

CURRENT MANAGEMENT OF ACUTE ISCHEMIC STROKE: ADVANCES IN INTRAVENOUS THROMBOLYSIS AND MECHANICAL THROMBECTOMY

TRATAMENTO ATUAL DO AVC ISQUÊMICO AGUDO: AVANÇOS NA TROMBÓLISE INTRAVENOSA E NA TROMBECTOMIA MECÂNICA

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ABSTRACT

Introduction: Acute ischemic stroke is a leading cause of mortality and disability worldwide, particularly in low- and middle-income countries. Cerebral arterial occlusion leads to progressive tissue ischemia, so early recognition and timely treatment are crucial for prognosis. Significant advances in the management of ischemic stroke have been achieved in recent decades, particularly with the development of reperfusion therapies such as intravenous thrombolysis and mechanical thrombectomy. The expansion of therapeutic windows and the use of neuroimaging-based criteria enable a more personalized approach, emphasizing the importance of critically synthesizing recent evidence.

Methodology: A systematic literature review was conducted in the PubMed and Virtual Health Library (VHL) databases, including studies published between 2020 and 2025. Descriptors related to ischemic stroke and reperfusion therapies were used, combined by Boolean operators. After applying filters and eligibility criteria and screening titles and abstracts, 16 studies were selected for full-text reading to comprise the final sample. The review included randomized clinical trials, meta-analyses, systematic reviews, and observational studies, in line with the PRISMA flowchart recommendations.

Results and discussion: The 16 analyzed studies demonstrated the consistent benefits of reperfusion therapies in acute ischemic stroke, particularly when employed early and in combination. Intravenous thrombolysis is effective both as a standalone therapy and as a bridge therapy to mechanical thrombectomy, resulting in improved recanalization rates and functional outcomes. Reducing the time between interventions was a decisive factor in achieving better clinical results. Tenecteplase has emerged as a promising alternative to alteplase, as it is associated with higher rates of early and first-pass reperfusion without a significant increase in bleeding risk. Mechanical thrombectomy has shown functional benefit even in patients with large infarct cores, expanding the traditional eligibility criteria. Recent evidence has also indicated that adjuvant intra-arterial thrombolysis after endovascular reperfusion can optimize microvascular perfusion and improve functional independence in selected patients. Despite the advances, methodological heterogeneity was observed across the studies, limiting the generalizability of the results.

Conclusion: The treatment of acute ischemic stroke has evolved into a multimodal, early, and individualized model. The integration of intravenous thrombolysis, mechanical thrombectomy, and adjuvant therapies has the potential to improve clinical outcomes and quality of life for patients significantly. However, further studies are needed to standardize protocols and refine selection criteria.

RESUMO

Introdução: O acidente vascular cerebral isquêmico agudo é uma das principais causas de mortalidade e incapacidade em todo o mundo, particularmente em países de baixa e média renda. A oclusão arterial cerebral leva à isquemia tecidual progressiva, portanto, o reconhecimento precoce e o tratamento oportuno são cruciais para o prognóstico. Avanços significativos no manejo do acidente vascular cerebral isquêmico foram alcançados nas últimas décadas, particularmente com o desenvolvimento de terapias de reperfusão, como a trombólise intravenosa e a trombectomia mecânica. A expansão da janela terapêutica e o uso de critérios baseados em neuroimagem permitem uma abordagem mais personalizada, enfatizando a importância da síntese crítica de evidências recentes.

Metodologia: Foi realizada uma revisão sistemática da literatura nas bases de dados PubMed e Virtual Health Library (VHL), incluindo estudos publicados entre 2020 e 2025. Descritores relacionados ao acidente vascular cerebral isquêmico e às terapias de reperfusão foram utilizados e combinados por operadores booleanos. Após a aplicação de filtros e critérios de elegibilidade e a triagem de títulos e resumos, 16 estudos foram selecionados para leitura completa para compor a amostra final. A revisão incluiu ensaios clínicos randomizados, meta-análises, revisões sistemáticas e estudos observacionais, em conformidade com as recomendações do fluxograma PRISMA.

