Ischemic Stroke and its Management

Module 2

Content

1. Introduction

Cerebrovascular diseases are frequently encountered by primary care physicians, with stroke being the most prevalent and severe manifestation. In the United States, stroke ranks as the fifth leading cause of death and remains a significant contributor to long-term disability. It is also the primary reason for hospital admissions related to neurological disorders (Feske SK. 2021). According to the 2020 American Heart Association report on Heart Disease and Stroke Statistics, the prevalence of stroke in the U.S. in 2016 was estimated at 2.5%, affecting approximately 7 million Americans over the age of 20. That year, nearly 800,000 stroke cases occurred, resulting in approximately 150,000 fatalities. Age serves as the most critical demographic risk factor, and while stroke incidence has declined in recent years, the lifetime risk has risen due to an aging population. Additionally, female sex and African American race are associated with an increased risk. The economic burden of stroke was estimated at $45.5 billion for the years 2014–2015 (Virani SS, et al.2020).

The etiology of ischemic stroke is influenced by multiple factors, with traditional modifiable risk factors like hypertension, smoking, diabetes, and hyperlipidemia receiving significant attention. However, genetic predisposition also plays a crucial role, particularly in early-onset strokes, which are often associated with a higher burden of disease-related single-nucleotide polymorphisms (SNPs). Due to this bias, older-onset cases may be attributed solely to modifiable risk factors without genetic testing.

To implement genetically personalized prevention and treatment strategies, stroke classification based on genetic risk is essential. While the widely used TOAST classification categorizes strokes based on phenotypic criteria after their occurrence, newer classification systems incorporate genetic information to refine stroke risk stratification. These systems align genetic data with TOAST-defined stroke subtypes, such as large-vessel, small-vessel, and cardioembolic strokes, further differentiating them into subphenotypes.

A modified classification adapted from Ilinca et al. categorizes genetic risk factors for ischemic stroke, excluding hemorrhagic stroke risk factors (Table 1).

Some genetic factors directly increase stroke risk, while others contribute to conditions such as hypertension, hyperlipidemia, structural heart abnormalities, and hypercoagulable states, further elevating stroke susceptibility (Ekkert A, et al.2021).

Table 1: Ischemic stroke subtypes classification by genetic risk

Large Artery Atherosclerosis	**Unspecified** **Hypercholesterolemia** **Hypertension**
Large artery structural abnormalities	Tortuosity/dolichoectasia Dissection Occlusion: Moyamoya-like/ fibromuscular dysplasia
Small-vessel disease	Isolated lacunar infarct Multiple lacunar infarcts White matter hyperintensities Hypertension
Cardioembolic	Arrhythmia: atrial fibrillation/flutter Morphological defect, such as patent foramen ovale Myopathy
Coagulopathy	Venous thrombosis Arterial thrombosis Hyperviscosity
Metabolic	Mitochondrial Defect of intermediary metabolism

Table adapted from: Ekkert A, et al.2021

2. Pathophysiology and classification of ischemic stroke

Ischemic stroke primarily results from cerebral infarction, which occurs due to an insufficient blood supply to brain tissue. Initially, this leads to a reversible loss of function, but prolonged ischemia results in irreversible neuronal damage and infarction. The ischemic cascade begins with the cessation of electrical activity in neurons, followed by cellular dysfunction caused by disruptions in membrane integrity. This disturbance triggers excessive calcium influx, initiating excitotoxicity, oxidative stress, and the eventual breakdown of cell membranes, leading to neuronal death.

The extent and duration of the blood flow deficit determine the severity of the infarction, highlighting the critical nature of timely intervention.

Different mechanisms contribute to vascular occlusion in ischemic stroke, with embolism being the most prevalent. In most cases, emboli originate from the heart due to underlying cardiac conditions such as atrial fibrillation, valvular heart disease, or cardiomyopathy caused by myocardial infarction or hypertension. Less commonly, cardiomyopathy may stem from viral infections, drug toxicity, genetic predisposition, or idiopathic causes, leading to left ventricular dysfunction, arrhythmias, and intracardiac thrombus formation. Infective or non-infective endocarditis can also generate emboli, while paradoxical embolism occurs when right-to-left shunting, typically due to a patent foramen ovale or congenital heart defect, allows venous thrombi to bypass pulmonary circulation and reach the brain.

In addition to cardioembolism, artery-to-artery embolism is a major contributor to ischemic stroke. This occurs when thrombotic material from large arteries dislodges and travels to smaller cerebral vessels, causing occlusion. Atherosclerotic plaques, often found in the carotid or vertebral arteries, serve as common sources of emboli. Another critical cause of stroke in younger individuals is arterial dissection, which can arise spontaneously or due to minor trauma, such as vigorous coughing or chiropractic manipulation. Certain connective tissue disorders further increase susceptibility to arterial dissections.

