UNIVERSAL JOURNAL OF MEDICAL AND NATURAL SCIENCES
ISSN 2992-8826
https://sr-journals.org/index.php/UJMANS

CLINICAL AND NEUROLOGICAL CHARACTERISTICS BEFORE AND AFTER REPERFUSION THERAPY IN ACUTE ISCHEMIC STROKE: A LITERATURE REVIEW

O.H.Dustmurodov[1], F.K.Shermukhamedova[2]
[1]Angioneurology unit of National Medical Center
[2]Neurology and medical psychology department of Tashkent State Medical University

Abstract. Acute ischemic stroke remains a leading cause of death and long-term disability worldwide, placing a substantial burden on patients, families, and healthcare systems. Reperfusion therapies, particularly intravenous thrombolysis and mechanical thrombectomy, have transformed acute stroke management by offering the possibility of salvaging ischemic brain tissue. Nevertheless, clinical outcomes after treatment vary widely, and early identification of patients at risk of poor recovery or complications continues to be a major challenge.

This review aims to synthesize current evidence on clinical and neurological indicators observed before and after reperfusion therapy, with a focus on their value in monitoring treatment response and predicting outcomes. The literature suggests that baseline neurological severity, early post-treatment changes such as neurological improvement or deterioration, and functional status over time are closely linked to prognosis. In parallel, laboratory and imaging markers provide additional insight into underlying pathophysiological processes, including reperfusion success and the risk of adverse events such as hemorrhagic transformation.

Taken together, these findings highlight that no single parameter is sufficient to capture the complexity of stroke evolution after reperfusion. A combined approach that integrates clinical assessment with laboratory and neuroimaging data appears to offer the most reliable framework for evaluating treatment effectiveness and guiding patient management

Keywords: Acute ischemic stroke, reperfusion therapy, thrombolysis, neurological outcomes, NIHSS, prognosis.

Annotatsiya. O‘tkir ishemik insult butun dunyo bo‘ylab o‘lim va uzoq muddatli nogironlikning asosiy sabablaridan biri bo‘lib qolmoqda hamda bemorlar, ularning oilalari va sog‘liqni saqlash tizimi zimmasiga katta og‘irlik tushirmoqda. Reperfuzion davo usullari, xususan, vena ichi trombolizisi va mexanik trombektomiya ishemik miya to‘qimasini saqlab qolish imkoniyatini berish orqali o‘tkir insultni davolash amaliyotini tubdan o‘zgartirdi. Shunga qaramay, davolanishdan keyingi klinik natijalar turlicha bo‘lib, tiklanish ehtimoli past bo‘lgan yoki asoratlar xavfi yuqori bo‘lgan bemorlarni erta aniqlash tibbiyotdagi asosiy muammolardan biri bo‘lib qolmoqda.

Ushbu sharhning maqsadi reperfuzion terapiyadan oldin va keyin kuzatiladigan klinik hamda nevrologik ko‘rsatkichlar bo‘yicha mavjud dalillarni umumlashtirish, shuningdek, ularning davolash samaradorligini monitoring qilish va natijalarni bashorat qilishdagi ahamiyatiga e’tibor qaratishdir. Adabiyotlar shuni ko‘rsatadiki, dastlabki nevrologik holatning og‘irlik darajasi, davolanishdan keyingi ilk o‘zgarishlar (masalan, nevrologik holatning yaxshilanishi yoki yomonlashishi) hamda vaqt o‘tishi bilan kuzatiladigan funksional holat prognoz bilan chambarchas bog‘liqdir. Bunga parallel ravishda, laboratoriya va neyrovizualizatsiya (tasvirlash) markerlari asosiy patofiziologik jarayonlar, jumladan, reperfuziyaning muvaffaqiyati va gemorragik transformatsiya kabi nojo‘ya hodisalar xavfi haqida qo‘shimcha tushuncha beradi.

Umuman olganda, ushbu xulosalar reperfuziyadan keyin insult kechishining murakkabligini to‘liq namoyon etish uchun hech bir parametr yakka o‘zi yetarli emasligini ta’kidlaydi. Klinik baholashni laboratoriya va neyrovizualizatsiya ma’lumotlari bilan birlashtirgan majmuaviy yondashuv davolash samaradorligini baholash va bemorlarni olib borish taktikasini belgilash uchun eng ishonchli asos bo‘lib xizmat qiladi.

