Original Research Article

Stroke Management: A Comprehensive, Evidence Based Review

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Abstract: Stroke is a leading cause of mortality and long-term disability worldwide and represents a major public health challenge. Contemporary stroke management spans hyperacute reperfusion therapies, acute medical and neurosurgical care, structured stroke-unit management, early multidisciplinary rehabilitation, and long-term secondary prevention. Over the last three decades, high-quality randomized controlled trials and guideline updates have transformed stroke care from predominantly supportive management to highly time-sensitive, evidence-driven interventions. The National Institute of Neurological Disorders and Stroke (NINDS) trial established intravenous alteplase within 3 hours as standard therapy for eligible ischemic stroke patients, while ECASS III extended benefit to the 3–4.5-hour window. In 2015, multiple landmark trials (MR CLEAN, ESCAPE, EXTEND-IA, SWIFT PRIME, REVASCAT) demonstrated major functional benefit from mechanical thrombectomy in anterior circulation large-vessel occlusion. Secondary prevention trials including PROGRESS, SPARCL, CHANCE, and POINT inform optimal blood-pressure control, lipid-lowering therapy, and antithrombotic strategies. This review synthesizes pivotal trials, international guideline recommendations, acute and long-term management strategies, rehabilitation principles, and current controversies, with structured tables summarizing the evidence base to support clinical practice.

Keywords: Stroke, Ischemic Stroke, Thrombolysis, Mechanical Thrombectomy, Secondary Prevention, Rehabilitation.

1. INTRODUCTION

Stroke is defined as a sudden onset of focal or global neurological deficit lasting more than 24 hours or leading to death, with a vascular cause. Globally, stroke is the second leading cause of death and a major contributor to long-term disability among adults [1]. Approximately 80–87% of strokes are ischemic, resulting from arterial occlusion, while the remainder are haemorrhagic, including intracerebral hemorrhage (ICH) and subarachnoid hemorrhage [2].

The concept of *"time is brain"* underscores the importance of rapid diagnosis and reperfusion in ischemic stroke, as neuronal loss increases with delayed treatment. Advances in neuroimaging, reperfusion therapies, stroke systems of care, and multidisciplinary rehabilitation have substantially improved outcomes. International guidelines, particularly from the American Heart Association/American Stroke Association (AHA/ASA), now provide structured algorithms for acute management and secondary prevention based on robust trial evidence [3].

2. METHODS OF THE REVIEW

This narrative review emphasizes landmark randomized controlled trials, major meta-analyses, and authoritative international guidelines that have shaped modern stroke management. Literature was identified through targeted searches of PubMed, MEDLINE, and guideline repositories. Priority was given to high-impact trials evaluating reperfusion therapies, secondary prevention strategies, and organized stroke care. Findings are synthesized narratively and summarized in tabular form.

3. Acute Ischemic Stroke: Hyperacute Reperfusion Therapies

3.1 Intravenous Thrombolysis

Intravenous thrombolysis with recombinant tissue plasminogen activator (rt-PA) represents a cornerstone of acute ischemic stroke management.

The NINDS rt-PA trial (1995) demonstrated that IV alteplase administered within 3 hours of symptom onset significantly improved functional outcomes at 90 days compared with placebo, despite an increased risk of symptomatic intracerebral hemorrhage [4]. This trial established thrombolysis as standard therapy for eligible patients.

The ECASS III trial (2008) extended the therapeutic window to 3–4.5 hours, reporting improved functional independence without increased mortality in carefully selected patients [5]. Subsequent pooled analyses confirmed that the benefit of alteplase is strongly time-dependent, with earlier treatment yielding greater absolute benefit [6].

3.2 Mechanical Thrombectomy

Before 2015, endovascular therapy showed inconsistent benefit. The advent of modern stent-retriever devices and optimized workflows transformed outcomes.

The MR CLEAN trial (2015) was the first modern randomized trial to demonstrate that mechanical thrombectomy within 6 hours significantly improved functional independence compared with best medical therapy alone [7]. This was followed by multiple positive trials—ESCAPE, EXTEND-IA, SWIFT PRIME, and REVASCAT—which consistently showed large functional benefits in patients with anterior circulation large-vessel occlusion [8–11].

Late-window trials DAWN and DEFUSE 3 further extended eligibility to 16–24 hours in selected patients using advanced perfusion imaging, shifting the paradigm from time-based to tissue-based selection [12, 13].

3.3 Imaging Selection

Non-contrast CT remains essential to exclude intracranial hemorrhage. CT angiography identifies large-vessel occlusion, while CT or MR perfusion imaging helps quantify ischemic core and penumbra. Advanced imaging enables individualized decision-making, particularly in late-presenting patients [14].