Large artery atherosclerosis remains a significant factor in ischemic stroke, with stenosis or occlusion commonly occurring in the internal carotid arteries, the vertebrobasilar system, or intracranial vessels. Arterial dissection, the second most common large vessel pathology, often leads to stroke in the absence of traditional risk factors. The primary mechanism by which large artery disease causes stroke is artery-to-artery embolism. However, severe stenosis can also result in reduced cerebral perfusion, leading to watershed infarcts in regions supplied by overlapping vascular territories.

Small vessel disease is another key cause of ischemic stroke, predominantly affecting penetrating arteries that supply deep brain structures. Chronic hypertension and other vascular risk factors contribute to progressive arterial narrowing, leading to lacunar infarcts.

These small, deep-seated infarcts commonly occur in the internal capsule, pons, thalamus, or cerebellum, resulting in distinct clinical syndromes such as pure motor hemiplegia, pure sensory stroke, ataxic hemiparesis, or dysarthria-clumsy hand syndrome.

Beyond these primary stroke mechanisms, a variety of less common causes exist. Hematologic disorders, including hypercoagulable states and sickle cell disease, can lead to thrombotic occlusions, while vasculitides may cause inflammatory damage to cerebral blood vessels. Additionally, non-thrombotic emboli, such as fat, air, tumor fragments, or septic material, can also precipitate ischemic strokes under specific clinical conditions.

The severity and progression of ischemic injury are dictated by both the extent and duration of cerebral blood flow reduction. When cerebral perfusion declines by approximately 50%, patients often remain asymptomatic. However, a further reduction leads to transient ischemic symptoms, where neuronal dysfunction is reversible if blood flow is quickly restored. If the ischemic period persists, irreversible neuronal injury occurs, culminating in infarction.

The rate at which infarction develops varies within different brain regions. In the core of the ischemic lesion, where perfusion is severely compromised, infarction may occur within minutes. However, in the surrounding penumbra, where perfusion is reduced but not completely halted, neuronal survival can be sustained for several hours. This creates a critical therapeutic window during which timely intervention can salvage at-risk tissue and minimize long-term neurological deficits. The variable progression of infarction underscores the importance of rapid stroke recognition and management, as prompt reperfusion therapies can significantly improve patient outcomes (Feske SK. 2021).

3. Risk factors for ischemic stroke

Ischemic stroke is a leading cause of morbidity and mortality worldwide, particularly in Western populations. It is estimated that up to 40% of stroke survivors suffer from severe disabilities, significantly impacting their quality of life and imposing a substantial economic burden on healthcare systems. Given its multifactorial nature, ischemic stroke is regulated by various modifiable and nonmodifiable risk factors. Identifying and addressing these risk factors is essential for effective primary and secondary prevention strategies.

3.1 Modifiable risk factors

Modifiable risk factors are those that can be managed or altered through lifestyle changes, medication, or medical interventions. Among these, hypertension stands as the most significant contributor to ischemic stroke. Elevated blood pressure damages blood vessels, increasing the likelihood of atherosclerosis, thrombus formation, and vessel rupture. Effective blood pressure control through dietary changes, regular exercise, and antihypertensive medications can significantly reduce stroke risk.

Diabetes mellitus is another critical risk factor, as chronic hyperglycemia promotes vascular inflammation and endothelial dysfunction, accelerating atherosclerosis and increasing the likelihood of cerebrovascular events. Proper glycemic control through lifestyle modifications and pharmacologic interventions can help mitigate this risk. Similarly, hyperlipidemia, characterized by elevated levels of low-density lipoprotein (LDL) cholesterol, contributes to plaque formation in the arteries, leading to reduced cerebral blood flow and an increased risk of stroke. The use of statins and lifestyle changes, such as a heart-healthy diet and regular physical activity, are crucial in managing lipid levels.

Coronary artery disease (CAD) is another closely related condition, as individuals with CAD have an increased risk of embolic strokes due to cardiac sources of embolism, such as atrial fibrillation. Antiplatelet and anticoagulant therapies play a significant role in preventing cardioembolic strokes in high-risk individuals. Other modifiable risk factors include smoking, excessive alcohol consumption, obesity, and physical inactivity, all of which contribute to vascular dysfunction and increased stroke susceptibility. Lifestyle interventions, such as smoking cessation, weight management, and regular exercise, can significantly reduce stroke risk.

