# An updated guide to treating stroke

**N Schellack,[1] N Smith,[1] L van Tonder,[2] EJ Fourie[1]**

[1] School of Pharmacy, Sefako Makgatho Health Sciences University, South Africa

[2] Netcare Femina Hospital, South Africa

**Corresponding author, email:** natalie.schellack@smu.ac.za

## Abstract

Stroke is one of the leading causes of mortality worldwide. Stroke can either be haemorrhagic (13%) or ischaemic (87%) in nature. Within the first few days of stroke, transient ischaemic attacks may occur and will require urgent intervention. However, this is often missed by healthcare workers. This article outlines the current evidence-based practice for stroke management and care. Based on the aetiology, this may include early reperfusion with a tissue plasminogen activator (t-PA), antiplatelet therapy and warfarin. This paper outlines many of the recommendations of the published National Clinical Guidelines for Stroke. It also covers aspects of multidisciplinary stroke care, from initial assessment and acute treatment, to rehabilitation strategies and the management of complications.

**Keywords:** stroke, hypertension, ischaemic stroke, haemorrhagic stroke, reperfusion, tissue plasminogen activator



S Afr Pharm J 2020;87(4):26-34

## Introduction

A stroke or cerebrovascular accident/incident (CVA/CVI) is defined as the damaging of, or death to brain cells that are starved of oxygen due to the sudden disruption of blood supply to certain areas of the brain.[1]

Stroke remains the second leading cause of death and disability, with an illustrative mortality rate of the seven million deaths that were reported globally in 2015. The World Health Organization (WHO) predicts the number of stroke-related deaths will increase to 7.8 million by 2030.[2] The upsurge in predicted deaths is mainly attributed to an increased exposure to stroke risk factors and an aging population.[3] South Africans have increased exposure too, with rapid epidemiological changes that predispose us to stroke risk factors. In SA, stroke is responsible for ~25 000 deaths annually and 95 000 years lived with disability. In 2000, stroke was the third most common cause of death in SA, after HIV/AIDS and coronary artery disease (CAD).

## Epidemiological background

There is an increased risk of stroke with advancing age; there are more stroke-related deaths in older South Africans, where stroke is the most common cause of death of people over the age of 50 years.[3] The Southern African Stroke Prevention Initiative (SASpi) study provided scientists and health professionals with the only community-based data on the prevalence of stroke in SA.[3] This study found that the age-standardised prevalence of stroke was 290 cases per 100 000 individuals in the population, and the crude prevalence in rural South Africans was found to be about 300 per 100 000. It is most likely that the stroke prevalence in urban areas is even higher than this. The SASpi study showed that there were far more disabled stroke survivors in rural SA than in Tanzania, for example, and a similar number in New Zealand, which has a high-income population, and which may probably have a higher incidence of stroke than SA. More recently, a crude stroke rate of 244 per 100 000 person-years was reported in the Agincourt subdistrict of the Mpumalanga Province, and 1 070 disability adjusted life years (DALYs) were lost as a result of people suffering strokes. This is indicative of very high rates of stroke incidence and disability in rural SA.[3] The SA National Burden of Disease Study estimated DALYs and years of life lost due to premature death and found that, despite the high prevalence of HIV/AIDS, violence and trauma, stroke is the eighth most important cause of years of life lost owing to illness, and the ninth most important cause of disability in SA.[3]

The SA Comparative Risk Assessment Collaborating Group estimated the contribution of eight risk factors to stroke and made the following findings in terms of each risk factor and its associated contribution (given as a percentage in brackets):[3]

- Uncontrolled hypertension (52%)
- Smoking/tobacco use (24%)
- Excess body weight/obesity (18%)
- High cholesterol levels (15%)
- Sedentary lifestyle/physical inactivity (12%)
- Inadequate intake of fresh fruit and vegetables (12%)
- Uncontrolled or poorly controlled diabetes mellitus (8%)
- Excessive alcohol consumption (8%)