Kalit so‘zlar: O‘tkir ishemik insult, reperfuzion terapiya, tromboliz, nevrologik oqibatlar, NIHSS, prognoz.

Аннотация. Острый ишемический инсульт остается одной из ведущих причин смертности и долгосрочной инвалидности во всем мире, создавая значительное бремя для пациентов, их семей и систем здравоохранения. Реперфузионная терапия, в частности внутривенный тромболизис и механическая тромбэктомия, коренным образом изменила подходы к лечению острого инсульта, предоставив возможность спасения ишемизированной ткани мозга. Тем не менее, клинические исходы после лечения сильно варьируют, и раннее выявление пациентов с риском неблагоприятного восстановления или развития осложнений продолжает оставаться серьезной проблемой.

Цель данного обзора — обобщить современные данные о клинических и неврологических показателях, наблюдаемых до и после реперфузионной терапии, с акцентом на их ценность для мониторинга ответа на лечение и прогнозирования исходов. Данные литературы свидетельствуют о том, что исходная тяжесть неврологического дефицита, ранние изменения после лечения (такие как неврологическое улучшение или ухудшение), а также функциональный статус в динамике тесно связаны с прогнозом. Параллельно с этим лабораторные и нейровизуализационные маркеры обеспечивают дополнительное понимание лежащих в основе патофизиологических процессов, включая успешность реперфузии и риск развития неблагоприятных событий, таких как геморрагическая трансформация.

В совокупности эти данные подчеркивают, что ни один отдельный параметр не является достаточным для отражения всей сложности течения инсульта после реперфузии. Комбинированный подход, объединяющий клиническую оценку с данными лабораторных исследований и нейровизуализации, по-видимому, предлагает наиболее надежную основу для оценки эффективности лечения и определения тактики ведения пациентов.

Ключевые слова: Острый ишемический инсульт, реперфузионная терапия, тромболизис, неврологические исходы, NIHSS, прогноз.

Introduction. Every year, around 800,000 individuals experience new or recurrent strokes, with most of these being new cases. Approximately 87% are ischemic, 10% reflect intracranial hemorrhage (ICH), and 3% are SAH. Over half of stroke survivors beyond 6 months are dependent on others for at least one activity of daily living. Annually, there are over 12 million incident cases of stroke, of which 65% are ischemic strokes. Patients with stroke with symptomatic steno-occlusive disease have a risk of recurrent stroke of at least 10–15% within 5 years[1]. Acute ischemic stroke occurs due to sudden obstruction of blood flow of a cerebral artery leading to lack of oxygenation of the downstream brain tissue. If the obstruction persists for a considerable time, it can result in permanent loss of neurological function mediated by the affected region of the brain. Pre-clinical studies have estimated that approximately 1.9 million neurons can undergo cell-death following each minute of ischemia. However, if the blockage is removed before substantial tissue injury occurs, reperfusion of the ischemic tissue may reverse such neuronal damage[2]. Thus, an important component of acute reperfusion therapies for acute ischemic stroke involves the concept of the infarct core, the region of the brain which has suffered irreversible damage, versus ischemic penumbra, defined as the critically hypo-perfused area of brain that is potentially salvageable but is progressing to complete infarction in the absence of timely reperfusion.

The aim of this review is to analyze the current evidence on the efficacy and safety of thrombolytic therapy in acute ischemic stroke, with particular emphasis on its impact on clinical and functional outcomes. Additionally, the review seeks to evaluate factors influencing therapeutic

response, including early neurological changes, time-to-treatment, and patient selection criteria, as well as to identify gaps in existing knowledge regarding variability in treatment effectiveness compared with standard medical therapy.

Materials and methods

This review was conducted using a structured search of major electronic databases, including PubMed, Scopus, and Web of Science. Articles published in the last 10 years were prioritized, with additional landmark studies included where relevant. Search terms combined keywords related to acute ischemic stroke, reperfusion therapy, thrombolysis, neurological outcomes, and prognostic markers. Only peer-reviewed studies in English focusing on adult populations were considered. Data were analyzed qualitatively, with emphasis on consistency of findings, clinical relevance, and methodological strength.