Resultados e discussão: Os 16 estudos analisados demonstraram os benefícios consistentes das terapias de reperfusão no acidente vascular cerebral isquêmico agudo, particularmente quando empregadas precocemente e em combinação. A trombólise intravenosa é eficaz tanto como terapia isolada quanto como terapia de ponte para a trombectomia mecânica, resultando em melhores taxas de recanalização e desfechos funcionais. A redução do intervalo entre as intervenções foi um fator decisivo para a obtenção de melhores resultados clínicos. O tenecteplase surgiu como uma alternativa promissora ao alteplase, pois está associado a taxas mais elevadas de reperfusão precoce e de primeira passagem, sem um aumento significativo no risco de sangramento. A trombectomia mecânica demonstrou benefício funcional mesmo em pacientes com grandes áreas de infarto, ampliando os critérios tradicionais de elegibilidade. Evidências recentes também indicam que a trombólise intra-arterial adjuvante após reperfusão endovascular pode otimizar a perfusão microvascular e melhorar a independência funcional em pacientes selecionados. Apesar dos avanços, observou-se heterogeneidade metodológica entre os estudos, limitando a generalização dos resultados.

Conclusão: O tratamento do AVC isquêmico agudo evoluiu para um modelo multimodal, precoce e individualizado. A integração da trombólise intravenosa, trombectomia mecânica e terapias adjuvantes tem o potencial de melhorar significativamente os desfechos clínicos e a qualidade de vida dos pacientes. No entanto, são necessários mais estudos para padronizar os protocolos e refinar os critérios de seleção.

Keywords: Ischemic Stroke; Reperfusion; Thrombolytic Therapy; Thrombectomy.

Palavras-chave: AVC Isquêmico; Reperfusão; Terapia Trombolítica; Trombectomia.

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INTRODUCTION

Acute ischemic stroke ranks among the most significant causes of mortality and disability globally and is a pressing public health concern, particularly in low- and middle-income countries. The majority of stroke cases originate from ischemia, stemming from occluded cerebral arteries and resulting in disrupted blood flow, tissue ischemia, and progressive neurological injury. Prompt recognition and rapid intervention, which are critical for prognosis, underscore the maxim "time is brain"¹.

In recent decades, significant advances have been observed in the management of acute ischemic stroke, particularly in reperfusion therapies. Intravenous thrombolysis with alteplase, initially restricted to a therapeutic window of up to 4.5 hours, has become standard treatment in eligible patients. However, limitations in efficacy, safety, and eligibility have spurred the development and investigation of new therapeutic strategies, including the use of alternative thrombolytic agents, such as tenecteplase, and the expansion of imaging-based criteria².

In parallel, mechanical thrombectomy emerged as a revolutionary intervention for acute ischemic stroke due to large vessel occlusion. It has shown substantial benefits in reducing functional disability in carefully selected patients³. Recent studies have extended the therapeutic window to 24 hours or more in some instances. This applies when guided by advanced neuroimaging methods, such as perfusion tomography and MRI. These advances allow for a more individualized and precise approach⁴.

Despite these advances, the management of acute ischemic stroke still faces significant challenges, including unequal access to reperfusion therapies, the need for well-structured protocols in the emergency room, and the continuous updating of healthcare professionals in light of new scientific evidence. In this context, a critical synthesis of recent literature is fundamental to guide clinical practice and support evidence-based decision-making⁵.

Therefore, this literature review aims to analyze current advances in the management of acute ischemic stroke, with an emphasis on reperfusion therapies, including intravenous thrombolysis and mechanical thrombectomy, and to discuss their indications, benefits, limitations, and clinical implications in contemporary neurology.

METHODOLOGY

This is a systematic literature review aimed at analyzing and synthesizing the available scientific evidence on the management of acute ischemic stroke, with emphasis on therapeutic advances in intravenous thrombolysis and mechanical thrombectomy.

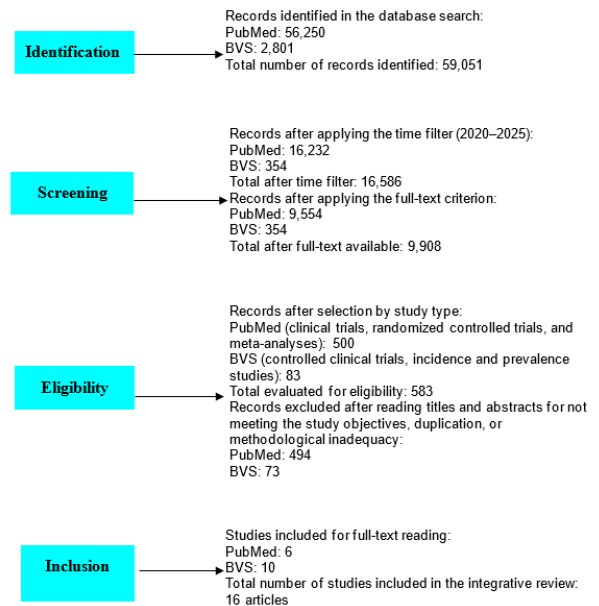
The bibliographic search was systematic and structured. PubMed (National Library of Medicine) and the

Virtual Health Library (VHL) were used. A combination of controlled descriptors and keywords was applied through Boolean operators: "Ischemic Stroke" AND "Reperfusion Therapy" OR "Thrombolytic Therapy" OR "Mechanical Thrombectomy".