3.2 Nonmodifiable risk factors

Nonmodifiable risk factors include age, sex, and genetic predisposition. Advancing age is the most significant demographic risk factor, with stroke incidence rising exponentially after the age of 55. The cumulative effect of vascular aging, coupled with the presence of comorbid conditions, makes older adults more vulnerable to ischemic stroke. Sex also plays a role in stroke risk, with men generally having a higher incidence of stroke, whereas women experience worse post-stroke outcomes.

3.3 Emerging and less-well-documented risk factors

Beyond traditional risk factors, several emerging contributors to ischemic stroke warrant attention. Geographic location and socioeconomic status have been linked to stroke prevalence, with individuals in lower-income regions exhibiting higher stroke rates due to inadequate healthcare access, poor dietary habits, and increased exposure to environmental stressors. Furthermore, chronic stress, depression, and excessive alcohol consumption have been implicated in stroke risk by exacerbating hypertension and metabolic dysfunction (Allen CL, et al. 2018).

Ischemic stroke occurs when a blood clot obstructs an artery supplying blood to the brain, leading to a sudden loss of neurological function. Recognizing the clinical presentation of ischemic stroke is crucial for prompt medical intervention, which can significantly improve outcomes.

4. Clinical presentation

4.1 Common signs and symptoms

The manifestations of an ischemic stroke depend on the affected brain region but commonly include:

- Sudden numbness or weakness: This often affects the face, arm, or leg, particularly on one side of the body.
- Confusion: Individuals may experience sudden confusion, trouble speaking, or difficulty understanding speech.
- Visual disturbances: There may be sudden trouble seeing in one or both eyes.
- Dizziness and loss of balance: Sudden dizziness, loss of balance, or lack of coordination are common.
- Severe headache: A sudden, severe headache with no known cause can occur.

4.2 Use of the "BE FAST" acronym for early recognition

The "BE FAST" acronym is a helpful tool for quickly identifying the signs of a stroke:

- B - Balance: Sudden loss of balance or coordination.
- E - Eyes: Sudden trouble seeing in one or both eyes.

- F - Face: Facial drooping or numbness on one side; ask the person to smile to observe asymmetry.
- A - Arms: Arm weakness or numbness; ask the person to raise both arms to see if one drifts downward.
- S - Speech: Slurred or garbled speech; ask the person to repeat a simple sentence to check for accuracy.
- T - Time: If any of these signs are present, it's time to call emergency services immediately.

Utilizing "BE FAST" facilitates the rapid recognition of stroke symptoms, enabling timely medical intervention (Clinic C.2025).

4.3 Differential diagnosis considerations

Several conditions can mimic the presentation of an ischemic stroke, making differential diagnosis essential:

- Transient Ischemic Attack (TIA): Often called a "mini-stroke," TIAs present with stroke-like symptoms that resolve within minutes to hours without permanent damage. However, they are a warning sign of potential future strokes and require immediate evaluation.
- Migraine with Aura: Some migraines can cause neurological deficits, such as visual disturbances or numbness, resembling stroke symptoms.
- Seizures: Postictal states following seizures can include temporary neurological deficits, known as Todd's paralysis, which may mimic stroke.
- Hypoglycemia: Low blood sugar levels can lead to confusion, weakness, and speech difficulties, similar to stroke presentations.
- Brain Tumors: Depending on their location, tumors can cause focal neurological deficits that develop more gradually than stroke symptoms.

Accurate and prompt differentiation between these conditions and ischemic stroke is vital, as treatment approaches vary significantly. Comprehensive clinical evaluation, including patient history, physical examination, and appropriate imaging studies, is essential to establish the correct diagnosis and initiate appropriate management (CDC, 2024).

5. Diagnostic evaluation

5.1 Pre-hospital assessment and the role of emergency medical services

Timely recognition and management of stroke symptoms in the pre-hospital setting are critical for optimizing patient outcomes. Emergency MedicalServices (EMS) play a pivotal role in identifying potential stroke cases, initiating pre-hospital care, and ensuring rapid transport to specialized stroke centers. Early intervention by EMS providers significantly impacts the administration of time-sensitive treatments such as thrombolysis and mechanical thrombectomy, which improve patient recovery and reduce long-term disability. Pre-hospital stroke assessment relies on validated screening tools designed to facilitate early stroke identification. The Face Arm Speech Time (FAST) test and the Cincinnati Prehospital Stroke Scale (CPSS) are widely used for their simplicity and effectiveness in recognizing common stroke symptoms. In addition, advanced tools like the Los Angeles Motor Scale (LAMS) and the Rapid Arterial Occlusion Evaluation (RACE) score assist in assessing stroke severity and identifying large vessel occlusions (LVO), which require urgent intervention such as mechanical thrombectomy. The use of these scales helps EMS personnel determine the most appropriate transport destination, ensuring that patients with severe strokes are directed to comprehensive stroke centers equipped for advanced care.

