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REPERFUSION THERAPY FOR ISCHEMIC STROKE

Yarashev A.R.[1], Eshonov O.Sh.[2]
1. Bukhara branch of the Republican Scientific Center for Emergency Medical Care.
2. Bukhara State Medical Institute.
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Resume: This literature review presents current data on reperfusion therapy for ischemic stroke, including systemic intravenous thrombolysis and mechanical thrombectomy. Indications, contraindications, therapeutic windows, patient selection criteria using modern neuroimaging methods, as well as the results of large randomized clinical trials and current international guidelines are discussed. The analysis demonstrates that timely use of reperfusion treatments can significantly improve clinical outcomes, reduce mortality, and enhance quality of life in patients with ischemic stroke.

Keywords: ischemic stroke, reperfusion therapy, thrombolysis, mechanical thrombectomy.

Relevance. Ischemic stroke (IS) remains one of the most pressing issues in modern medicine and healthcare [1, 2]. Despite significant progress in the prevention of cardiovascular diseases, advancements in neuroimaging techniques, and the implementation of high-tech treatment methods, stroke continues to be a leading cause of mortality and permanent disability among the adult population worldwide [11–13]. The high prevalence of the disease, the significant number of patients of working age, the prolonged loss of functional independence, and the need for costly medical and social rehabilitation underscore the exceptional medical, social, and economic significance of this condition [1–4, 15, 22, 37, 40].

According to the Global Burden of Disease (GBD) 2021 study, stroke remains the second leading cause of death and a major cause of disability worldwide. Between 1990 and 2021, the absolute number of stroke cases, deaths, and disability-adjusted life years (DALYs) continued to rise, primarily due to population aging and the increasing prevalence of vascular risk factors. Ischemic stroke accounts for approximately 85–87% of all acute cerebrovascular events and is characterized by the greatest potential for effective pathogenetic treatment through the timely restoration of cerebral perfusion [4–10].

According to current epidemiological data, more than 12 million new cases of stroke are recorded worldwide each year, and the number of people living with the aftereffects of a stroke exceeds 100 million. Despite a certain decline in age-standardized mortality rates in a number of high-income countries, the absolute burden of the disease continues to rise, particularly in low- and middle-income countries, which are experiencing the greatest increases in incidence, disability, and mortality [11–16].

The trend toward an increasing prevalence of stroke among middle-aged and even young individuals is a cause for particular concern. This is driven by the rising incidence of arterial hypertension, diabetes mellitus, obesity, atrial fibrillation, dyslipidemia, smoking, and other modifiable risk factors. Concurrently, there is a growing number of patients with comorbid cardiovascular conditions, which significantly complicates treatment and worsens functional outcomes [17–20].

The social impact of ischemic stroke is determined not only by high mortality rates but also by the significant disability experienced by patients. According to the World Stroke Organization, a substantial proportion of stroke survivors are left with persistent motor, cognitive, and speech impairments that require long-term medical, psychological, and social support. The loss of independence significantly reduces the quality of life for patients and their families and entails substantial economic costs for the healthcare system [21–32].

Over the past two decades, approaches to treating ischemic stroke have undergone fundamental changes. While therapy was previously aimed primarily at limiting secondary brain injury and providing symptomatic support for vital functions, the cornerstone of treatment today is the rapid restoration of blood flow in the occluded cerebral artery. This shift was made possible by the development of the concept of reperfusion therapy—comprising intravenous thrombolysis and mechanical thrombectomy—the efficacy of which has been convincingly confirmed by numerous randomized clinical trials and international guidelines [33–39].

Modern stroke medicine regards ischemic stroke as an emergency in which the outcome largely depends on the speed at which cerebral perfusion is restored. For this reason, the "Time is Brain" concept has become a fundamental principle in the care of patients with acute ischemic stroke. Every minute of persistent cerebral vessel occlusion is associated with progressive neuronal death, a worsening functional prognosis, and reduced efficacy of reperfusion therapy. This drove the improvement of the specialized care delivery system, the establishment of stroke centers, the implementation of telemedicine technologies, and the development of modern patient routing algorithms [12, 23, 27, 39–45].