Initially, 56,250 studies were identified in PubMed and 2,801 studies in VHL. After applying the time filter to the period 2020-2025, 16,232 studies remained in PubMed and 354 in BVS. Next, the full-text availability criterion was used, yielding 9,554 publications in PubMed and 354 studies in BVS.

In the subsequent step, selection was conducted by study type, in accordance with the previously defined eligibility criteria. In BVS, controlled clinical trials, incidence studies, and prevalence studies were included, totaling 83 articles. In PubMed, clinical trials, randomized controlled trials, and meta-analyses were selected, yielding 500 studies.

Subsequently, the titles and abstracts were screened to assess their thematic relevance, methodological consistency, and suitability to the objectives of the systematic review. After this stage, 6 articles from PubMed and 10 articles from BVS were selected for full-text reading, totaling 16 studies, which comprised the final sample of the systematic review, as presented in the PRISMA flowchart (Flowchart 1).



Flowchart 1 - Study Selection

Source: Rother; Gonçalves et al., (2026)

RESULTS

Sixteen studies evaluating different reperfusion strategies for the management of acute ischemic stroke were included, comprising randomized clinical trials, meta-analyses, systematic reviews, observational studies, and secondary analyses. Overall, the findings demonstrated

consistent benefits of reperfusion therapies, primarily when performed early and in combination.

Studies that evaluated intravenous (IV) thrombolysis highlighted its relevance both as a standalone therapy and as part of bridging therapy. Wang et al. (2022) demonstrated that combining IV thrombolysis with mechanical thrombectomy resulted in higher recanalization rates and better functional outcomes than thrombolysis alone, without a significant increase in mortality⁶.

Complementarily, Kaesmacher et al. (2024) observed that shorter intervals between IV thrombolysis and thrombectomy were associated with better functional outcomes and lower mortality, reinforcing the critical role of timing in treatment⁷.

Intravenous tenecteplase has proven to be an effective alternative to alteplase. Qiu et al. (2025) demonstrated that administering IV tenecteplase before thrombectomy was associated with higher rates of early reperfusion and better functional outcomes, without a significant increase in the risk of intracranial hemorrhage⁸. Corroborating these findings, Diprose et al. (2025) reported higher first-pass reperfusion rates in patients treated with tenecteplase than with alteplase⁹.

Mechanical thrombectomy offers significant functional benefit even for patients with large infarct cores, as shown by Romoli et al. (2024)¹⁰. However, this comes with a higher absolute risk of hemorrhagic complications. Cao et al. (2025) reported that achieving first-pass reperfusion was associated with lower mortality, better recovery, and fewer hemorrhagic complications¹¹.

Adjuvant intra-arterial thrombolysis after successful endovascular reperfusion has been evaluated in several recent studies. Mortezaei et al. (2025) observed greater functional independence without a significant increase in symptomatic intracranial hemorrhage¹². Similar results were reported by Hou et al. (2025) and Huang et al. (2025 – POST-TNK), in which intra-arterial administration of tenecteplase after thrombectomy was associated with improved functional outcomes at 90 days and a safety profile comparable to that of the control group^{13,14}. Liu et al. (2025 – POST-UK) demonstrated that intra-arterial urokinase promoted greater microvascular reperfusion and better functional outcomes, without a statistically significant increase in bleeding¹⁵.

In situations of unsuccessful mechanical reperfusion, Faizy et al. (2023) identified that prior IV thrombolysis was associated with better clinical outcomes and lower mortality, suggesting a benefit even in the absence of effective recanalization¹⁶. The systematic review by Doheim et al. (2025) reinforced that adjuvant thrombolytics can improve microvascular perfusion and functional outcomes when used in appropriately selected patients¹⁷.

The Cochrane systematic review by Gottlieb et al. (2025) compared thrombectomy with and without IV thrombolysis, demonstrating a slight functional advantage

of the combined therapy. However, there was no significant difference in mortality and heterogeneity among the included studies¹⁸.

