfarin (target INR, 2-3) is reasonable. Antiplatelet agents would not normally be added to warfarin unless patients experience recurrent embolism despite a therapeutic INR. The benefit of warfarin after stroke or TIA in patients with sinus rhythm and cardiomyopathy characterized by systolic dysfunction has not been established.

In mitral valve prolapse, long-term antiplatelet therapy is reasonable. In mitral annular calcification, antiplatelet therapy can be considered. Patients with mitral regurgitation can be considered for warfarin or antiplatelet therapy.

In aortic valve disease, antiplatelet therapy may be considered. For patients with mechanical prosthetic valves, oral anticoagulation with warfarin (target INR, 2.5-3.5) is recommended. For those who experience TIAs despite therapeutic INR, aspirin 75-100 mg/day can be added to the regimen. Patients with bioprosthetic valves and no other source of thromboembolism who experience TIAs can be considered for oral anticoagulation with warfarin (target INR, 2-3).

Intracranial atherosclerosis

The 2014 AHA/ASA guidelines state the following for patients with stroke or TIA due to 50-99% stenosis of a major intracranial artery:

- Aspirin 50-325 mg/day, rather than warfarin, is recommended
- Maintenance of blood pressure below 140/90 mm Hg and total cholesterol below 200 mg/dL is recommended
- Extracranial or intracranial bypass surgery is not recommended
- Angioplasty and stent placement are investigational and of unknown utility

A randomized trial has shown that aggressive medical management (antiplatelet therapy combined with intensive management of vascular risk factors) is safer than percutaneous transluminal angioplasty and stenting (PTAS) in patient with 70-99% stenosis of a major intracranial artery. Enrollment in this trial was stopped after 451 patients underwent randomization because the 30-day rate of stroke

or death was 14.7% in the PTAS group and 5.8% in the medical-management group.

Long-Term Monitoring

Patients selected for outpatient care should have a clear follow-up plan and stroke prevention initiated as described, including antiplatelet medication and risk-factor modification. Antiplatelet agents typically should be initiated as soon as intracranial bleeding is ruled out. As noted (see above), the agent to be used varies with the patient and the specific indication.

The following measures should be included in any long-term monitoring of TIA patients:

- Antihypertensive control should be optimized for patients with hypertension
- Lipid control should be initiated, potentially including a statin agent
- Blood glucose control should be optimized for patients with diabetes

- A smoking-cessation strategy, which may include medication, should be initiated
- Heavy drinkers should eliminate or reduce alcohol consumption
- Overweight patients should be encouraged to lose weight
- All patients should be encouraged to exercise

Recommendations

These guidelines cover both ischaemic stroke and transient ischaemic attacks (TIAs). Separate guidelines exist or are being prepared for intracerebral haemorrhage and subarachnoid haemorrhage. The classes of evidence and levels of recommendations used in these guidelines are defi ned according to the criteria of the European Federation of Neurological Societies

Table 9.1 Classification of evidence for diagnostic and for therapeutic measures (from [583]).

	Evidence classification scheme for a diagnostic measure	Evidence classification scheme for a therapeutic intervention
Class I	A prospective study in a broad spectrum of persons with the suspected condition, using a 'gold standard' for case definition, where the test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy	An adequately powered, prospective, randomized, controlled clinical trial with masked outcome assessment in a representative population or an adequately powered systematic review of prospective randomized controlled clinical trials with masked outcome assessment in representative populations. The following are required: **a.** randomization concealment **b.** primary outcome(s) is/are clearly defined **c.** exclusion/inclusion criteria are clearly defined **d.** adequate accounting for dropouts and crossovers with numbers sufficiently low to have a minimal potential for bias; and **e.** relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences
Class II	A prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a broad spectrum of persons with an established condition (by 'gold standard') compared to a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy	Prospective matched-group cohort study in a representative population with masked outcome assessment that meets a–e above or a randomized, controlled trial in a representative population that lacks one criterion a–e
Class III	Evidence provided by a retrospective study where either persons with the established condition or controls are of a narrow spectrum, and where test is applied in a blinded evaluation	All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment
Class IV	Evidence from uncontrolled studies, case series, case	Evidence from uncontrolled studies, case series, case

Table 9.2 Definitions for levels of recommendation (from [583]).