Pathophysiology of Ischemic Stroke

Ischemic stroke (IS) immediately triggers a complex molecular and cellular process known as the ischemic cascade. The process sequentially develops several mechanisms as a consequence of the deprivation of blood and oxygen supply to the ischemic core [3]. Patients with ischemic stroke often display the ischemic penumbra, which surrounds the ischemic core and has been identified for up to 48 h. The ischemic penumbra exhibits intermediate perfusion, where cells depolarize intermittently [4]. Without treatment, the penumbra often progresses to infarction due to the effects of ongoing excitotoxicity, spreading depolarization and post-ischemic inflammation.Excitotoxic synaptic transmission, facilitated by glutamate through the activation of N-methyl-D-aspartate (NMDA) and alpha-amino-3-hydroxy-5-methyl-4-propionate (AMPA) receptors, is a process where the influx of Na^{+} and Ca^{2+} upon glutamate release depolarizes the membrane (Figure 1). While this mechanism is essential for neuronal plasticity, excessive receptor activation can lead to neuronal death. In ischemic areas, glutamate is released uncontrollably. This unregulated release triggers the glutamate–calcium cascade, resulting in a necrotic lesion, where Ca^{2+}-mediated excitotoxicity plays a crucial role in the development of brain infarction. The export of Ca^{2+} from neurons into the extracellular space is intricately tied to energy consumption. In instances of brain energy depletion during hypoxia, there is a passive efflux of K+ from cells, amplifying the entry of Ca^{2+} into neurons. The uncontrolled elevation of intracellular cytoplasmic Ca^{2+} connects glutamate excitotoxicity to biochemical pathways that lead to additional damage, specifically oxidative stress[4, 5].

UNIVERSAL JOURNAL OF MEDICAL AND NATURAL SCIENCES
ISSN 2992-8826
https://sr-journals.org/index.php/UJMANS

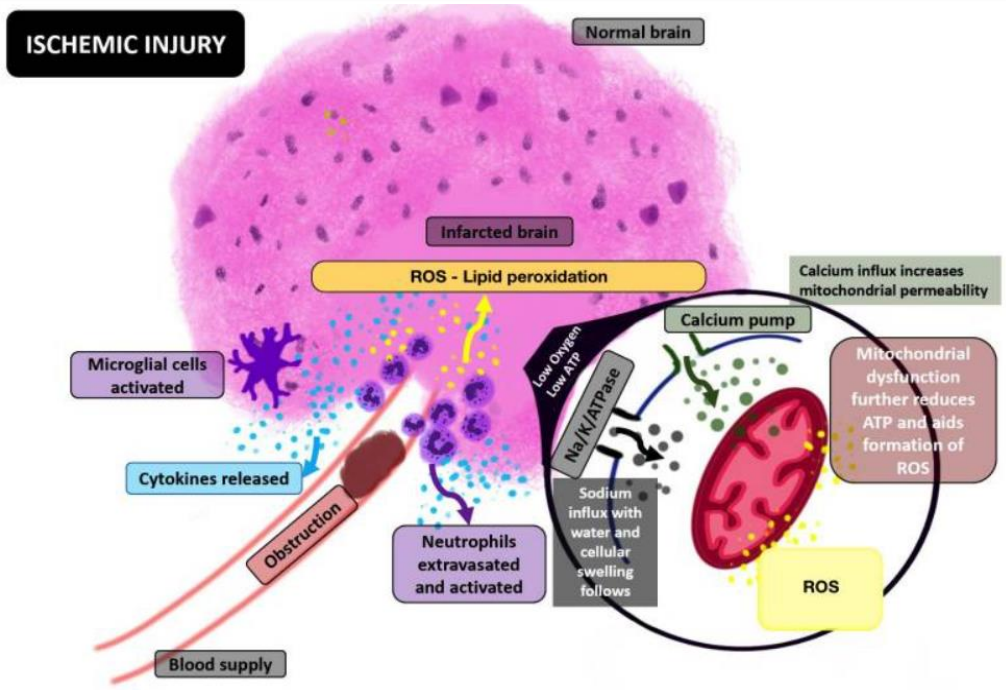


Figure 1. Ischemic Injury and its Molecular Consequences. Abbreviation: ROS, reactive oxygen species.