Aspects related to perioperative management were also analyzed. Sarraj et al. (2025) did not observe significant differences in functional outcomes between general and non-general anesthesia during thrombectomy, indicating that the choice of anesthetic strategy should be individualized¹⁹. Finally, Doncel-Moriano Cubero et al. (2025) showed a growing trend in the use of combined revascularization therapies, accompanied by an overall improvement in clinical outcomes over time.²⁰

Table 1 – Summary of the main results of the included studies on reperfusion therapies in acute ischemic stroke

Author / Year	Study Type	Population / Sample	Intervention Evaluated	Main Results
Cao et al., 2025	Secondary analysis of RCTs	Data from three Chinese multicenter trials	First-pass reperfusion	Associated with lower mortality, better functional recovery, and a lower rate of hemorrhagic complications.
Diprose et al., 2025	Comparative observational study	Patients undergoing thrombectomy	Tenecteplase vs. alteplase	Tenecteplase showed higher first-pass reperfusion rates compared to alteplase.
Doheim et al., 2025	Systematic review	Studies on endovascular reperfusion	Adjuvant thrombolytics post-thrombectomy	Showed improvement in microvascular perfusion and functional outcomes, with an acceptable safety profile.
Doncel-Moriano Cubero et al., 2025	Observational study of trends	Patients with ischemic stroke	Revascularization strategies	An increase in the use of combination therapies and progressive improvement in clinical outcomes were observed.
Faizy et al., 2023	Multicenter observational study	Ischemic stroke with unsuccessful mechanical reperfusion	Prior IV thrombolysis	Associated with better clinical outcomes and lower mortality, even without effective mechanical reperfusion.
Gottlieb et al., 2025	Systematic review (Cochrane)	Patients with acute ischemic stroke	Thrombectomy with vs. without IV thrombolysis	Slight functional advantage with associated thrombolysis; no significant difference in mortality.
Hou et al., 2025	Randomized clinical trial	Successful endovascular reperfusion	Intra-arterial tenecteplase	Increased functional independence without a significant increase in bleeding risk.
Huang et al., 2025 (POST-TNK)	Randomized clinical trial	Stroke due to large vessel occlusion	Adjuvant intra-arterial tenecteplase	Improved functional outcomes at 90 days, with a safety profile similar to the control group.
Kaesmacher et al., 2024	Meta-analysis	Patients undergoing thrombectomy	Time to IV thrombolysis	Shorter time to IV thrombolysis was associated with better functional outcomes and lower mortality.
Liu et al., 2025 (POST-UK)	Randomized clinical trial	Acute ischemic stroke	Adjuvant intra-arterial urokinase	Associated with greater microvascular reperfusion and improved functional outcomes, without a significant increase in bleeding.
Martins et al., 2023	Updated narrative review	Recent evidence on ischemic stroke	IV thrombolysis and thrombectomy	Highlighted advances in image selection, expansion of therapeutic windows, and improvement in clinical outcomes.
Mortezaei et al., 2025	Meta-analysis of RCTs	Large vessel occlusion	Post-reperfusion intra-arterial thrombolysis	Associated with greater functional independence, without a significant increase in symptomatic intracranial hemorrhage.
Qiu et al., 2025	Randomized clinical trial	Large vessel occlusion	IV tenecteplase before thrombectomy	Resulted in higher rates of early reperfusion and better functional outcomes, with similar safety.
Romoli et al., 2024	Meta-analysis of RCTs	Stroke with a large infarct nucleus	Mechanical thrombectomy	Demonstrated significant functional benefit, despite the higher absolute risk of hemorrhagic complications.
Sarraj et al., 2025	Randomized clinical trial	Patients undergoing thrombectomy	General vs. non-general anesthesia	No significant difference in functional outcomes; decision should be individualized.
Wang et al., 2022	Meta-analysis	Patients with ischemic stroke	IV thrombolysis alone vs. bridging therapy	Bridge therapy showed better recanalization rates and functional outcomes, without increased mortality.

Source: Rother; Gonçalves et al., (2026)

DISCUSSION

The integrated analysis of the 16 studies included in this systematic review shows a significant evolution in the management of acute ischemic stroke, marked by the consolidation of mechanical thrombectomy, the reassessment of the role of intravenous thrombolysis, and the incorporation of adjuvant strategies to optimize cerebral reperfusion and functional outcomes. In general, the findings converge on the conclusion that combined approaches, when performed early and in appropriately selected patients, result in better clinical outcomes.

The studies evaluating intravenous thrombolysis in combination with thrombectomy yielded complementary results. Wang et al. (2022) and Gottlieb et al. (2025) compared bridging therapy with isolated thrombectomy and found a slight functional superiority of the combined approach, with no significant increase in mortality^{6,18}. These findings are reinforced by Kaesmacher et al. (2024), who demonstrated that reducing the time between IV thrombolysis and thrombectomy is associated with better functional outcomes, corroborating the synergistic role between the two strategies when there is no delay in endovascular treatment⁷. Furthermore, Faizy et al. (2023) add relevant evidence by demonstrating the benefit of IV thrombolysis even in cases of unsuccessful mechanical reperfusion, suggesting a positive effect on microcirculation or collateral circulation¹⁶.

