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Modern Stroke Management: An Evidence-Based Approach To Pharmacological Therapy, Neurointervention, Regenerative Medicine, and Rehabilitation

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Abstract

Stroke is a major neurological disorder requiring rapid, evidence-based management to reduce mortality, disability, and long-term complications. This study aimed to review evidence-based approaches to stroke management, focusing on pharmacological therapy, neurointervention, regenerative medicine, and rehabilitation. This study employed a narrative literature review by synthesizing relevant evidence on acute treatment, secondary prevention, neurointervention, regenerative approaches, and rehabilitation. The population consisted of scientific literature addressing stroke management, while the sample comprised selected studies and clinical guidelines relevant to the research objectives. Data were collected through literature review and analyzed descriptively by comparing and synthesizing findings across the selected sources. The results showed that intravenous thrombolysis and mechanical thrombectomy are essential interventions for eligible patients with acute ischemic stroke, while antiplatelet therapy, anticoagulation, and high-intensity statin therapy contribute to secondary prevention. Regenerative approaches, acupuncture, herbal therapy, physiotherapy, and Tuina may provide complementary benefits, particularly during rehabilitation. In conclusion, optimal stroke management requires an integrated and evidence-based strategy that combines timely acute intervention, secondary prevention, rehabilitation, and selected complementary approaches to improve functional outcomes and reduce recurrence.

Keywords*: *Anticoagulation, Neurointervention, Rehabilitation, Stroke, Thrombolysis

INTRODUCTION

Stroke is one of the neurological emergencies caused by impaired blood flow to the brain, resulting in damage to neurons and brain tissue. This condition is one of the leading causes of death and disability worldwide. Based on its pathophysiology, stroke is classified into ischemic stroke, which accounts for approximately 85% of cases, and hemorrhagic stroke, which accounts for approximately 15% of cases (WHO, 2022; Kumar & Clark, 2022).

Advances in medical science over the past two decades have led to various developments in stroke management, particularly through early reperfusion strategies, neurointerventional techniques, multidisciplinary rehabilitation, and regenerative therapies. The *Time is Brain* principle is an important foundation in stroke management because delayed reperfusion can result in rapid neuronal loss, making time a critical factor in determining treatment success (Saver, 2006).

Despite the development of various modern therapies, stroke management continues to face challenges in determining the appropriate intervention based on the disease phase and the patient's condition. *Intravenous thrombolysis* with *recombinant tissue plasminogen activator* (rt-PA) remains the standard therapy for acute ischemic stroke, while *mechanical thrombectomy* is used in patients with large vessel occlusion within the appropriate therapeutic time window. The effectiveness of both approaches is highly influenced by the speed of diagnosis and treatment administration (Powers et al., 2019; Nogueira et al., 2018).

Another challenge concerns the prevention of recurrent stroke and the recovery of neurological function after the acute phase. The use of *antiplatelet* agents, *anticoagulant*s, and high-intensity statins plays an important role in secondary prevention, while rehabilitation through *physiotherapy* is necessary to support functional recovery. However, post-stroke recovery also requires a broader approach because neurological impairments may persist and affect the patient's functional abilities (Wang et al., 2013; Winstein et al., 2016).

On the other hand, regenerative therapies and complementary approaches have increasingly gained attention in post-stroke management. Mesenchymal stem cell therapy has the potential to support neuroprotection, neurogenesis, angiogenesis, synaptogenesis, and neuroplasticity, but it remains investigational. *Acupuncture*, *herbal therapy*, and *tuina* have also been investigated as adjunctive therapies in rehabilitation, although their use should be positioned as complementary to conventional therapy based on the available evidence (Hess & Borlongan, 2008; Yang et al., 2016).

Based on these conditions, this study aims to review the development of stroke management based on the principles of *Evidence-Based Medicine*, encompassing pharmacological therapy, neurointervention, prevention of recurrent stroke, regenerative therapy, complementary medicine, and rehabilitation. This review is important for providing an integrated overview of various approaches that can be used in stroke management from the acute phase through recovery. The novelty of this review lies in integrating conventional therapy, neurointervention, regenerative therapy, Eastern medicine approaches, and rehabilitation within a single evidence-based framework for stroke management.

RESEARCH METHODS

This study employed an *Evidence-Based Medicine* (EBM)-based literature review method to examine the development of integrated stroke management. The review covered pharmacological therapy, neurointervention, regenerative therapy, complementary medicine, and rehabilitation based on the available scientific evidence (Powers et al., 2019; Winstein et al., 2016).