Level A	Established as useful/predictive or not useful/predictive for a diagnostic measure or established as effective, ineffective or harmful for a therapeutic intervention; requires at least one convincing Class I study or at least two consistent, convincing Class II studies
Level B	Established as useful/predictive or not useful/predictive for a diagnostic measure or established as effective, ineffective, or harmful for a therapeutic intervention; requires at least one convincing Class II study or overwhelming Class III evidence
Level C	Established as useful/predictive or not useful/predictive for a diagnostic measure or established as effective, ineffective or harmful for a therapeutic intervention; requires at least two Class III studies
Good Clinical Practice (GCP) points	Recommended best practice based on the experience of the guideline development group. Usually based on Class IV evidence indicating large clinical uncertainty, such GCP points can be useful for health workers

Stroke services and stroke unit

Recommendations

- It is recommended that all stroke patients should be treated in a stroke unit (Class I, Level A).
- It is recommended that healthcare systems ensure that acute stroke patients have access to high technology medical and surgical stroke care when required (Class III, Level B).
- The development of clinical networks, including telemedicine, is recommended to expand access to high-technology specialist stroke care (Class II, Level B).

Diagnostic imaging

Recommendations

- In patients with suspected TIA or stroke, urgent cranial CT (Class I), or alternatively MRI (Class II), is recommended (Level A).
- If MRI is used, the inclusion of diffusion-weighted imaging (DWI) and T2*-weighted gradient echo sequences is recommended (Class II, Level A).
- In patients with TIA, minor stroke, or early spontaneous recovery immediate diagnostic work-up, including urgent vascular imaging (ultrasound, CT-angiography, or MR angiography) is recommended (Class I, Level A).

Other Doagnosis Tests

Recommendations

- In patients with acute stroke and TIA, early clinical evaluation, including physiological parameters and routine blood tests, is recommended (Class I, Level A).
- For all stroke and TIA patients, a sequence of blood tests is recommended (table 9.3, table 9.5).
- It is recommended that all acute stroke and TIA patients should have a 12-lead ECG. In addition continuous ECG recording is recommended for ischaemic stroke and TIA patients (Class I, Level A).
- It is recommended that for stroke and TIA patients seen after the acute phase, 24-h Holter ECG monitoring should be performed when arrhythmias are suspected and no other causes of stroke are found (Class I, Level A).
- Echocardiography is recommended in selected patients (Class III, Level B).

Management of Vascular Risk

Recommendations

- Blood pressure should be checked regularly. It is recommended that high blood pressure should be managed with lifestyle modification and individualized pharmacological therapy (Class I, Level A) aiming at normal levels of 120/80 mmHg (Class IV, GCP). For prehypertensive (120–139/80–90 mmHg) with congestive heart failure, MI, diabetes, or chronic renal failure, antihypertensive mediation is indicated (Class I, Level A).
- Blood glucose should be checked regularly. It is recommended that diabetes should be managed with lifestyle modification and individualized pharmacological therapy (Class IV, Level C). In diabetic patients, high blood pressure should be managed intensively (Class I, Level A) aiming for levels below 130/80 mmHg (Class IV, Level C). Where possible, treatment should include an angiotensin converting enzyme inhibitor or angiotensin receptor antagonist (Class I, Level A).
- Blood cholesterol should be checked regularly. It is recommended that high blood cholesterol (e.g. LDL> 150 mg/dl [3.9 mmol/l]) should be managed with lifestyle modification (Class IV, Level C) and a statin (Class I, Level A).
- It is recommended that cigarette smoking be discouraged (Class III, Level B).
- It is recommended that heavy use of alcohol be discouraged (Class II, Level B).
- Regular physical activity is recommended (Class III, Level B).
- A diet low in salt and saturated fat, high in fruit and vegetables and rich in fibre is recommended (Class II, Level B).
- Subjects with an elevated body mass index are recommended to take a weight-reducing diet (Class II, Level B).
- Antioxidant vitamin supplements are not recommended (Class I, Level A).
- Hormone replacement therapy is not recommended for the primary prevention of stroke (Class I, Level A).