4. Acute Haemorrhagic Stroke Management

Management of spontaneous intracerebral hemorrhage focuses on rapid blood-pressure control, reversal of anticoagulation, management of raised intracranial pressure, and selective neurosurgical intervention. Trials such as STICH and STICH II produced mixed results regarding surgical evacuation, emphasizing patient-specific decision-making [15, 16]. Rapid reversal of warfarin with vitamin K and prothrombin complex concentrate, or specific reversal agents for direct oral anticoagulants, is critical [3].

5. In-Hospital Supportive Care

Comprehensive stroke-unit care includes airway and respiratory support, avoidance of hypotension, glucose and temperature control, early venous thromboembolism prophylaxis, swallow screening, prevention of aspiration, and early mobilization. Evidence consistently demonstrates that organized stroke-unit care reduces mortality and long-term dependency compared with general medical wards [17].

6. Secondary Prevention of Stroke

6.1 Antiplatelet Therapy

Aspirin remains the foundation of secondary prevention for non-cardioembolic ischemic stroke. Short-term dual antiplatelet therapy (DAPT) with aspirin and clopidogrel has been evaluated in patients with minor stroke or high-risk transient ischemic attack.

The CHANCE trial (2013) demonstrated that short-term DAPT reduced 90-day stroke recurrence without significant increase in major bleeding in a Chinese population [18]. The POINT trial (2018) confirmed reduced ischemic events but noted increased major bleeding, supporting short-duration DAPT (approximately 21 days) in selected patients [19].

6.2 Anticoagulation for Cardioembolic Stroke

For atrial fibrillation–related stroke, direct oral anticoagulants (DOACs) are preferred over warfarin based on large randomized trials demonstrating at least non-inferior efficacy and reduced intracranial hemorrhage [20–22].

6.3 Blood-Pressure Control
  The PROGRESS trial showed that a perindopril-based blood-pressure-lowering regimen reduced recurrent stroke risk by approximately 28% in patients with prior stroke or TIA, regardless of baseline blood pressure [23].

6.4 Lipid-Lowering Therapy
  The SPARCL trial established that high-dose atorvastatin significantly reduced recurrent stroke and major cardiovascular events following recent ischemic stroke or TIA [24].

7. Rehabilitation and Recovery
  Early, intensive, multidisciplinary rehabilitation is essential for maximizing recovery after stroke. Physiotherapy, occupational therapy, speech and language therapy, and neuropsychological support promote neuroplasticity, functional independence, and quality of life. Rehabilitation planning should begin during the acute phase and continue across inpatient and community settings [25].

8. Review of Literature

S. No.	Year	Authors	Study	Methodology	Population	Outcomes	Key Findings
1	1995	NINDS rt-PA Group	IV rt-PA Trial	RCT, double blind	AIS ≤3 h	mRS, NIHSS	Improved functional outcome; ↑ sICH [4]
2	2008	Hacke *et al.*,	ECASS III	RCT	AIS 3–4.5 h	mRS at 90 d	Extended thrombolysis benefit [5]
3	2015	Berkhemer *et al.*,	MR CLEAN	RCT	LVO ≤6 h	Functional independence	Thrombectomy superior to medical care [7]
4	2015	Goyal *et al.*,	ESCAPE	RCT	LVO ≤6 h	mRS	Improved outcomes with rapid workflow [8]
5	2015	Saver *et al.*,	SWIFT PRIME	RCT	LVO ≤6 h	mRS	Benefit of stent-retriever thrombectomy [10]
6	2018	Albers *et al.*,	DEFUSE 3	RCT	LVO 6–16 h	mRS	Late-window benefit with perfusion selection [12]
7	2013	Wang *et al.*,	CHANCE	RCT	Minor stroke/TIA	Stroke recurrence	Reduced recurrence with short DAPT [18]
8	2018	Johnston *et al.*,	POINT	RCT	Minor stroke/TIA	Ischemic events	Benefit with ↑ bleeding risk [19]
9	2001	PROGRESS Group	PROGRESS	RCT	Prior stroke/TIA	Recurrent stroke	BP lowering reduced risk [23]
10	2006	Amarenco *et al.*,	SPARCL	RCT	Stroke/TIA	Stroke recurrence	High-dose statin beneficial [24]

9. DISCUSSION
  The transformation of stroke care reflects successful translation of randomized evidence into guideline-driven practice. Key challenges remain, including optimization of hemorrhagic stroke therapies, balancing antithrombotic benefit against bleeding risk, and ensuring equitable access to advanced stroke care. Implementation science, tele-stroke services, and regionalized stroke systems are critical for maximizing population-level benefit [26].

10. CONCLUSION
  Modern stroke management is firmly evidence-based and multidisciplinary. Landmark trials and international guidelines emphasize rapid reperfusion, structured stroke-unit care, aggressive secondary prevention, and early rehabilitation. Ongoing research and system-level improvements are essential to further reduce the global burden of stroke.

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