Beyond stroke identification, EMS providers play a crucial role in initiating early management. They establish intravenous access, monitor vital signs, and gather essential patient information, including the last known well time and symptom progression, which are critical for determining treatment eligibility. Effective communication between EMS personnel and hospital stroke teams facilitates rapid decision-making and minimizes delays upon hospital arrival. Additionally, some EMS systems utilize pre-notification protocols, allowing stroke teams to prepare for immediate patient evaluation and intervention. Innovative solutions, such as mobile stroke units (MSUs), are emerging to enhance pre-hospital stroke care. These specialized ambulances are equipped with point-of-care imaging, laboratory testing, and telemedicine capabilities, enabling real-time consultation with stroke specialists.

5.2 Imaging modalities

5.2.1 Non-contrast CT scans

Non-contrast computed tomography (NCCT) is the first-line imaging modality for suspected acute ischemic stroke (AIS). NCCT is widely available, fast, and cost-effective, primarily used to differentiate ischemic from hemorrhagic stroke. It also helps determine early ischemic changes and assess stroke severity using the Alberta Stroke Program Early CT Score (ASPECTS).

Despite its advantages, NCCT has limitations, including low sensitivity for detecting early infarcts within the first three hours. Additionally, NCCT cannot provide detailed vascular information, necessitating further imaging such as CT angiography (CTA) or perfusion studies for comprehensive assessment.

5.2.2 CT and MR angiography

CT angiography (CTA) is a crucial imaging tool for identifying large vessel occlusions (LVOs) and evaluating collateral circulation. Single-phase CTA offers rapid assessment, while multiphase CTA provides time-resolved imaging, enhancing visualization of collateral status. CTA is often combined with NCCT for a more complete evaluation of stroke patients, aiding in the selection of candidates for endovascular therapy (EVT).

Magnetic resonance angiography (MRA) serves as an alternative to CTA, particularly in patients with contraindications to iodinated contrast. Contrast-enhanced MRA improves detection accuracy for intracranial arterial occlusions, but it is less commonly used in acute stroke due to limited availability and longer imaging times.

5.2.3 MRI and diffusion-weighted imaging

Magnetic resonance imaging (MRI) provides superior sensitivity in detecting AIS, even within 30 minutes of symptom onset. Diffusion-weighted imaging (DWI) is the gold standard for identifying acute infarcts by detecting areas of restricted water diffusion, making it highly effective in diagnosing early-stage ischemic stroke.

However, MRI is not widely available in emergency settings and has limitations such as prolonged scan times, patient compatibility issues (e.g., metal implants), and higher costs. Despite these drawbacks, DWI is invaluable in evaluating stroke mimics and posterior circulation strokes, where NCCT sensitivity is limited.

5.2.4 CT perfusion (CTP) and MR perfusion (MRP)

CT perfusion (CTP) imaging assesses cerebral blood flow (CBF), cerebral blood volume (CBV), and time-based perfusion metrics such as mean transit time (MTT) and time to maximum (Tmax). These parameters help differentiate infarcted core from salvageable penumbra, guiding treatment decisions for thrombolysis and EVT.

MR perfusion (MRP) offers similar capabilities but is less commonly used due to longer acquisition times. Advanced automated software has improved the efficiency of CTP and MRP analysis, facilitating rapid interpretation in acute stroke settings.

5.3 Laboratory tests and biomarkers

Laboratory tests play a crucial role in stroke diagnosis, helping to rule out stroke mimics and identify underlying risk factors. Routine blood work includes a complete blood count (CBC), coagulation profile (prothrombin time [PT], international normalized ratio [INR], activated partial thromboplastin time [aPTT]), blood glucose levels, renal function tests, and electrolyte panels. These tests are essential for assessing thrombolysis eligibility, as coagulation abnormalities or severe metabolic disturbances may influence treatment decisions. For instance, hypoglycemia can mimic stroke symptoms, while hyperglycemia is associated with worse stroke outcomes. Additionally, infectious markers, such as white blood cell count and C-reactive protein (CRP), can help identify infections that may contribute to stroke risk.

Emerging stroke biomarkers are being investigated for their potential to provide rapid, point-of-care diagnosis and prognostic insights. Neuron-specific enolase (NSE), S100 calcium-binding protein B (S100B), and glial fibrillary acidic protein (GFAP) are being studied for their ability to differentiate ischemic from hemorrhagic stroke. GFAP, in particular, has shown promise in detecting intracerebral hemorrhage, while NSE and S100B may indicate neuronal damage and blood-brain barrier disruption. Additionally, inflammatory markers, such as interleukins (IL-6, IL-10) and oxidative stress indicators like 8-isoprostane, are being explored for their role in stroke pathophysiology and prognosis.