Stroke management, especially in younger South Africans, is often complicated by the high prevalence of HIV/AIDS. In 2010, the SA Stroke Society (SASS) published guidelines on the management of stroke and transient ischaemic attacks (TIAs) – their objective was to place the recommendations in the current SA context, and to grade the existing evidence at the time according to the applicable levels of scientific rigour. Most South African patients with stroke that are seen in the primary healthcare setting struggle to regularly access basic medicine, such as aspirin, statins, antihypertensive and antidiabetic medications. Moreover, because of the limited number of specialised stroke units in the country, which are situated almost exclusively in the larger urban centres, there are significant disparities in the quality of care that stroke patients invariably receive in this country. The appropriate access to reperfusion therapies is not universally available, even in urban centres.[3]

**Table I:** Ischaemic versus haemorrhagic stroke

| Ischaemic stroke | | | Haemorrhagic stroke | |
|---|---|---|---|---|
| Ischaemic stroke is the most common type of stroke and accounts for 85% of all stroke cases. This type of stroke occurs when one of the arteries supplying the brain of oxygenated blood is obstructed, thus reducing the blood flow to certain areas in the brain.[4] Ischaemic strokes can be further sub-divided into: | | | Haemorrhagic strokes account for 15% of all stroke cases and occur when a blood vessel in the brain becomes weak and ruptures, causing blood to leak into the brain, damaging surrounding tissue.[4] The prognosis of a haemorrhagic stroke is far less optimistic than that of an ischaemic stroke, with death occurring in 38% of patients within the first 30 days.[5] Haemorrhagic strokes can be sub-divided into: | |
| **Thrombotic stroke** | **Embolic stroke** | **Transient ischaemic attack (TIA)** | **Intracerebral haemorrhage** | **Subarachnoid haemorrhage** |
| When a blood clot forms in a vessel that supplies the brain with blood and disrupts the blood flow from the site where the clot formation occurred.[4] | When a blood clot or a fragment from an atherosclerotic plaque, usually in the heart or large arteries leading to the brain, loosens, and travels until it reaches a small-enough blood vessel that it is then able to occlude, thus disrupting blood flow to the brain.[4] Embolic strokes account for 20% of all acute strokes.[4] | An acute episode of temporary neurological dysfunction that results from ischaemia and is not associated with acute tissue infarction. 80% of TIAs resolve within 60 minutes. TIA can result from the same mechanisms as ischaemic stroke. 10% of patients with TIA will suffer a stroke within 90 days and of those, half suffer a stroke within 2 days.[6] | When a small blood vessel inside the brain ruptures, causing bleeding inside the brain tissue. Hypertension is one of the main causes for the weakened state of the vessel.[4] | A blood vessel that ruptures and results in bleeding into the subarachnoid space between the pia mater and arachnoid mater of the meninges. 85% of this type of haemorrhage is caused by an aneurysm.[4] |

Therefore, the burden of stroke is high, and it is vital to educate patients on the risk factors for the development of stroke, and on the associated preventative measures that should be commonly available or instituted, and that should be actively promoted.

## Pathophysiology

The interruption of blood flow to the brain that arises during a stroke is due to either ischaemia or haemorrhage. These two major types of stroke are elucidated in Table I.

## Risk factors associated with stroke

The individual risk factors for stroke may coexist and the prevalence of these risk factors varies greatly amongst different population groups in South Africa. They may be modifiable (i.e. risk factors that may be reduced by lifestyle changes and/or medication) or non-modifiable (e.g. increased risk with increasing age). The main risk factors are summarised in Tables II and III.[3]

**Table II:** Lifestyle-related risk factors

| Lifestyle-related risk factors | Impact on stroke risk |
|---|---|
| Cigarette smoking | Smokers are 2–4 times more likely to suffer from ischaemic heart disease or stroke compared to non-smokers.[2] |
| Physical inactivity | Patients who are physically active less than four (4) times a week, have a 20% increase in stroke risk after 5.7 years, compared to physically active patients.[2] |
| Body weight and fat distribution | Patients with a body mass index (BMI) of more than 25 kg/m$^2$, with increased abdominal fat, have an increased stroke risk, regardless of the country they live in.[3] |
| Alcohol | Heavy alcohol consumption has shown to increase the risk of both ischaemic and haemorrhagic stroke.[3] |