The research instruments consisted of relevant scientific literature sources concerning stroke management. The data were analyzed descriptively through the identification, classification, and synthesis of information based on the types of interventions and evidence of their effectiveness (Nogueira et al., 2018; Yang et al., 2016).

The population and sample in this study did not consist of patients or respondents but rather scientific literature concerning stroke management. The literature included clinical guidelines, clinical trials, systematic reviews, and meta-analyses related to stroke therapy (Powers et al., 2019; Saver, 2006).

The research procedure involved identifying the literature, categorizing information based on the types of therapies, examining evidence of effectiveness, and systematically organizing the synthesized findings. The review covered thrombolysis, *mechanical thrombectomy*, prevention of recurrent stroke, stem cell therapy, *acupuncture*, *herbal therapy*, *physiotherapy*, and *tuina* (Albers et al., 2018; Hess & Borlongan, 2008).

RESULTS AND DISCUSSION

Modern Pharmacological Therapy

Intravenous thrombolysis

Intravenous administration of recombinant tissue plasminogen activator (rt-PA, alteplase) remains the standard treatment for acute ischemic stroke. Although the greatest therapeutic benefit is achieved when treatment is initiated within the first 3 hours of symptom onset, current guidelines recommend its administration for up to 4.5 hours (Powers et al., 2019; The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group, 1995). Alteplase exerts its therapeutic effect by converting plasminogen into plasmin, thereby promoting fibrinolysis, facilitating thrombus dissolution, and restoring cerebral blood flow (The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group, 1995). The efficacy of *intravenous thrombolysis* has been established by landmark clinical trials, including the National Institute of Neurological Disorders and Stroke (NINDS) trial and the European Cooperative Acute Stroke Study III (ECASS III), which demonstrated significantly improved neurological outcomes compared with conventional therapy

(The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group, 1995; Hacke et al., 2008).

Mechanical thrombectomy

Mechanical thrombectomy represents one of the most significant advances in the management of acute ischemic stroke caused by large vessel occlusion (LVO). Current guidelines recommend that the procedure be performed within 6 hours of symptom onset, while the therapeutic window may be extended to 24 hours in selected cases based on advanced perfusion imaging findings. The DWI or CTP Assessment with Clinical Mismatch in the Triage of Wake-Up and Late Presenting Strokes Undergoing Neurointervention (DAWN) trial and the Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke 3 (DEFUSE-3) trial demonstrated that *mechanical thrombectomy* significantly improved functional independence compared with medical therapy alone. In addition, the procedure achieved recanalization rates of 70–90%, enabled 45–60% of patients to attain functional independence, defined as a modified Rankin Scale (mRS) score of 0–2, and was associated with lower mortality (Nogueira et al., 2018; Albers et al., 2018).

Digital Subtraction Angiography (DSA)

Digital subtraction angiography (DSA) remains the gold standard for evaluating the cerebral vasculature and is fundamental to modern neurointerventional management. The technique enables accurate identification of vascular occlusions, assessment of collateral circulation, guidance during *mechanical thrombectomy*, and evaluation of reperfusion outcomes. Although DSA is not a therapeutic modality, it plays a critical role in optimizing the success of *mechanical thrombectomy* and other endovascular interventions (Osborn & Jacobs, 1999).

Prevention Of Recurrent Stroke

Antiplatelet

Aspirin remains the first-line *antiplatelet* agent for the secondary prevention of non-cardioembolic ischemic stroke. It exerts its antithrombotic effect through irreversible inhibition of cyclooxygenase-1 (COX-1), leading to reduced thromboxane A_2 production, decreased platelet aggregation, and a lower risk of recurrent stroke. The addition of clopidogrel as dual *antiplatelet* therapy (DAPT) further enhances *antiplatelet* activity by irreversibly blocking the P2Y12 receptor, thereby inhibiting platelet activation and aggregation. Based on findings from the Clopidogrel in High-Risk Patients with Acute Nondisabling Cerebrovascular Events (CHANCE) trial and the Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke (POINT) trial, DAPT is recommended for patients with minor ischemic stroke or high-risk transient ischemic attack (TIA) (Wang et al., 2013; Johnston et al., 2018).