This time duration of ischemic tissue viability varies considerably and depends on several factors such as the location of cerebral artery occlusion, extent of the occlusion (partial versus complete), degree of cerebral collateral blood flow, and cerebral perfusion pressure. In particular, the extent of recruitment of cerebral collaterals has been demonstrated to be one of the strongest predictors of favorable outcome in ischemic stroke patients. Several studies have suggested favorable collateral flow with slowed progression of ischemic penumbra to infarct core and better clinical outcomes following acute interventions Understanding their role in cases of acute ischemic stokes has also been pivotal in garnering utility of acute reperfusion therapeutics beyond the previously recognized time windows. Despite administration of intravenous (IV) thrombolysis (alteplase or tenecteplase) within the standard hour time window, ischemic stroke outcomes vary significantly, ranging from complete recovery to death or severe disability. While prompt treatment improves functional outcomes overall—with a "number needed to treat" (NNT) to prevent 1 death or disability of 7 when treated within 3 hours—a substantial minority of patients still experience poor outcomes[6, 7]. Thrombectomy is currently recommended for eligible patients with stroke who are treated within 6 hours after the onset of symptoms.But some studies show that endovascular thrombectomy performed 6–16 hours after stroke onset in carefully selected patients may significantly improve functional outcomes and independence compared with medical therapy alone, without increasing major complications[2]. The interval from ischemic stroke onset to completion varies widely from patient to patient, reflecting interindividual differences in site of vessel occlusion, degree of ischemic preconditioning, richness and patency of collaterals, systemic blood pressure, blood volume, serum glucose, and many other factors[8]. Even when treatment is given on time, the following factors contribute to poor outcomes (defined as 90-day modified Rankin Scale ≥2 or death)[9].

Large Vessel Occlusions (LVOs): Intravenous tissue plasminogen activator (tPA) is less effective at dissolving large clots, such as those in the proximal middle cerebral artery (M1/M2) or internal carotid artery. These LVOs, which account for 25-30% of strokes, require faster or combined therapy (e.g., endovascular thrombectomy) to achieve high recanalization rates. Initial Stroke Severity (NIHSS Score): A higher baseline National Institutes of Health Stroke Scale (NIHSS) score is the strongest predictor of poor outcome, despite treatment.

Hemorrhagic Transformation: Symptomatic intracranial hemorrhage (sICH) is a major risk, with incidence rates sometimes reaching 2.75–4.25 times higher in thrombolysed patients compared to non-thrombolysed controls.

Blood Pressure and Glucose Levels: High systolic blood pressure (SBP) and high blood glucose at admission are independent risk factors for poor functional outcomes and mortality.

Collateral Circulation: The ability of the brain to maintain blood flow to the ischemic area through alternative vessels varies significantly between individuals. Poor collateral circulation can lead to faster infarct growth despite opening the main blocked vessel.

Comorbidities: Pre-existing conditions such as atrial fibrillation, congestive heart failure, diabetes, and previous stroke increase mortality and reduce the likelihood of a favorable outcome.

Age: Older patients (octogenarians and nonagenarians) often have lower functional success rates than younger patients, partly due to reduced rehabilitation potential, although the safety profile (hemorrhage risk) is often similar[10-12].

Ischemia-reperfusion injury (IRI) presents a clinical challenge characterized by the exacerbation of cellular dysfunction and death upon restoration of blood flow to previously ischemic tissues. Despite the necessity of restoring blood flow to salvage ischemic tissues, reperfusion paradoxically induces further damage, thereby impeding the function and viability of the affected organ. This phenomenon is observed across various organs, including the heart, lungs, kidneys, gut, skeletal muscles, and brain. Furthermore, IRI may extend beyond the primary ischemic site, triggering systemic damage that culminates in multisystem organ failure. The multifaceted nature of reperfusion injury involves intricate molecular and cellular mechanisms, culminating in extensive tissue destruction (Figure2,3).