**Table III:** Medical risk factors

| Medical risk factors | Impact on stroke risk |
|---|---|
| Hypertension | Elevated blood pressure (BP) (> 130/85 mmHg) is the most prevalent risk factor in both ischaemic and haemorrhagic strokes.[2] |
| Diabetes mellitus (DM) (uncontrolled) | Uncontrolled DM is an independent risk factor for ischaemic strokes.[3]<br><br>Diabetic ischaemic stroke patients tend to be younger, and are more likely to have hypertension, dyslipidaemia and myocardial infarctions than non-diabetic stroke patients. Tight glycaemic control is crucial.[2] |
| Dyslipidaemia | Dyslipidaemia is strongly associated with atherosclerosis, a prevalent risk factor for ischaemic stroke. Triglyceride levels, total cholesterol, HDL cholesterol and LDL cholesterol should be evaluated in a fasting state in high-risk patients.[2] |
| Cardiac conditions | Certain cardiac conditions may increase the risk of an ischaemic stroke by predisposing the patient to future embolic events.<br><br>These cardiac conditions include: atrial fibrillation (AF)*, valvular disease, mitral stenosis, structural anomalies that allow for right-to-left shunting (e.g. a patent foramen ovale) of blood, and atrial and ventricular enlargement.[2]<br><br>*Patients with AF have uncoordinated atrial contractions, which predisposes the left atrium to thrombus formation, thereby causing a five-fold increase in the risk of developing an ischaemic stroke.[5] |
| Chronic kidney disease (CKD) | There is a 43% increased risk for ischaemic stroke in patients with a chronic GFR < 60 mL/min–1/1.73 m.[2] |

GFR – glomerular filtration rate

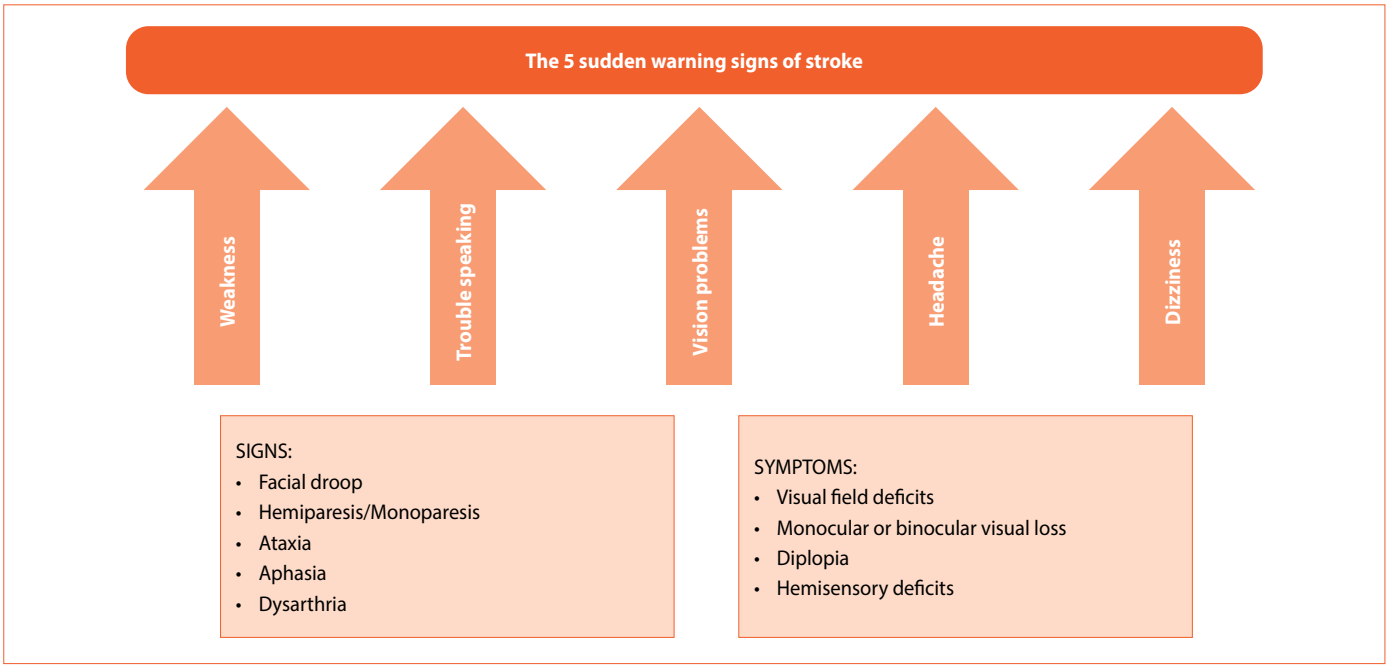


**Figure 1:** The general signs and symptoms of stroke[6]

## Clinical presentation

For any patient that presents with a sudden, altered level of consciousness (LOC), or an acute neurological deficit, stroke should be considered.[6] Nausea, vomiting, headache and a sudden, altered level of consciousness are more prevalent in haemorrhagic strokes. Figure 1 illustrates the signs and symptoms of both an ischaemic and a haemorrhagic stroke.[6]