Despite significant research progress, no single biomarker has been widely adopted in clinical practice due to variability in sensitivity and specificity. The heterogeneity of stroke subtypes and patient populations further complicates biomarker validation.

Ongoing studies are focused on developing biomarker panels with high diagnostic accuracy that can complement neuroimaging modalities and enhance early stroke detection, risk stratification, and treatment decisions (Patil S, et al.2022).

6. Acute management strategies

6.1 Rapid reperfusion therapy

The primary goal of acute ischemic stroke management is to restore cerebral perfusion as quickly as possible to salvage ischemic but viable brain tissue and improve functional outcomes. The two main reperfusion strategies are intravenous thrombolysis and endovascular thrombectomy, both of which have revolutionized stroke care by significantly reducing long-term disability. Intravenous thrombolysis with recombinant tissue plasminogen activator (rtPA, alteplase) remains the first-line treatment for eligible patients presenting within the recommended time frame. Timely administration of thrombolytic therapy is critical, as its efficacy diminishes with each passing minute after symptom onset. The eligibility criteria for rtPA administration are stringent and include symptom onset within 4.5 hours, absence of major hemorrhage or extensive infarction on neuroimaging, and no contraindications such as recent major surgery, active bleeding, or a history of intracranial hemorrhage. Given the narrow therapeutic window, hospitals must implement well-structured stroke protocols to ensure rapid patient evaluation and minimize door-to-needle time. Despite its benefits, intravenous thrombolysis has limitations, particularly in cases of large vessel occlusions (LVOs), where clot burden may be too extensive for rtPA alone to achieve recanalization. Furthermore, symptomatic intracerebral hemorrhage remains a significant concern, necessitating vigilant monitoring and appropriate reversal strategies in case of bleeding complications.

6.2 Endovascular thrombectomy

For patients with large vessel occlusions (LVOs), endovascular thrombectomy (EVT) has revolutionized the management of acute ischemic stroke and is now regarded as the gold standard treatment. LVOs, which commonly involve major intracranial arteries such as the middle cerebral artery (MCA), internal carotid artery (ICA), or basilar artery, can lead to severe neurological deficits and long-term disability if not treated promptly.

This procedure is particularly beneficial for occlusions of the internal carotid artery (ICA) and the proximal middle cerebral artery (MCA). The decision to proceed with EVT is based on imaging criteria that assess clot location, infarct core size, and the presence of salvageable brain tissue. While initial trials demonstrated benefits within a 6-hour treatment window, more recent studies have expanded this window up to 24 hours in selected patients, as determined by advanced perfusion imaging techniques such as CT perfusion or diffusion-weighted MRI. EVT involves mechanical clot retrieval using stent retrievers or aspiration catheters, typically accessed via a femoral or radial artery approach. The procedure has demonstrated remarkable efficacy, with substantial improvements in disability outcomes at 90 days post-stroke. However, achieving successful reperfusion does not guarantee functional recovery, emphasizing the need for comprehensive post-procedural management, including neurocritical monitoring, hemodynamic stabilization, and secondary prevention strategies. Although EVT has transformed the treatment landscape for LVO strokes, access to this intervention remains a challenge in many regions due to the need for specialized neurointerventional expertise and infrastructure.

6.3 Antithrombotic therapy

In addition to reperfusion therapies, antithrombotic treatment plays a crucial role in preventing stroke progression and early recurrence. For patients who are ineligible for thrombolysis or thrombectomy, early administration of antiplatelet agents is the standard of care. Aspirin, initiated within 24–48 hours of stroke onset, significantly reduces the risk of early stroke progression. In cases of minor stroke or high-risk transient ischemic attacks (TIAs), dual antiplatelet therapy (DAPT) with aspirin and clopidogrel has been shown to provide additional benefits in reducing short-term recurrence risk, particularly within the first 21 days. However, prolonged use of DAPT beyond 90 days is generally not recommended due to an increased risk of bleeding complications. Anticoagulation is indicated in specific circumstances, particularly for cardioembolic strokes resulting from atrial fibrillation. In such cases, direct oral anticoagulants (DOACs) such as apixaban, rivaroxaban, and dabigatran are preferred over warfarin due to their superior safety profile and reduced risk of intracranial hemorrhage. The timing of anticoagulation initiation in patients with atrial fibrillation-related strokes depends on stroke severity.