Thus, the high prevalence of ischemic stroke, its significant contribution to mortality and disability, and the rapid evolution of methods for restoring cerebral blood flow necessitate a systematic analysis of modern advances in reperfusion therapy. In recent years, results from major clinical trials have been published, international guidelines updated, and patient selection criteria for intravenous thrombolysis and mechanical thrombectomy expanded—developments that require a synthesis and critical evaluation of the accumulated evidence base.

Evolution and current trends in the development of reperfusion therapy

Fundamental changes in the treatment of ischemic stroke have been made possible by advances in the understanding of the pathophysiology of cerebral ischemia. It has been established that, following the occlusion of a cerebral artery, two functionally distinct zones are formed: a central ischemic core, where irreversible neuronal death rapidly ensues due to a critical reduction in cerebral blood flow, and a surrounding zone of ischemic penumbra, characterized by the preservation of tissue structural integrity despite marked impairment of functional activity. It is the viability of the penumbra that determines the potential for the recovery of neurological functions upon the timely restoration of blood supply. Therefore, the primary goal of modern ischemic stroke therapy is to restore perfusion to the ischemic brain tissue as rapidly as possible, before irreversible morphological changes occur [16–18].

The modern concept of reperfusion therapy is based on the principle of achieving the earliest possible recanalization of an occluded cerebral artery. The most widely used methods for restoring cerebral blood flow are intravenous thrombolysis with recombinant tissue plasminogen activator and endovascular mechanical thrombectomy. Although these methods operate via different mechanisms, they share a common goal: restoring cerebral perfusion, limiting the volume of the cerebral infarct, preserving viable tissue, and improving functional outcomes [7, 9, 18, 43, 46].

Over the past five years, the development of reperfusion therapy has been characterized by a significant expansion of diagnostic and therapeutic capabilities. One of the most notable advances

has been the implementation of multimodal neuroimaging, including CT perfusion imaging and MRI with diffusion- and perfusion-weighted sequences. The use of modern imaging techniques has enabled a shift from patient selection based solely on time-based criteria to an individualized assessment of brain tissue viability. This approach has significantly expanded the scope for reperfusion therapy in specific categories of patients with an unknown stroke onset time or those presenting outside the traditional therapeutic window [4, 8, 19–21].

The advancement of endovascular technologies has been a significant milestone in the development of modern stroke medicine. The use of new generations of stent retrievers, large-bore aspiration catheters, and combined clot-removal techniques, alongside the standardization of endovascular interventions, has enabled a substantial increase in the rate of successful recanalization of major cerebral arteries. Modern clinical studies convincingly demonstrate that mechanical thrombectomy is highly effective in treating patients with large-vessel occlusion, both within the standard time window and in carefully selected patients presenting at later time points after symptom onset [22–24].

Another promising area is the optimization of pharmacological reperfusion. Although alteplase remains the first-line agent for intravenous thrombolysis, the use of tenecteplase has attracted significant interest in recent years due to its greater fibrin specificity, longer half-life, and suitability for single-bolus administration. Results from large randomized trials and meta-analyses indicate that tenecteplase is non-inferior to alteplase in terms of efficacy and safety for the majority of patients with acute ischemic stroke, a finding that has led to the revision of several international clinical guidelines and the active adoption of this drug into clinical practice [13, 16, 25–27].

Alongside the refinement of reperfusion methods, significant attention is being paid to optimizing the organization of specialized medical care. The "Time is Brain" concept has now evolved into a comprehensive system of organizational measures aimed at minimizing the time from the onset of initial symptoms to the restoration of blood flow. A leading role is played by specialized stroke centers, the development of telemedicine technologies, the optimization of patient routing, the standardization of "door-to-needle" and "door-to-groin" metrics, and the implementation of automated systems for analyzing neuroimaging data using artificial intelligence. The comprehensive implementation of these measures has significantly reduced the time to the initiation of reperfusion therapy and improved treatment outcomes for patients with ischemic stroke [14, 25, 28–30].