## Public education on stroke prevention

Educating the public on how to recognise the signs and symptoms of a stroke can greatly decrease the high mortality rate associated with this debilitating condition. Raising stroke awareness is particularly useful in areas where the incidence is high, such as old age homes. The public should be aware of the sudden onset of such signs and symptoms as depicted by Figure 2.[6]

The early recognition of symptoms will lead to the rapid diagnosis and treatment of the stroke, which increases the patient's likelihood of survival. The American Stroke Association released the 'FAST' acronym as part of their stroke public awareness campaign, to educate carers and the public on the early warning signs of a stroke and to contact the relevant emergency services at once.[6]

**F:** **Face drooping** (i.e. one side of the face is drooping, or the patient finds it really difficult to move the affected side)

**A:** **Arm weakness** (i.e. the inability of the patient to fully lift one of his/her arms)

**S:** **Speech difficulty** (i.e. the patient is battling to produce speech or comprehend verbal communication)

**T:** **Time**, time to call 911 (i.e. call the local emergency services or transport the patient to an emergency department at once).

Their message is to 'stop stroke' by recognising the 'FAST' signs.

Suitable pre-hospital care that would need to be provided by ambulance personnel or paramedics, should include the following measures:[3]

- maintaining physiological homeostasis (in vital functions),

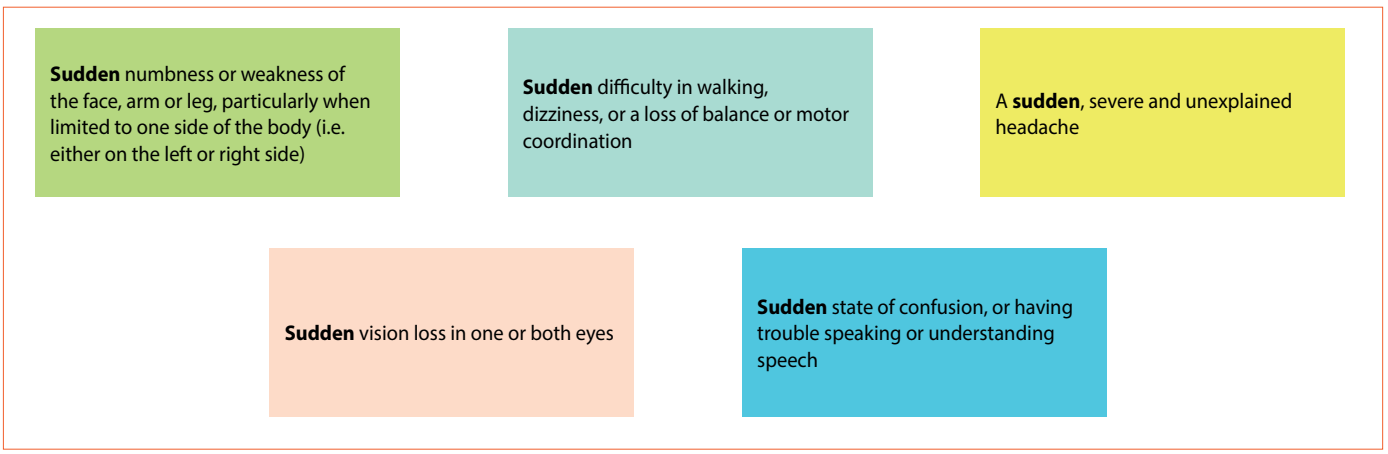


**Figure 2:** Recognising the signs and symptoms of stroke[6]

- taking history of the events (time of onset, signs and symptoms and previous medical history), and
- alerting the nearest stroke unit [or emergency department] and alert priority transport.