In the context of thrombolytic agents, the studies by Qiu et al. (2025) and Diprose et al. (2025) converge on the advantages of tenecteplase over alteplase, especially regarding early and first-pass reperfusion^{8,9}. These results align with those of Cao et al. (2025), who demonstrated a robust association between first-pass reperfusion, lower mortality, and better functional outcomes¹¹. Thus, it is suggested that the choice of thrombolytic agent may influence not only initial recanalization but also the overall efficiency of thrombectomy.

Mechanical thrombectomy, in turn, has shown benefits even in scenarios traditionally considered unfavorable. Romoli et al. (2024) demonstrated significant functional improvement in patients with large infarct cores, thereby expanding the previously adopted eligibility criteria¹⁰. This finding is consistent with the trend observed by Doncel-Moriano Cubero et al. (2025), who identified a progressive increase in the use of more aggressive and combined revascularization strategies, accompanied by an overall improvement in clinical outcomes over time²⁰.

One of the central points of this review concerns the role of adjuvant intra-arterial thrombolysis after successful endovascular reperfusion. The POST-TNK clinical trials (Huang et al., 2025) and the study by Hou et al. (2025) demonstrated consistent improvement in functional independence with intra-arterial tenecteplase, without a significant increase in bleeding risk^{14,13}. Similarly, the POST-UK trial (Liu et al., 2025) showed that intra-arterial urokinase

promotes microvascular reperfusion¹⁵. These results are corroborated by the meta-analysis of Mortezaei et al. (2025) and the systematic review by Doheim et al. (2025), which point to functional benefits of adjuvant thrombolytic therapies, suggesting that isolated macrovascular recanalization may be insufficient to ensure optimal neurological recovery^{12,17}.

Aspects related to perioperative management were also considered. Sarraj et al. (2025) observed no significant differences in functional outcomes between general and non-general anesthesia during thrombectomy, which aligns with the need for therapeutic individualization advocated by Martins et al. (2023) and highlights the importance of adaptable, patient-centered protocols^{19,21}.

The integration of the studies reveals an apparent convergence towards the concept that the treatment of acute ischemic stroke should be multimodal, early, and individualized, combining IV thrombolysis, mechanical thrombectomy, and, in selected cases, adjuvant intra-arterial thrombolysis. However, despite overall consistency in the findings, methodological heterogeneity is observed across studies, including differences in inclusion criteria, outcomes evaluated, and populations studied, which limit direct comparisons and generalization of the results.

Together, the 16 articles analyzed point to a paradigm shift in the management of acute ischemic stroke, with an expansion of therapeutic indications and increasing sophistication of reperfusion strategies. These advances reinforce the need for specialized centers, well-defined protocols, and future research to refine patient selection and consolidate the role of adjuvant therapies in clinical practice.

CONCLUSION

This systematic review shows that the contemporary management of acute ischemic stroke has evolved significantly, with the expansion of reperfusion strategies and improvements in patient selection criteria. The findings of the 16 included studies consistently demonstrate that the combination of therapies, when delivered early and individually, is associated with better functional outcomes and reduced neurological disability.

Intravenous thrombolysis maintains a fundamental role, especially when combined with mechanical thrombectomy, underscoring the importance of bridging therapy. Tenecteplase emerges as a promising alternative to alteplase, offering advantages in early and first-pass reperfusion without a significant increase in hemorrhagic risk. Mechanical thrombectomy has demonstrated benefits even in subgroups traditionally considered to have a worse prognosis, such as patients with a large infarct nucleus, provided that there is careful clinical and imaging evaluation.

Additionally, the most recent evidence indicates that adjuvant intra-arterial thrombolysis after successful

endovascular reperfusion can optimize microvascular perfusion and improve functional outcomes in selected patients. These results suggest that isolated macrovascular recanalization may not be sufficient in all cases, reinforcing the importance of complementary therapeutic approaches.

Despite the observed advances, challenges persist regarding the methodological heterogeneity of studies, the standardization of therapeutic protocols, and the definition of subgroups that benefit most from adjuvant strategies. Thus, future randomized clinical trials and multicenter studies are needed to consolidate the evidence, refine the eligibility criteria, and guide the definitive incorporation of these approaches into clinical guidelines.

In summary, the treatment of acute ischemic stroke is moving towards an increasingly multimodal, early, and personalized model, in which the integration between intravenous thrombolysis, mechanical thrombectomy, and adjuvant therapies represents a concrete opportunity to improve clinical outcomes and the quality of life of patients.

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