Despite significant progress in reperfusion therapy, a number of unresolved issues remain. Access to modern treatment methods varies across different regions of the world, and the proportion of patients receiving reperfusion therapy remains limited due to delayed medical attention, inadequate equipment in specialized centers, and organizational challenges. Furthermore, efforts continue to identify optimal patient selection algorithms, refine criteria for the use of intravenous thrombolysis and mechanical thrombectomy, and develop new technologies capable of enhancing the efficacy of restoring cerebral blood flow [41–47].

Thus, reperfusion therapy represents one of the most rapidly evolving fields in modern vascular neurology. Continuous advancements in intravenous thrombolysis, endovascular interventions, neuroimaging technologies, and organizational models of care delivery are accompanied by an expansion of indications for reperfusion treatment and improved clinical outcomes. At the same time, the rapid accumulation of new scientific data, the regular updating of international guidelines, and the emergence of new therapeutic approaches necessitate a systematic analysis of the current evidence base.

The **aim** of this review is to conduct a comprehensive analysis of contemporary domestic and international scientific publications from 2020–2026 regarding reperfusion therapy for ischemic stroke, to summarize current data on the efficacy of intravenous thrombolysis and mechanical thrombectomy, and to examine recent advances, existing limitations, and promising directions for the future development of reperfusion technologies.

Materials and methods. This study is an analytical review of current scientific literature. A search for publications was conducted in the international bibliographic databases PubMed/MEDLINE, Scopus, Web of Science, and the Cochrane Library, as well as among current international clinical guidelines published between January 2020 and June 2026. The following keywords and their combinations were used for the search: acute ischemic stroke, reperfusion therapy, intravenous thrombolysis, alteplase, tenecteplase, mechanical thrombectomy, endovascular therapy, stroke guidelines, perfusion imaging, artificial intelligence in stroke [1–4].

Inclusion criteria comprised systematic reviews, meta-analyses, randomized controlled trials, multicenter prospective studies, large national and international registries, and current clinical guidelines from international professional societies. Priority was given to publications providing a high level of evidence that reflect the current state of reperfusion therapy for ischemic stroke. The literature analysis employed comparative, analytical, and systemic approaches, involving a critical assessment of study results and their clinical significance [11–14, 21–24].

The pathophysiological basis of the concept of reperfusion therapy for ischemic stroke. Ischemic stroke develops as a result of acute cerebral artery occlusion, leading to a critical reduction in cerebral blood flow and impaired delivery of oxygen and energy substrates to nervous tissue. The sequence of pathological processes triggered by the cessation of blood supply includes energy depletion, ion pump dysfunction, cellular edema, excitotoxicity, activation of inflammatory responses, and neuronal death. The rate of progression of these processes depends on the degree of reduction in cerebral perfusion, the location of the vascular occlusion, and the status of collateral circulation [10, 26].

Modern approaches to the treatment of ischemic stroke are based on the concepts of the ischemic core and the ischemic penumbra. The ischemic core is an area of critically reduced blood flow where irreversible structural changes and cell death have already occurred. Surrounding the core is the ischemic penumbra—a region of the brain characterized by markedly reduced perfusion and impaired neuronal function, yet one that retains potential viability if blood flow is restored in a timely manner. Preserving and salvaging the penumbra is the primary goal of modern reperfusion therapy [12, 27, 33, 46].

The classic "time is brain" concept is based on the premise that the volume of the ischemic core continuously expands through the recruitment of penumbral tissue. The longer an arterial occlusion persists, the less viable brain tissue remains and the lower the likelihood of a favorable functional outcome. However, modern neuroimaging techniques have demonstrated that the rate of ischemic injury progression varies significantly among patients and is largely determined by the efficiency of collateral circulation. This led to the development of a new concept, according to which the decision regarding reperfusion therapy must take into account not only the time from symptom onset but also the state of the brain tissue [32, 37, 43].