Mild strokes warranting earlier initiation and severe strokes requiring a delayed approach to mitigate hemorrhagic transformation risk.

Stroke therapeutics are therefore, broadly categorized into 3 types based on their mode of action—activity-based, drug therapies and cell therapies as described in Figure 1.

Figure 1: The three different types of stroke treatment strategies

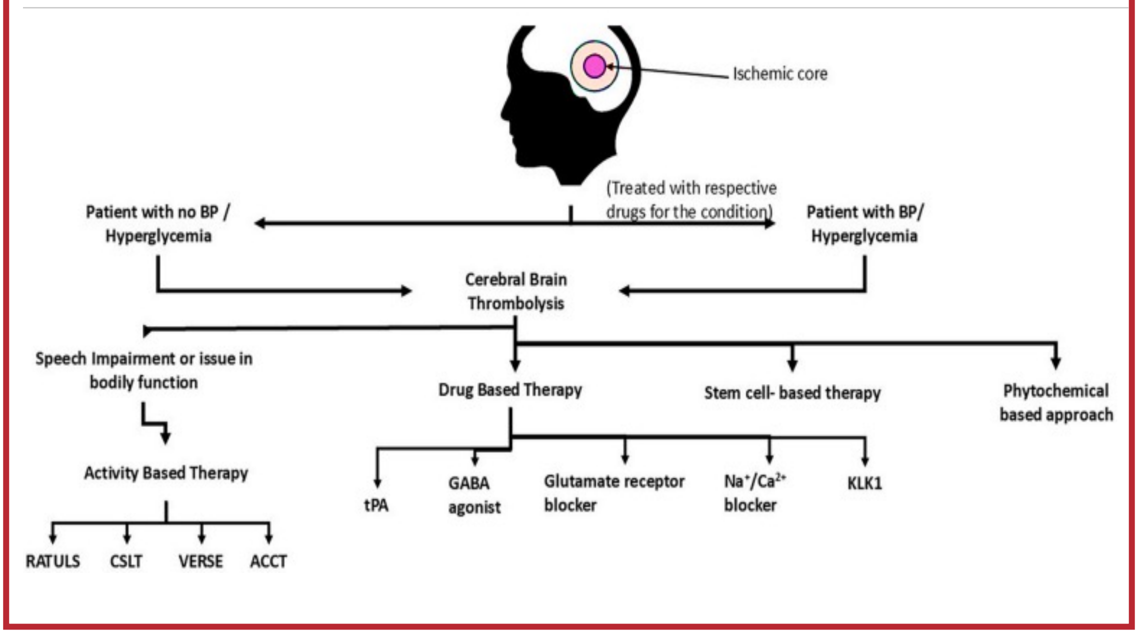

Figure adapted from: Majumder D. 2024

6.4 Hemodynamic management

Optimal hemodynamic management is a cornerstone of acute stroke care, as both excessive hypertension and aggressive blood pressure lowering can negatively impact cerebral perfusion. In the early phase of ischemic stroke, permissive hypertension is often recommended to maintain adequate blood flow to the penumbra, the region of at-risk but still viable brain tissue. Current guidelines suggest withholding antihypertensive therapy unless systolic blood pressure exceeds 220 mmHg in non-thrombolysis candidates or 185/110 mmHg in patients undergoing thrombolysis. However, in patients with comorbid conditions such as acute coronary syndrome, heart failure, or aortic dissection, blood pressure control may be necessary to prevent complications.

For patients who have undergone EVT, individualized blood pressure targets are often required, as excessive reductions may compromise collateral circulation.

6.5 Metabolic and supportive care

Beyond reperfusion and hemodynamic control, metabolic and supportive care measures play a crucial role in improving stroke outcomes. Hyperglycemia is commonly observed in the acute phase of stroke and is associated with poor outcomes due to increased infarct size and hemorrhagic transformation risk. Strict glucose control with insulin therapy is recommended in patients with persistent hyperglycemia, aiming to maintain blood glucose levels between 140–180 mg/dL while avoiding hypoglycemia. Temperature management is also critical, as fever can exacerbate neuronal injury by increasing metabolic demand and promoting inflammatory processes. Early identification and treatment of infections, particularly pneumonia and urinary tract infections, are essential in preventing systemic complications that contribute to worse neurological outcomes. Stroke patients are also at high risk of deep vein thrombosis (DVT) due to prolonged immobility. Therefore, prophylactic measures such as intermittent pneumatic compression devices and, in selected cases, low-dose anticoagulation should be implemented.