Anticoagulant

Warfarin exerts its *anticoagulant* effect by inhibiting vitamin K epoxide reductase (VKORC1), thereby reducing the synthesis of vitamin K-dependent coagulation factors. In contrast, direct oral *anticoagulant*s (DOACs), including apixaban, rivaroxaban, edoxaban, and dabigatran, directly inhibit specific coagulation factors involved in thrombus formation. Compared with warfarin, DOACs have demonstrated a more favorable safety profile, particularly by reducing the risk of major bleeding, while maintaining efficacy in the prevention of recurrent stroke (Powers et al., 2019; Ruff et al., 2014).

High-Intensity Statin Therapy

The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial demonstrated that atorvastatin reduced the risk of recurrent stroke by 16% through stabilization of atherosclerotic plaques, improvement of endothelial function, attenuation of vascular inflammation, and prevention of thrombus formation. Based on these findings, *high-intensity statin therapy* with atorvastatin (40–80 mg/day) or rosuvastatin (20–40 mg/day) is recommended for secondary stroke prevention.

Stem Cell Therapy: A New Hope For Neuronal Regeneration

Mesenchymal stem cells (MSCs) represent a promising regenerative strategy for improving post-stroke recovery. MSCs derived from bone marrow, adipose tissue, and placental tissue exert

therapeutic effects through multiple mechanisms, including neuroprotection, neurogenesis, angiogenesis, synaptogenesis, immunomodulation, and enhancement of neuroplasticity. The optimal therapeutic window for MSC administration appears to be during the subacute phase (7–30 days) and early chronic phase (1–6 months) after stroke (Hess & Borlongan, 2008; Yang et al., 2016). Meta-analyses have demonstrated that stem cell therapy improves neurological outcomes, including National Institutes of Health Stroke Scale (NIHSS), Barthel Index, and Fugl-Meyer Motor Scale scores, compared with control groups. However, stem cell therapy remains an investigational approach and requires further clinical validation before becoming part of standard stroke management (Powers et al., 2019; Hess & Borlongan, 2008).

Evidence-Based Eastern Medicine Approaches

Acupuncture

Acupuncture is one of the most commonly used complementary therapies for post-stroke rehabilitation. Its therapeutic effects are mediated through several mechanisms, including enhancement of cerebral blood flow, stimulation of neuroplasticity, modulation of neurotransmitter activity, and reduction of neuroinflammation. Recent systematic reviews and meta-analyses have demonstrated that the combination of *acupuncture* and *physiotherapy* improves motor recovery outcomes compared with *physiotherapy* alone, supporting its potential role as an adjunctive rehabilitation strategy after stroke (Yang et al., 2016; Wu et al., 2010).

Herbal Therapy

Herbal-derived therapies, including Ginkgo biloba, Panax ginseng, curcumin, and Bacopa monnieri, have been investigated as potential adjunctive approaches in post-stroke management. Their proposed mechanisms involve antioxidant activity, regulation of inflammatory pathways, neuroprotection, and modulation of neuroregenerative processes (Adami & Bottai, 2022; Chandel et al., 2026).

Modern Rehabilitation

Physiotherapy

Physiotherapy remains a fundamental component of post-stroke rehabilitation, utilizing evidence-based approaches such as task-specific training, constraint-induced movement therapy, gait training, and robot-assisted rehabilitation. The American Heart Association/American Stroke Association (AHA/ASA) recommends early and intensive rehabilitation to promote functional recovery and preserve neuroplasticity after stroke (Winstein et al., 2016).

Tuina Therapy

Tuina is a traditional Chinese manual therapy involving therapeutic massage techniques and stimulation of specific meridian points. Recent meta-analytic evidence indicates that combining *tuina therapy* with conventional *physiotherapy* may result in superior motor functional outcomes compared with *physiotherapy* alone among patients with chronic stroke (Ji et al., 2022).

CONCLUSION

Multidisciplinary approaches in post-stroke management and rehabilitation integrate reperfusion therapies, DSA-guided neurointervention, intensive rehabilitation, secondary prevention, and regenerative strategies. Reperfusion therapies, including thrombolysis and *mechanical thrombectomy*, provide the greatest benefit during the acute phase within the optimal therapeutic window, whereas multidisciplinary rehabilitation remains essential for long-term functional recovery. Complementary approaches, including *acupuncture*, *herbal therapy*, and tuina, may support neuroplasticity as adjunctive strategies, whereas stem cell-based therapies offer a promising future direction for neuronal repair and regeneration.

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