The evolution of the concept of ischemic stroke treatment. For many decades, the treatment of ischemic stroke was primarily symptomatic in nature. Efforts were mainly directed toward maintaining vital functions, correcting hemodynamic disturbances, and preventing complications. However, this approach did not make it possible to significantly influence the extent of the developing cerebral infarction or the outcome of the disease [22, 31, 45].

Significant progress was achieved through the evolution of concepts regarding the feasibility of restoring blood flow in an occluded artery. A modern reperfusion strategy gradually emerged, centered on the earliest possible recanalization of the vascular bed. Restoring cerebral perfusion became the key pathogenetic approach to treating ischemic stroke.

In recent years, the concept of reperfusion therapy has continued to evolve. While treatment decisions were previously based primarily on the time elapsed since symptom onset, the individual assessment of brain tissue viability now plays a pivotal role. This approach has significantly expanded the scope for administering reperfusion therapy to patients with unknown stroke onset times and those presenting within extended time windows.

The primary goals of reperfusion therapy are: recanalization of the occluded cerebral artery; restoration of cerebral perfusion; preservation of the viable ischemic penumbra; limitation of the cerebral infarct volume; prevention of neurological deficit progression; reduction of mortality; and improvement of functional outcomes and patients' quality of life.

Restoring adequate blood flow within the territory of an occluded artery before irreversible brain tissue damage occurs is the primary objective of reperfusion therapy for ischemic stroke. Contemporary studies convincingly demonstrate a direct link between successful reperfusion and the likelihood of achieving functional independence 90 days post-stroke. For this reason, the extent of blood flow restoration is considered one of the most critical prognostic factors for the disease outcome.

Modern methods of reperfusion therapy. Currently, the primary methods of reperfusion therapy are intravenous thrombolysis and mechanical thrombectomy. Intravenous thrombolysis is a pharmacological approach to vessel recanalization involving the administration of a thrombolytic agent. This method is characterized by high accessibility and the ability to initiate treatment rapidly; it remains the initial step in reperfusion therapy for the majority of patients who meet the selection criteria [5, 18, 27, 39, 43].

Mechanical thrombectomy is an endovascular method for removing a thrombus from an occluded vessel and is currently considered the standard of care for patients with large cerebral artery occlusion. The implementation of modern endovascular technologies has significantly increased the rate of successful recanalization and improved functional treatment outcomes [22, 23].

Further development has been seen in the combined reperfusion strategy, which involves a combination of intravenous thrombolysis and subsequent mechanical thrombectomy. This approach ensures the most rapid initiation of reperfusion therapy while simultaneously achieving high rates of blood flow restoration in patients with large-vessel occlusion.

The "Time is Brain" concept. One of the key principles in modern stroke medicine is the "Time is Brain" concept. Its essence lies in the fact that every minute of ongoing ischemia is accompanied by the progressive loss of viable nervous tissue and a worsening of the functional prognosis [39]. The practical outcome of this concept has been the establishment of specialized stroke centers, the implementation of standardized diagnostic and treatment algorithms, and a continuous effort to reduce the time intervals between symptom onset and the initiation of reperfusion therapy. The most critical quality indicators for care delivery are considered to be the "door-to-needle" time for intravenous thrombolysis and the "door-to-groin puncture" time for mechanical thrombectomy [2, 15, 21].

At the same time, current data indicate that the "Time is Brain" concept is gradually evolving into the "Time and Tissue" concept. The use of perfusion neuroimaging makes it possible to identify patients with salvageable penumbra—even many hours after symptom onset—and to administer reperfusion therapy within extended time windows.

Modern patient selection strategy. The success of reperfusion therapy is largely determined by appropriate patient selection. Currently, clinical decision-making is based on a comprehensive assessment of clinical, laboratory, and neuroimaging data [5, 6, 21–24].