## Diagnosing a stroke

A medical practitioner will diagnose a stroke based on the above-mentioned signs and symptoms.[7] Thereafter a thorough medical history is needed to consider possible risk factors as discussed earlier.[7]

### *Diagnostic tests and procedures*

The following options need to be considered and utilised as needed:

***A brain CT (computed tomography) scan:***

A minimally invasive diagnostic procedure that uses x-rays to take clear, detailed images of the brain. This procedure is performed immediately after a stroke is suspected.[7]

***Magnetic resonance imaging (MRI):***

This diagnostic procedure detects changes in brain tissue and damage to brain cells. This procedure may be performed in addition to a CT scan.[7]

***Computed tomography arteriogram (CTA) and magnetic resonance arteriogram (MRA):***

These procedures allow for the visualisation of the large blood vessels in the brain. They enable the medical practitioner to identify the site of a blood clot and the flow of blood through the brain.[7]

***Carotid ultrasound:***

A non-invasive diagnostic procedure that shows the inside of the carotid arteries that supply oxygen to the brain. This test will indicate if an atherosclerotic plague has narrowed or blocked these carotid arteries. This procedure may include a Doppler ultrasound.[7]

***Doppler ultrasound:***

The Doppler will show the speed and direction of blood flowing through the vessels.[7]

***Carotid angiography:***

An invasive procedure during which contrast dye and special x-rays are used to visualise the inside of the carotid arteries.[7]

### *Complementary and additional investigations*

***Electrocardiogram (ECG):***

An ECG records the heart's electrical activity, the heart rate and rhythm. This test may detect cardiac problems that could have contributed to a stroke.[7]

***Echocardiography of the heart:***

Also referred to as ultrasound, this test uses sound waves to create a picture of the heart. It can detect possible blood clots in the heart and any aorta-related problems.[7]

***Blood tests:***

- Blood glucose: This test measures the amount of glucose in the blood. A patient with low glucose levels may present with some of the same symptoms that are associated with stroke.[7]
- Platelet count: A platelet count measures the number of platelets in the blood. Abnormal levels may be a sign of either a bleeding disorder or a thrombotic disorder.[7]
- Partial thromboplastin time or activated partial thromboplastin time (PTT or aPTT): These tests measure the time it takes for the blood to clot.[7]
- Antiphospholipid antibodies: Measuring the antiphospholipid antibodies should be reserved for patients < 50 years of age, with a history of venous/arterial thrombotic events or *livedo reticularis*, which is a common skin finding consisting of a mottled, reticulated vascular pattern that appears as a lace-like purplish discoloration of the skin. The discoloration is caused by swelling of the venules as a result of obstruction of the capillaries by small blood clots.[8]

Thus, the timely diagnosis of stroke at the initial examination is extremely important given the disease morbidity and narrow time window for effective intervention.[9]

## Treatment goals

If stroke is diagnosed timeously and appropriate treatment is utilised, the goals mentioned below should be within reach. The broad treatment goals are:[11]

- firstly, to prevent or reduce ongoing neurological injury,
- to reduce mortality and long-term disability.
- to further prevent complications that are secondary to immobility and neurological dysfunction, and
- to prevent the recurrence of stroke in the same patient.

The steps towards attaining these goals are depicted in Figure 3.

Intravenous thrombolysis may offer patients that suffered ischaemic stroke with an effective treatment option, when and if such intravenous recombinant tissue plasminogen activator (*r*t-PA) therapy can be delivered within 4.5 hours following the onset of symptoms.[8-10] Recent advances indicate that mechanical thrombectomy, performed in the specialised vascular catheterisation laboratory, where the occluding cerebral vessel clot is extracted, may be a highly effective treatment option as well, and thus preventing death and disability.[8-10] However, it is important to note that treatment should not only be directed at finding a suitable cure, but those patients that survive the initial neurological insult with disability, should be offered suitable reha-bilitation as well. Rehabilitation will assist with optimal recovery and help them to achieve their maximum potential, as well as to reintegrate into society.[8-10] For patients to benefit from these advances, however, they need to be directed towards the most suitable healthcare facilities early on and in time for the appropriate treatments to be delivered. This requires coordination of services, including the emergency assessment, transfer and a fast transfer to a suitable stroke centre.[8-10]

The rehabilitation programme following a stroke should be delivered by an interdisciplinary team with experience in the process,