Primary Prevention - Antithrpmbic Therapy

Recommendations

- Low-dose aspirin is recommended in women aged 45 years or more who are not at increased risk for intracerebral haemorrhage and who have good gastrointestinal tolerance; however, its effect is very small (Class I, Level A).
- It is recommended that low-dose aspirin may be considered in men for the primary prevention of myocardial infarction; however, it does not reduce the risk of ischaemic stroke (Class I, Level A).
- Antiplatelet agents other than aspirin are not recommended for primary stroke prevention (Class IV, GCP).
- Aspirin may be recommended for patients with non-valvular AF who are younger than 65 years and free of vascular risk factors (Class I, Level A).
- Unless contraindicated, either aspirin or an oral anticoagulant (international normalized ratio [INR] 2.0–3.0) is recommended for patients with non-valvular AF who are aged 65–75 years and free of vascular risk factors (Class I, Level A).
- Unless contraindicated, an oral anticoagulant (INR 2.0–3.0) is recommended for patients with non-valvular AF who are aged >75, or who are younger but have risk factors such as high blood pressure, left ventricular dysfunction, or diabetes mellitus (Class I, Level A).
- It is recommended that patients with AF who are unable to receive oral anticoagulants should be offered aspirin (Class I, Level A).
- It is recommended that patients with AF who have mechanical prosthetic heart valves should receive long-term anticoagulation with a target INR based on the prosthesis type, but not less than INR 2–3 (Class II, Level B).
- Low-dose aspirin is recommended for patients with asymptomatic internal carotid artery (ICA) stenosis >50% to reduce their risk of vascular events (Class II, Level B).

Secondary Prevention
Optimal management of vascular risk factors

Recommendations

- It is recommended that blood pressure be checked regularly. Blood pressure lowering is recommended after the acute phase, including in patients with normal blood pressure (Class I, Level A).
- It is recommended that blood glucose should be checked regularly. It is recommended that diabetes should be managed with lifestyle modification and individualized pharmacological therapy (Class IV, GCP).
- In patients with type 2 diabetes who do not need insulin, treatment with pioglitazone is recommended after stroke (Class III, Level B).
- Statin therapy is recommended in subjects with non-cardioembolic stroke (Class I, Level A).
- It is recommended that cigarette smoking be discouraged (Class III, Level C).
- It is recommended that heavy use of alcohol be discouraged (Class IV, GCP).
- Regular physical activity is recommended (Class IV, GCP).
- A diet low in salt and saturated fat, high in fruit and vegetables, and rich in fibre is recommended (Class IV, GCP).
- Subjects with an elevated body mass index are recommended to adopt a weight-reducing diet (Class IV, Level C).
- Antioxidant vitamin supplements are not recommended (Class I, Level A).
- Hormone replacement therapy is not recommended for the secondary prevention of stroke (Class I, Level A).
- It is recommended that sleep-disordered breathing such as obstructive sleep apnoea be treated with continuous positive airway pressure breathing (Class III, Level GCP).
- It is recommended that endovascular closure of PFO be considered in patients with cryptogenic stroke and high risk PFO (Class IV, GCP).

Antithrombotic therapy

Recommendations

- It is recommended that patients receive antithrombotic therapy (Class I, Level A).
- It is recommended that patients not requiring anticoagulation should receive antiplatelet therapy (Class I, Level A). Where possible, combined aspirin and dipyridamole, or clopidogrel alone, should be given. Alternatively, aspirin alone or triflusal alone may be used (Class I, Level A).
- The combination of aspirin and clopidogrel is not recommended in patients with recent ischaemic stroke, except in patients with specific indications (e.g. unstable angina or non-Q-wave MI, or recent stenting); treatment should be given for up to 9 months after the event (Class I, Level A).
- It is recommended that patients who have a stroke on antiplatelet therapy should be re-evaluated for pathophysiology and risk factors (Class IV, GCP).
- Oral anticoagulation (INR 2.0–3.0) is recommended after ischaemic stroke associated with AF (Class I, Level A). Oral anticoagulation is not recommended in patients with comorbid conditions such as falls, poor compliance, uncontrolled epilepsy, or gastrointestinal bleeding (Class III, Level C). Increasing age alone is not a contraindication to oral anticoagulation (Class I, Level A).
- It is recommended that patients with cardioembolic stroke unrelated to AF should receive anticoagulants (INR 2.0–3.0) if the risk of recurrence is high (Class III, Level C).
- It is recommended that anticoagulation should not be used after non-cardioembolic ischaemic stroke, except in some specific situations, such as aortic atheromas, fusiform aneurysms of the basilar artery, cervical artery dissection, or patent foramen ovale in the presence of proven deep vein thrombosis (DVT) or atrial septal aneurysm (Class IV, GCP).
- It is recommended that combined low dose aspirin and dipyridamole should be given if oral anticoagulation is contraindicated (Class IV, GCP).

Conclusion

Pharmacologic management for transient ischemic attacks (TIAs) is aimed at reducing both short-term and long-term risk of stroke. In view of the high short-term risk of stroke after TIA, antithrombotic therapy should be initiated as soon as intracranial hemorrhage has been ruled out.

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