Neuroimaging methods play a pivotal role. Non-contrast computed tomography (CT) allows for the exclusion of intracranial hemorrhage and the assessment of early signs of ischemia. CT angiography is used to detect occlusion of major vessels, whereas CT perfusion and advanced magnetic resonance imaging (MRI) techniques enable the determination of the volume of the ischemic core and penumbra. The implementation of perfusion imaging has been a key factor in expanding the scope of reperfusion therapy in recent years.

Another promising area is the use of artificial intelligence technologies for the automated analysis of neuroimaging data. Modern software systems enable faster interpretation of examination results, improved accuracy in assessing the volume of ischemic lesions, and reduced time for clinical decision-making [15–20].

The history of the development of intravenous thrombolysis. Intravenous thrombolysis (IVT) is the first treatment for acute ischemic stroke with a sound pathophysiological basis, the efficacy of which has been confirmed by numerous randomized clinical trials. The introduction of thrombolytic therapy has been one of the most significant achievements in modern vascular neurology, radically transforming approaches to the management of patients with acute cerebrovascular accidents.

The first attempts to use fibrinolytic agents for ischemic stroke were made as early as the second half of the 20th century. However, the use of streptokinase and urokinase was associated with a high incidence of intracranial hemorrhage and a lack of convincing evidence regarding clinical efficacy; consequently, these drugs did not gain widespread adoption. Advances in genetic engineering and the development of recombinant tissue plasminogen activator (rt-PA) ushered in a new era in reperfusion therapy [16, 23].

A turning point was the introduction into clinical practice of alteplase—a recombinant tissue plasminogen activator with high fibrin specificity. Results from the first large-scale randomized trials convincingly demonstrated that the timely administration of alteplase facilitates recanalization of the occluded cerebral artery, limits the volume of the cerebral infarct, and leads to a significant improvement in functional outcomes. These studies laid the foundation for current international guidelines on the treatment of acute ischemic stroke [6, 13].

In subsequent years, the evidence base for intravenous thrombolysis steadily expanded. Patient selection criteria were refined, the therapeutic window was extended, and modern neuroimaging techniques were introduced, enabling a shift from a purely time-based approach to the assessment of ischemic brain tissue viability. The development of this method was significantly influenced by the results of the WAKE-UP and EXTEND trials, as well as a number of subsequent studies, which confirmed the feasibility of administering thrombolytic therapy to carefully selected patients based on MRI and CT perfusion criteria [15–20].

The current stage of development in intravenous thrombolysis is characterized by the further personalization of treatment. Alongside the refinement of patient selection criteria, new thrombolytic agents with more favorable pharmacological properties are being actively investigated. Tenecteplase—a modified variant of tissue plasminogen activator—is of particular interest, distinguished by greater fibrin specificity, resistance to plasminogen activator inhibitor-1, and a longer half-life. Due to these characteristics, the drug can be administered as a single bolus, which significantly simplifies thrombolytic therapy, particularly in the pre-hospital setting and during patient transport to specialized stroke centers. Contemporary reviews and meta-analyses indicate

that tenecteplase is non-inferior to alteplase in terms of efficacy and safety, and—in certain patient subgroups, particularly those with large vessel occlusion—may achieve higher rates of early recanalization [30–32].

Thus, the evolution of intravenous thrombolysis reflects the general developmental trajectory of modern stroke medicine—moving from the use of early fibrinolytic agents to personalized reperfusion therapy grounded in evidence-based medicine, advanced neuroimaging technologies, and an individualized assessment of the potential treatment benefit for each patient.

Pathophysiological rationale for intravenous thrombolysis. The pathogenetic basis of intravenous thrombolysis is the rapid restoration of blood flow in an occluded cerebral artery through the pharmacological lysis of the thrombus. In most cases, ischemic stroke is caused by the thrombotic or thromboembolic occlusion of a cerebral vessel, leading to a sharp reduction in regional cerebral blood flow and the development of ischemia. In the absence of timely recanalization, the volume of irreversible damage progressively increases as tissue from the ischemic penumbra becomes involved.