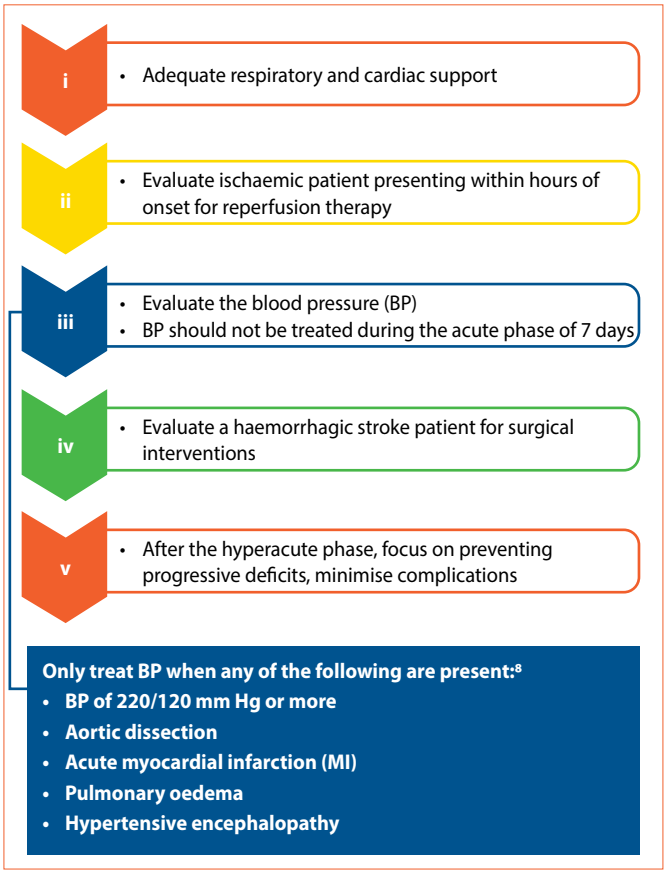


**Figure 3:** Steps to achieving the intended treatment goals.[11]

and with the aim of improving patient outcomes by minimising the chances of developing secondary complications. They also need to try and maximise a patient's level of independence de-spite their impairments.[8-10]

## Stroke treatment

- Supportive care to maintain homeostasis and treatment of acute complications should be prioritised to increase the patient's probability of making a full, or as near as possible to a complete recovery. More than half of all the ischaemic strokes, as well as ischaemic heart disease, worldwide, may be attributable to poorly controlled hypertension. The two key factors in the successful management of hypertension, are the selection of the most appropriate medications for individual patients, and their adherence to their treatment regimens. Diuretics remain an important drug class with a large amount of evidence for their efficacy. Although these agents constitute a highly-affordable option in the management of high blood pressure, they do have the potential for adverse metabolic side-effects. When used as monotherapy, they are often stopped during the first year of their use, with only 34% of such patients able to persist with their treatment beyond the first year.[11,12]
- Medications that act on the renin-angiotensin-aldosterone system (RAAS) are often prescribed for the management of hypertension because they block important renal mechanisms that play an important role in maintaining normal homeostasis of sodium levels and water in the body, and because of their additional extrarenal actions. They have also been shown to reduce the incidence of major cardiovascular events in high-risk patients.[11,12]

The calcium antagonists have regained some level of their former acceptance in this setting, in spite of worries about the short-acting drugs in this class. Over the years, several combinations with fixed-dosage drugs have been developed and shown to be effective. Some of these fixed-dose combinations have had specific indications based on certain haemodynamic and metabolic criteria. Examples of these include the following:[11,12]

- Suitable thiazide diuretics, combined with either a beta blocker, an ACE inhibitor, or an ARB, and used for uncomplicated hypertension, heart failure, or left ventricular hypertrophy, respectively.
- A calcium-channel blocker (CCB) and a beta blocker for hypertension and coronary artery disease, or a CCB and an ACE inhibitor for hypertension with kidney disease or in patients that exhibit a high level of cardiovascular risk.