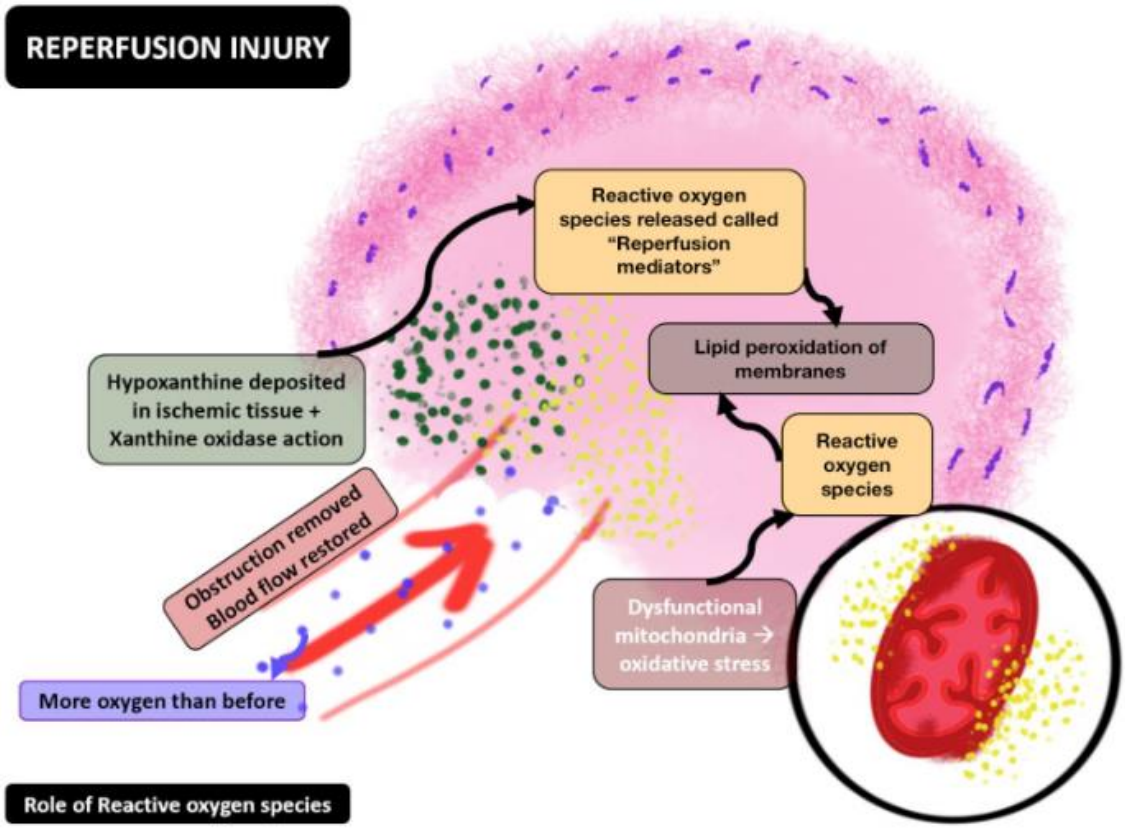


Figure2. Ischemia-Reperfusion Injury, Reactive Oxygen Species. The image explores the involvement of reactive oxygen species in ischemia-reperfusion injury.

Complications arising from IRI in AIS patients can significantly impact clinical outcomes and long-term prognosis. While reperfusion therapies are vital for restoring blood flow to ischemic brain tissue, they can paradoxically exacerbate tissue damage through mechanisms such as oxidative stress, inflammation, and excitotoxicity. These complications may manifest as penumbral damage,

ischemia expansion, hemorrhagic transformation, malignant cerebral edema and herniation, seizures, and disruption of the BBB, leading to secondary brain injury and neurological deterioration. Moreover, reperfusion injury can contribute to post-stroke complications such as recurrent ischemic events, vasospasm, and systemic inflammatory response syndrome. Managing these complications requires a multifaceted approach, including close monitoring for early detection, tailored interventions to mitigate further damage, and comprehensive rehabilitation strategies to optimize recovery and minimize long-term disability. Healthcare professionals can improve patient outcomes and enhance the quality of care for affected patients by addressing the complexities of IRI and its associated complications.