6.6 Acute stroke unit care

A dedicated stroke unit with a multidisciplinary team approach significantly enhances the quality of acute stroke care and improves survival and functional recovery. These units provide comprehensive care, including continuous neurological monitoring, early rehabilitation planning, and coordinated secondary prevention strategies. The presence of a specialized stroke team ensures rapid assessment, streamlined workflows, and adherence to evidence-based treatment protocols. Early mobilization, initiated within 24–48 hours of stroke onset, has been associated with improved functional outcomes, although overly aggressive mobilization may be detrimental in some cases. Effective communication between neurologists, interventional radiologists, intensivists, rehabilitation specialists, and nursing staff is crucial in optimizing patient outcomes.

6.7 Risk factor management in stroke prevention

A significant reduction in stroke incidence over recent decades has been largely attributed to advancements in managing key vascular risk factors. These include smoking cessation, effective control of hypertension, lipid management, and diabetes treatment. Addressing these risk factors is essential for both primary prevention—reducing the likelihood of a first stroke—and secondary prevention—minimizing the risk of recurrence in individuals with a history of stroke or transient ischemic attack (TIA).

Hypertension remains one of the most critical modifiable risk factors for stroke, and strict blood pressure control significantly lowers the risk of both ischemic and hemorrhagic strokes. Patients should be advised to adhere to antihypertensive therapy tailored to their individual cardiovascular profile. Similarly, dyslipidemia management is a cornerstone of stroke prevention, particularly in individuals with atherosclerotic disease. Current guidelines recommend high-intensity statin therapy, aiming for a low-density lipoprotein (LDL) cholesterol target of less than 70 mg/dL, to reduce the risk of recurrent cerebrovascular events. In addition to lipid-lowering therapy, lifestyle modifications play a pivotal role in stroke prevention. Adopting a heart-healthy diet—such as the Mediterranean or DASH diet—has been shown to improve vascular health. Regular physical activity, including moderate-intensity exercise for at least 150 minutes per week, supports overall cardiovascular function and metabolic health. Weight reduction in overweight or obese individuals further reduces stroke risk by improving blood pressure, lipid profiles, and insulin sensitivity.

Beyond these traditional risk factors, other conditions have been increasingly recognized as contributors to stroke risk. Obstructive sleep apnea (OSA), for instance, is highly prevalent among stroke patients and is associated with an increased risk of both initial and recurrent strokes due to intermittent hypoxia, sympathetic activation, and vascular dysfunction. Screening for OSA in high-risk individuals, followed by appropriate management—such as continuous positive airway pressure (CPAP) therapy—can improve cardiovascular outcomes and potentially lower the risk of stroke recurrence.

Comprehensive stroke prevention strategies should integrate both pharmacological and lifestyle-based interventions to achieve optimal risk factor control.

Encouraging patients to actively participate in their own risk reduction through smoking cessation programs, dietary modifications, exercise regimens, and adherence to prescribed medications can significantly reduce the burden of stroke on both individuals and healthcare systems (SPARCL, 2006; Amarenco P, et al.2019).

7. Surgical therapies for stroke prevention

A. Carotid endarterectomy and carotid artery stenting

Carotid endarterectomy (CEA) is beneficial for patients with symptomatic stenosis of the cervical internal carotid artery of 50% or greater, provided that surgical risk remains low. In selected cases, endovascular placement of carotid artery stents (CAS) may serve as an alternative to CEA. Earlier studies conducted nearly two decades ago indicated that CEA could also be advantageous for patients with asymptomatic carotid stenosis. However, with the decline in overall stroke risk since these studies were conducted, the effectiveness of both CEA and CAS in asymptomatic individuals has been called into question. This uncertainty is being addressed through an ongoing large-scale clinical trial. Until conclusive results are available, it is advisable for patients to consult a vascular neurologist for individualized recommendations regarding the appropriateness of CEA or CAS.

B. Patent foramen ovale (PFO) closure

Patent foramen ovale (PFO) is a prevalent condition, found in approximately 25% of the general population, and is generally considered benign. In patients with embolic strokes and minimal vascular risk factors, the presence of PFO raises the question of whether device closure would be beneficial. The Risk of Paradoxical Embolism (RoPE) score is a valuable tool in assessing the likelihood that a PFO contributed to the stroke. While early clinical trials demonstrated that PFO closure could be performed safely, they failed to establish clear clinical benefit. However, more recent studies have shown that PFO closure may reduce the risk of recurrent stroke in appropriately selected patients. As a result, consultation with a vascular neurologist and an interventional cardiologist experienced in the procedure is now recommended for patients with embolic stroke or transient ischemic attack (TIA) without an identifiable alternative cause.