The side-effects of diuretics, beta blockers, and ACE inhibitors may limit the usefulness and clinical benefits of fixed-dose combination therapies that make use of these drugs and may also decrease the levels of patient adherence to such treatment options.[11,12]

**Table IV:** Non-pharmacological and pharmacological treatment of stroke

| Non-pharmacological | | Pharmacological | | |
|---|---|---|---|---|
| | | Ischaemic stroke | | |
| Ischaemic stroke | Haemorrhagic stroke | *Acute treatment* | *Secondary prevention* | Haemorrhagic stroke |
| Surgical decompression to reduce intracranial pressure (ICP)<br><br>Early rehabilitation can reduce long-term disability | Surgical intervention to clip or ablate vascular abnormality<br><br>External ventricular drain with ICP monitoring | Tissue plasminogen activator (t-PA):<br>• Alteplase **0.9 mg/kg** IV (max 90 mg) over 1 hour – 3 hours after onset of stroke<br>• Alteplase **0.9 mg/kg** IV (max 90 mg) over 1 hour – 3 to 4.5 hours after onset of stroke<br><br>Anti-platelet therapy:<br>• Aspirin **160 mg to 325mg** daily – started 48 hours after onset of stroke | Anti-platelet therapy:<br>• Aspirin **50 mg to 325 mg** daily<br>• Clopidogrel **75 mg** daily<br>• Aspirin **25 mg** daily with extended release dipyridamole **200 mg BD**<br><br>Cardio-embolic:<br>• Dabigatran **150 mg BD**<br>• Vitamin K-antagonist, warfarin<br><br>Atherosclerosis:<br><br>Statin therapy | Nimodipine:<br><br>**60 mg every 4 hours** for 21 days with maintenance of intravascular volume via pressor therapy |

The combination of amlodipine and valsartan was developed to try and improve both the efficacy and the tolerability of the resultant fixed-dose combination product, and thus deliver the promise of better treatment. Both amlodipine and valsartan have favourable side-effect profiles, making the promise of combining these two drugs much more favourable than some of the earlier treatment options. The two drugs each act on a different mechanism that underlies the pathophysiology of hypertension. Therefore, they could offer a clear benefit in terms of their expected complementary mechanisms of action.[11,12]

The management of acute complications may include:

- Fluid imbalance – Hypovolaemia in stroke patients is associated with poor outcome and should be corrected with 0.9% normal saline. Atrial fibrillation or any cardiac arrhythmias may reduce the cardiac output and should be corrected.[3]
- Glucose metabolism – Hyperglycaemia in stroke patients has been associated with reduced functional outcome and the goal is to achieve normoglycaemia.[2]
- Hyperthermia – Increased body temperature after a stroke has been associated with poorer neurological outcome. Fever of more than 38 ºC should be treated with paracetamol.[2]
- Swallowing and nutrition – Patients who have difficulty swallowing have a high risk of aspiration. All patients should be kept nil per mouth until their ability to swallow has been assessed. In patients who remain unable to swallow or who are unconscious, a nasogastric tube may be required.[3]

The acute pharmacological and non-pharmacological treatment measures are summarised in Table IV.

**To Alteplase or NOT to Alteplase? – That is the question**

| Include Alteplase[11] | Exclude Alteplase[11] |
|---|---|
| • ≥ 18 years of age<br>• Clinical diagnosis causing measurable neurological deficit<br>• Time of symptom onset well before 4.5 hours before treatment | • Evidence of intracranial haemorrhage<br>• Minor/rapid improving symptoms<br>• Clinical suspicion of SAH – even when CT is clear<br>• Active internal bleed (21 days)<br>• Heparin within last 48 hours, increased aPTT<br>• Recent anticoagulant therapy, increased PT (> 15s)/INR<br>• Intracranial surgery, head trauma, or stroke 3 months ago<br>• Major surgery/stroke/serious trauma within 14 days<br>• Lumbar puncture within 7 days<br>• History of increased ICP, haemorrhage or arteriovenous malformation (AVM)<br>• Recent acute MI<br>• SBP > 185 mmHg or DBP > 110 mmHg |

## Prevention of stroke

Primary stroke prevention measures reduce the risk of stroke and should be actively promoted. Secondary prevention measures, reduce the risk of recurrence of stroke.[3]