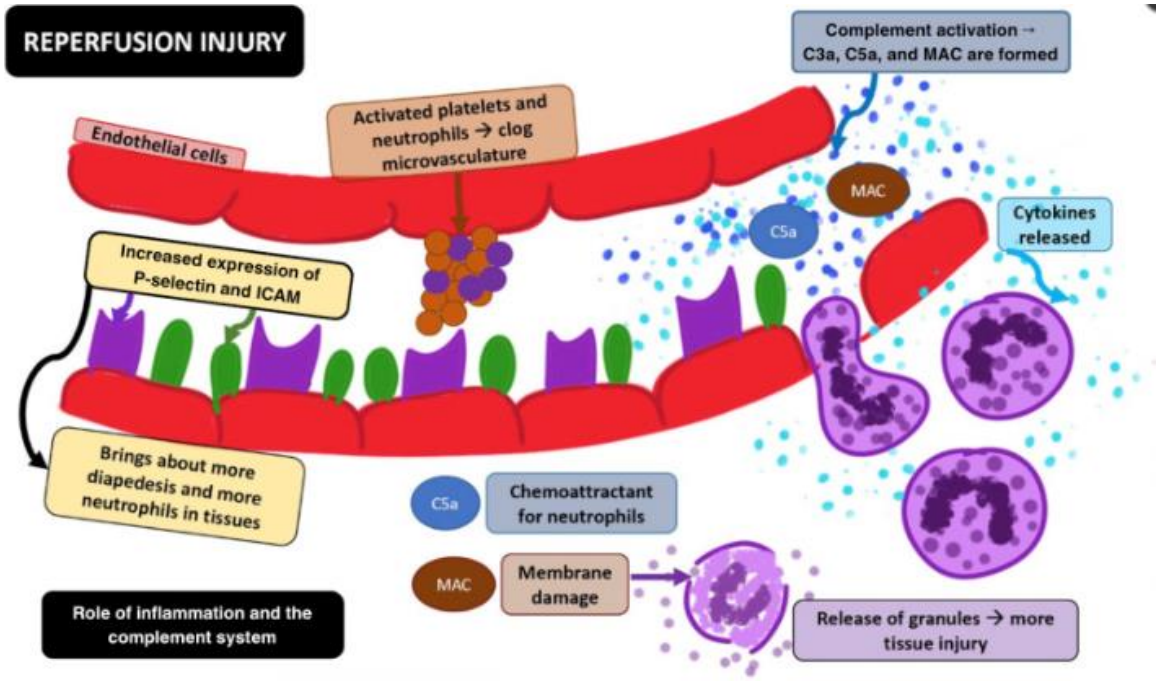


Figure 3. Ischemia-Reperfusion Injury, Inflammation and the Complement System. This image elucidates the involvement of inflammation and the complement system in ischemia-reperfusion injury. Abbreviations: ICAM, intercellular adhesion molecule; MAC, membrane attack complex.

Initial clinical assessment

The baseline clinical and neurological status of patients presenting with acute ischemic stroke (AIS) serves as the primary foundation for determining treatment eligibility and predicting future functional recovery. The National Institutes of Health Stroke Scale (NIHSS) is the globally recognized standard for assessing initial stroke severity, where scores of 5 or less typically indicate a minor stroke. However, initial clinical assessment can be deceptive, as nearly one-third of minor stroke patients who do not receive intravenous thrombolysis (IVT) experience neurological progression or recurrence within 90 days, leading to severe disability. Key predictors identified before the initiation of therapy include advanced age, which significantly increases the risk of complications, and a history of comorbidities such as hypertension, diabetes mellitus, and atrial fibrillation. Furthermore, the Onset-to-Treatment Time (OTT) remains a critical variable, as longer delays are directly associated with an increased likelihood of early neurological deterioration (END). Prompt neurological and physiological assessment is therefore essential to salvage the ischemic penumbra and optimize the therapeutic window.

Monitoring after reperfusion therapy

Following the administration of reperfusion therapy, clinical monitoring focuses on identifying two divergent paths: Early Neurological Improvement (ENI) or Early Neurological Deterioration (END). ENI is generally defined as a significant reduction in NIHSS scores within the first 24 hours, whereas END is defined as an increase of 4 points or more on the same scale. Statistics

indicate that the overall incidence of END after reperfusion therapy is approximately 14%, with slightly higher rates observed after endovascular treatment compared to thrombolysis alone. The occurrence of END is a grave prognostic sign, as it increases the risk of 90-day mortality and functional dependency by nearly 2.5 times. Functional outcomes at three months are evaluated using the modified Rankin Scale (mRS), where scores of 0–1 signify an "excellent" recovery and independent living. Factors such as the successful recanalization of the occluded vessel and the absence of symptomatic intracranial hemorrhage (sICH) are the strongest independent predictors of clinical success.

Laboratory biomarkers provide an objective layer of monitoring that complements clinical observation. Fibrinogen levels measured 24 hours after IVT have emerged as a powerful predictor; an elevation in these levels is independently associated with more severe brain injury, larger infarct volumes, and poor long-term functional outcomes. Similarly, D-dimer serves as a crucial marker of the fibrinolytic system's activation, with the change from baseline (ΔD-dimer) being a superior predictor for sICH and poor outcomes compared to single measurements. Inflammatory markers, particularly the Platelet-to-Neutrophil Ratio (PNR), reflect the balance between thrombosis and the inflammatory response; a low post-IVT PNR is a herald of hemorrhagic transformation and neurological worsening. Additionally, electrolyte imbalances play a role in prognosis, with lower calcium (Ca^{2+}) concentrations linked to a higher risk of END and higher sodium (Na^{+}) levels associated with adverse long-term outcomes in hypertensive patients.