Administration of a thrombolytic agent activates the body's endogenous fibrinolytic system. Recombinant tissue plasminogen activator binds to the fibrin within the thrombus and catalyzes the conversion of plasminogen into plasmin—the primary enzyme responsible for breaking down the thrombus's fibrin scaffold. This results in the gradual dissolution of thrombotic masses, restoration of patency in the occluded artery, and re-establishment of blood supply to the ischemic brain tissue [4, 16, 29, 37, 45].

The clinical efficacy of intravenous thrombolysis depends directly on the speed at which reperfusion is achieved. The most pronounced effect is observed when treatment is initiated as soon as possible after the onset of stroke symptoms. However, recent studies have shown that the efficacy of therapy is determined not only by time but also by the condition of the cerebral tissue. The use of CT perfusion and magnetic resonance imaging makes it possible to identify patients with a persisting viable penumbra who may benefit from intravenous thrombolysis even within extended time windows.

Currently, intravenous thrombolysis is regarded not only as a standalone treatment modality but also as a crucial component of a comprehensive reperfusion strategy. In patients with large cerebral artery occlusion, pharmacological reperfusion often precedes mechanical thrombectomy (bridging therapy), facilitating partial or complete vessel recanalization prior to the endovascular intervention and potentially improving functional outcomes. At the same time, research continues into optimizing the choice between combined and direct endovascular treatment strategies across various clinical scenarios [7, 11, 28, 36].

Alteplase: mechanism of action, pharmacodynamics, pharmacokinetics, and clinical application. For nearly three decades, alteplase (recombinant tissue plasminogen activator, rt-PA) has remained the first-line agent for systemic intravenous thrombolysis in acute ischemic stroke. Despite the emergence of new thrombolytic agents—most notably tenecteplase—alteplase continues to be regarded as the benchmark against which all modern pharmacological reperfusion regimens are compared. Its efficacy and safety have been confirmed by numerous randomized trials, meta-analyses, and international clinical guidelines, making alteplase central to the modern treatment strategy for ischemic stroke [3, 8, 20, 41].

Molecular mechanism of action. Alteplase is a recombinant form of human tissue plasminogen activator (rt-PA) produced via genetic engineering. Under physiological conditions, tissue plasminogen activator is synthesized primarily by vascular endothelial cells and plays a key role in regulating the endogenous fibrinolytic system. The primary mechanism of action of

alteplase involves the selective activation of plasminogen bound to the fibrin of the thrombus. Upon binding to the fibrin scaffold, alteplase catalyzes the conversion of plasminogen into plasmin, a serine protease that degrades fibrin. Disruption of the fibrin network leads to the gradual destabilization and fragmentation of the thrombus, as well as the restoration of patency in the occluded artery [9, 17, 28, 39, 44].

Unlike first-generation agents (streptokinase and urokinase), alteplase exhibits significantly higher fibrin specificity. This means its activity increases substantially upon binding to fibrin, resulting in markedly less systemic plasmin activation. This property reduces the risk of generalized fibrinolysis and systemic hemorrhagic complications, although it does not entirely eliminate them. Restoration of blood flow following successful thrombolysis is accompanied by several beneficial effects: recanalization of the occluded artery; restoration of cerebral perfusion; preservation of the ischemic penumbra; limitation of cerebral infarct expansion; improvement of microcirculation; and an increased likelihood of functional recovery for the patient [7, 16, 28, 39, 47].

It should be emphasized that the efficacy of alteplase is determined not only by its ability to dissolve the thrombus but also by the timeliness of its administration. As the duration of ischemia increases, the volume of irreversibly damaged tissue grows, and the efficacy of thrombolytic therapy predictably declines [6, 14, 23, 32, 46].