C. Extracranial-intracranial (ec-ic) bypass and indirect surgical revascularization

Controlled trials evaluating the use of EC-IC bypass for carotid artery occlusion have not demonstrated significant clinical benefit. Nevertheless, in specialized surgical centers, these procedures may be advantageous for select patients with high-risk vascular stenosis, particularly in cases of moyamoya syndrome. While this approach remains unproven in broader clinical practice, symptomatic patients with significant vascular occlusions should be evaluated by experienced neurologists and neurosurgeons to determine the most appropriate treatment strategy.

D. Intracranial stenting

Clinical trials investigating the use of intracranial arterial stents for symptomatic intracranial stenosis have not shown clear benefits. In fact, some studies have reported a higher rate of adverse events in patients undergoing stenting procedures compared to those receiving medical therapy. Currently, management of such patients follows the protocol established in the medical arm of the SAMMPRIS trial, reserving interventional treatment for exceptional cases where a significantly elevated risk of stroke is identified (Keyhani S, et al.2020; Alexander MJ,et al.2019; Patil S, et al.2022).

8. Conclusion

Diagnostic evaluation of stroke relies on a multimodal approach combining pre-hospital assessment, neuroimaging, and laboratory testing. Rapid EMS response, NCCT for initial stroke assessment, CTA/MRA for vascular imaging, and perfusion studies for ischemic penumbra evaluation are integral components of stroke diagnosis. While MRI provides superior sensitivity, its limited availability remains a challenge. Future advancements in stroke biomarkers and portable imaging technologies may further enhance diagnostic accuracy and expedite treatment in acute stroke management. The acute management of ischemic stroke has undergone significant advancements, with rapid reperfusion therapy through intravenous thrombolysis and endovascular thrombectomy at the forefront of treatment strategies. While timely intervention remains the most critical determinant of success, comprehensive supportive care—including hemodynamic optimization, metabolic control, and prevention of complications—plays an equally important role in improving outcomes. Antithrombotic therapy further reduces the risk of stroke progression and recurrence, while specialized stroke unit care ensures a multidisciplinary approach to early rehabilitation and secondary prevention. Despite these advancements, challenges remain in ensuring widespread access to timely stroke treatment, particularly in resource-limited settings. Future efforts should focus on expanding stroke networks, improving public awareness, and implementing innovative strategies such as telestroke services to enhance the delivery of acute stroke care.

References

1. Alexander MJ, Zauner A, Chaloupka JC, et al. for the WEAVE Trial Sites and Interventionalists. WEAVE trial: Final results in 152 on-label patients. Stroke. 2019;50(4):889-94.
2. Allen CL, Bayraktutan U. Risk factors for ischaemic stroke. International journal of stroke : official journal of the International Stroke Society [Internet]. 2008;3(2):105–16.
3. Amarenco P, Kim JS, Labreuche J, et al. A Comparison of Two LDL Cholesterol Targets after Ischemic Stroke. New England Journal of Medicine. 2019 Nov 18;382(1).
4. CDC. Signs and Symptoms of Stroke. Stroke. 2024. Available from: https://www.cdc.gov/stroke/signs-symptoms/index.html?utm_source
5. Clinic C. Signs of a Stroke: Act Quickly With "BE FAST". Cleveland Clinic. 2025. Available from: https://health.clevelandclinic.org/be-fast-stroke?utm_source
6. Ekkert A, Šliachtenko A, Grigaitė J, Burnytė B, Utkus A, Jatužis D. Ischemic Stroke Genetics: What Is New and How to Apply It in Clinical Practice? Genes. 2021;13(1):48.
7. Feske SK. Ischemic stroke. The American Journal of Medicine. 2021;134(12):1457–64.
8. Keyhani S, Cheng EM, Hoggatt KJ, et al. Comparative effectiveness of carotid endarterectomy vs initial medical therapy in patients with asymptomatic carotid stenosis. JAMA Neurol. 2020.1427: e201427.
9. Majumder D. Ischemic Stroke: Pathophysiology and Evolving Treatment Approaches. Neuroscience Insights. 2024 Jan 1;19.
10. Patil S, Rossi R, Jabrah D, Doyle K. Detection, Diagnosis and Treatment of Acute Ischemic Stroke: Current and Future Perspectives. Frontiers in Medical Technology. 2022 Jun 24;4(4):748949.
11. The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Investigators. High-dose atorvastatin after stroke or transient ischemic attack. N Engl J Med 2006;355(6):349 59.

12. Virani SS, Alonso A, Benjamin EJ, et al. Heart Disease and Stroke Statistics – 2020 Update: A report of the American Heart Association. Circulation 2020;141(9): xxxx

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