| Primary stroke prevention |
|---|
| Cessation of smoking reduces the risk of stroke by 50% after 1 year.[3] |
| Moderate to vigorous physical activity for 30 minutes at least four times a week, has shown a 35% reduction in stroke risk.[2] |
| Weight reduction to a BMI of between 20 and 25 kg/m$^2$ has been shown to reduce the systolic blood pressure, thus reducing the risk of stroke. |
| Light to moderate alcohol consumption (< 2 drinks per day for men and < 1 drink for women) has been associated with a lower stroke risk.[3] |
| **Secondary stroke prevention** |
| High blood pressure (BP) is the most common modifiable stroke risk factor. Results from both the ACCORD and SPRINT trails indicated that intensive BP control of a systolic blood pressure (SBP) of < 120 mmHG, resulted in a significant lower relative risk, compared to the traditional approach of < 140 mmHG.[2] |
| Diabetes mellitus is an independent risk factor for stoke recurrence. Tight BP control (SBP < 120 mmHG) with cholesterol management is crucial. Analysis from prospective random control trial of interventions that targeted patients with prediabetes, show a 23% relative risk reduction in fatal and nonfatal strokes.[2] |
| Heart rhythm disorders such as AF independently increases the relative risk for stroke fivefold. The $CHADS_2$ scoring system is used to identify AF patients and assist with the appropriate selection of anticoagulant therapy.[3] |
| Dyslipidaemia is associated with atherosclerosis, which is a major risk factor in ischaemic stroke. In high-risk patients with vascular disease and a total fasting cholesterol of > 3.5 mmol/l, statin therapy is strongly suggested, and is associated with reduced rates in both myocardial infarction and reduced risk of ischaemic stroke.[3] |

## Conclusion

There have been major advances in recent years in the management of stroke both acutely and during rehabilitation. Secondary prevention that is effectively implemented is likely to significantly reduce the risk of stroke. The pharmacist needs to recognise stroke early and help to implement treatment timeously, as this can greatly reduce mortality. Patients with acute stroke should be monitored for the development of neurological deterioration, which may take the form of thromboembolism or infection. The role of the pharmacist is especially important in recognising adverse effects from both pharmacological and non-pharmacological interventions.

## References


1. Rudd A, Bowen A, Young G, James M. The latest national clinical guideline for stroke. Clinical Medicine. 2016;17(2):154-155.
2. Benjamin EJ, Muntner P, Alonso A, et al; for the American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics-2019 update: a report from the American Heart Association [published online January 31, 2019]. Circulation. https://doi.org/10.1161/CIR.0000000000000659.
3. Taylor A, Ntusi NAB. Guest Editorial. Evolving concepts of stroke and stroke management in South Africa: Quo vadis? S Afr Med J. 2019;109(2):69-71. https://doi.org/10.7196/SAMJ.2019.v109i2.00009.
4. Shari N. Allen M. Pharmacologic Management of Stroke [Internet]. Uspharmacist.com. 2017 [Accessed 2 July 2017]. Available from: https://www.uspharmacist.com/article/pharmacologic-management-of-stroke.
5. Schellack N, Schellack G, Esterhuizen H. Understanding anticoagulation therapy for stroke prevention and atrial fibrilation. South African Pharmacy Journal. 2013;80(7):13-19.
6. Jauch E, Al Kasab S, Stettler B. Ischemic Stroke Clinical Presentation: History, Physical Examination [Internet]. Emedicine.medscape.com. 2017 [Accessed 2 July 2017]. Available from: http://emedicine.medscape.com/article/1916852-clinical.
7. Nhlbi.nih.gov [Internet]. How Is a Stroke Diagnosed? – NHLBI, NIH. 2017 [Accessed 3 July 2017]. Available from: https://www.nhlbi.nih.gov/health/health-topics/topics/stroke/diagnosis.
8. Bateman K. Medical management of acute ischaemic stroke. S Afr Med J. 2019;109(2):72-76. https://doi.org/10.7196/SAMJ. 2019. v109i2.00008.
9. Harrichandparsad R. Mechanical thrombectomy for acute ischaemic stroke. S Afr Med J. 2019;109(2):77-80. https://doi.org/10.7196/SAMJ.2019.v109i2.00010.
10. Whitehead S, Baalbergen E. Post-stroke rehabilitation. S Afr Med J. 2019;109(2):81-83. https://doi.org/10.7196/SAMJ. 2019. v109i2.00011.
11. Wells B, DiPiro J, Schwinghammer T, DiPiro C. Pharmacotherapy Handbook, 9th ed. New York, N.Y: McGraw-Hill Education; 2014.
12. Abedi V, Goyal N, Tsivgoulis G, et al. Novel Screening Tool for Stroke Using Artificial Neural Network. Stroke. 2017;48(6):1678-1681.