Pharmacodynamics. The pharmacodynamic properties of alteplase are closely linked to the functioning of the hemostatic system. Following intravenous administration, the drug rapidly distributes within the vascular compartment and binds to the fibrin of the thrombus. Maximal local plasminogen activation occurs directly at the site of the occluded vessel, where fibrin concentration is highest. The resulting plasmin brings about the sequential breakdown of the fibrin scaffold, the cross-links between fibrin molecules, and the structure of the thrombotic mass. Simultaneously, fibrin degradation products are released and subsequently cleared by the mononuclear phagocyte system. The pharmacodynamic effect manifests within just a few minutes of starting the infusion; however, the rate of recanalization depends significantly on the age and size of the thrombus, the location of the occlusion, the thrombus composition, and the status of collateral circulation. The highest efficacy is observed with fibrin-rich emboli of cardiogenic origin, whereas dense atherothrombotic occlusions of large vessels often prove less responsive to pharmacological lysis [11, 17, 27, 35, 45].

Pharmacokinetics. The pharmacokinetic properties of alteplase determine the specifics of its clinical use. Following intravenous administration, the drug is characterized by extremely rapid plasma clearance. The majority of alteplase is cleared from the circulation by the liver via receptor-mediated uptake by hepatocytes. The drug's elimination half-life comprises two phases: an initial phase (α-phase) of approximately 4–6 minutes and a terminal phase (β-phase) of approximately 35–40 minutes. It is precisely this short half-life that necessitated the use of a combined administration regimen. The standard regimen comprises: 10% of the total dose administered as an intravenous bolus over 1 minute, and 90% of the dose administered as an intravenous infusion over 60 minutes. The recommended dose is 0.9 mg/kg of body weight, with a maximum total dose of 90 mg. This regimen ensures the rapid attainment of a therapeutic drug concentration and its maintenance throughout the period of active thrombolysis [719, 24, 34, 42].

Clinical application. Currently, alteplase remains the standard for systemic thrombolytic therapy in patients with acute ischemic stroke who meet the eligibility criteria. The primary conditions for administration are: confirmed ischemic stroke; presence of a clinically significant neurological deficit; absence of intracranial hemorrhage on neuroimaging; and adherence to time-

based criteria or the presence of viable brain tissue as indicated by CT or MR perfusion imaging [12, 19, 24, 31, 44].

Current guidelines emphasize that maximum clinical efficacy is achieved when treatment is initiated as early as possible. At the same time, the use of multimodal neuroimaging has made it possible to safely expand the indications for thrombolysis in select stroke patients with unknown onset times or delayed presentation, provided a significant volume of ischemic penumbra remains. A practically important advantage of alteplase is the ability to use it either as a standalone reperfusion therapy or as part of a combined strategy (bridging therapy) prior to mechanical thrombectomy in patients with large cerebral artery occlusion. This approach is recommended by most current international guidelines, provided there are no contraindications to intravenous thrombolysis [33–36].

Current evidence base. Despite the active adoption of tenecteplase, alteplase remains the comparator drug in virtually all modern studies of thrombolytic therapy. Major systematic reviews and meta-analyses from 2024 have demonstrated that alteplase maintains high efficacy in achieving favorable functional outcomes, and its safety profile is well established. At the same time, accumulated data indicate that tenecteplase at a dose of 0.25 mg/kg is comparable to alteplase in terms of efficacy and safety, and may achieve higher rates of early recanalization in certain patient subgroups—a finding that reflects the current trend toward a gradual revision of standards for pharmacological reperfusion.

Conclusion. Modern reperfusion therapy is a pathogenetically grounded strategy for treating ischemic stroke, aimed at the earliest possible restoration of cerebral blood flow and the preservation of viable brain tissue. The evolution of the ischemic penumbra concept, the implementation of multimodal neuroimaging, advancements in endovascular treatment techniques, and a personalized approach to patient selection have significantly expanded the capabilities for providing specialized care. Alteplase remains the cornerstone of modern intravenous thrombolytic therapy for ischemic stroke. At the same time, advances in neuroimaging, refined patient selection criteria, and the emergence of new thrombolytic agents offer opportunities to further optimize pharmacological reperfusion. Further research into combined reperfusion and neuroprotection strategies is needed.

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