Instrumental and neuroimaging technologies are indispensable for selecting patients for therapy, especially in extended time windows[13]. The DWI-FLAIR mismatch—where a lesion is visible on diffusion-weighted imaging but not on fluid-attenuated inversion recovery—is a validated surrogate for identifying strokes that occurred within the last 4.5 hours, making it vital for treating "wake-up" strokes. Advanced perfusion imaging further allows clinicians to identify the "imaging mismatch" between the infarct core and the salvageable penumbra, extending the treatment window up to 9 hours for eligible patients. The presence of a Large Vessel Occlusion (LVO) on baseline imaging is a strong predictor of potential deterioration if left untreated. Post-procedure success is quantified by the modified Thrombolysis in Cerebral Ischemia (mTICI) scale, where achieving mTICI 2b/3 (successful reperfusion) significantly improves the probability of excellent functional recovery.

Transcranial Doppler (TCD) and Transcranial Color-Coded Duplex (TCCD) sonography serve as vital bedside tools for the continuous and comprehensive monitoring of patients following acute reperfusion therapies like intravenous **Instrumental and neuroimaging technologies** are indispensable for selecting patients for therapy, especially in extended time windows[13]. The DWI-FLAIR mismatch—where a lesion is visible on diffusion-weighted imaging but not on fluid-attenuated inversion recovery—is a validated surrogate for identifying strokes that occurred within the last 4.5 hours, making it vital for treating "wake-up" strokes. Advanced perfusion imaging further allows clinicians to identify the "imaging mismatch" between the infarct core and the salvageable penumbra, extending the treatment window up to 9 hours for eligible patients. The presence of a Large Vessel Occlusion (LVO) on baseline imaging is a strong predictor of potential deterioration if left untreated. Post-procedure success is quantified by the modified Thrombolysis in Cerebral Ischemia (mTICI) scale, where achieving mTICI 2b/3 (successful reperfusion) significantly improves the probability of excellent functional recovery.

Transcranial Doppler (TCD) and Transcranial Color-Coded Duplex (TCCD) sonography serve as vital bedside tools for the continuous and comprehensive monitoring of patients following acute reperfusion therapies like intravenous **Instrumental and neuroimaging technologies** are indispensable for selecting patients for therapy, especially in extended time windows[13]. The DWI-FLAIR mismatch—where a lesion is visible on diffusion-weighted imaging but not on fluid-attenuated inversion recovery—is a validated surrogate for identifying strokes that occurred within the last 4.5 hours, making it vital for treating "wake-up" strokes. Advanced perfusion imaging further allows clinicians to identify the "imaging mismatch" between the infarct

core and the salvageable penumbra, extending the treatment window up to 9 hours for eligible patients. The presence of a Large Vessel Occlusion (LVO) on baseline imaging is a strong predictor of potential deterioration if left untreated. Post-procedure success is quantified by the modified Thrombolysis in Cerebral Ischemia (mTICI) scale, where achieving mTICI 2b/3 (successful reperfusion) significantly improves the probability of excellent functional recovery.

Transcranial Doppler (TCD) and Transcranial Color-Coded Duplex (TCCD) sonography serve as vital bedside tools for the continuous and comprehensive monitoring of patients following acute reperfusion therapies like intravenous thrombolysis (IVT) and mechanical thrombectomy (MT). Unlike static imaging, these modalities allow for real-time assessment of cerebral hemodynamics through several key parameters:

TIBI Grading and Recanalization: The **Thrombolysis in Brain Ischemia (TIBI) grading system** is the primary metric used to quantify residual flow at the site of an occlusion, ranging from grade 0 (complete absence of flow) to grade 5 (normal flow). Monitoring these grades in real-time allows clinicians to identify the speed and timing of recanalization; for instance, a shift from TIBI grades 0/I to IV/V indicates successful reperfusion with high accuracy. Conversely, a worsening of the TIBI grade by ≥ 1 is a diagnostic sign of **arterial re-occlusion**, a major cause of early neurological deterioration.

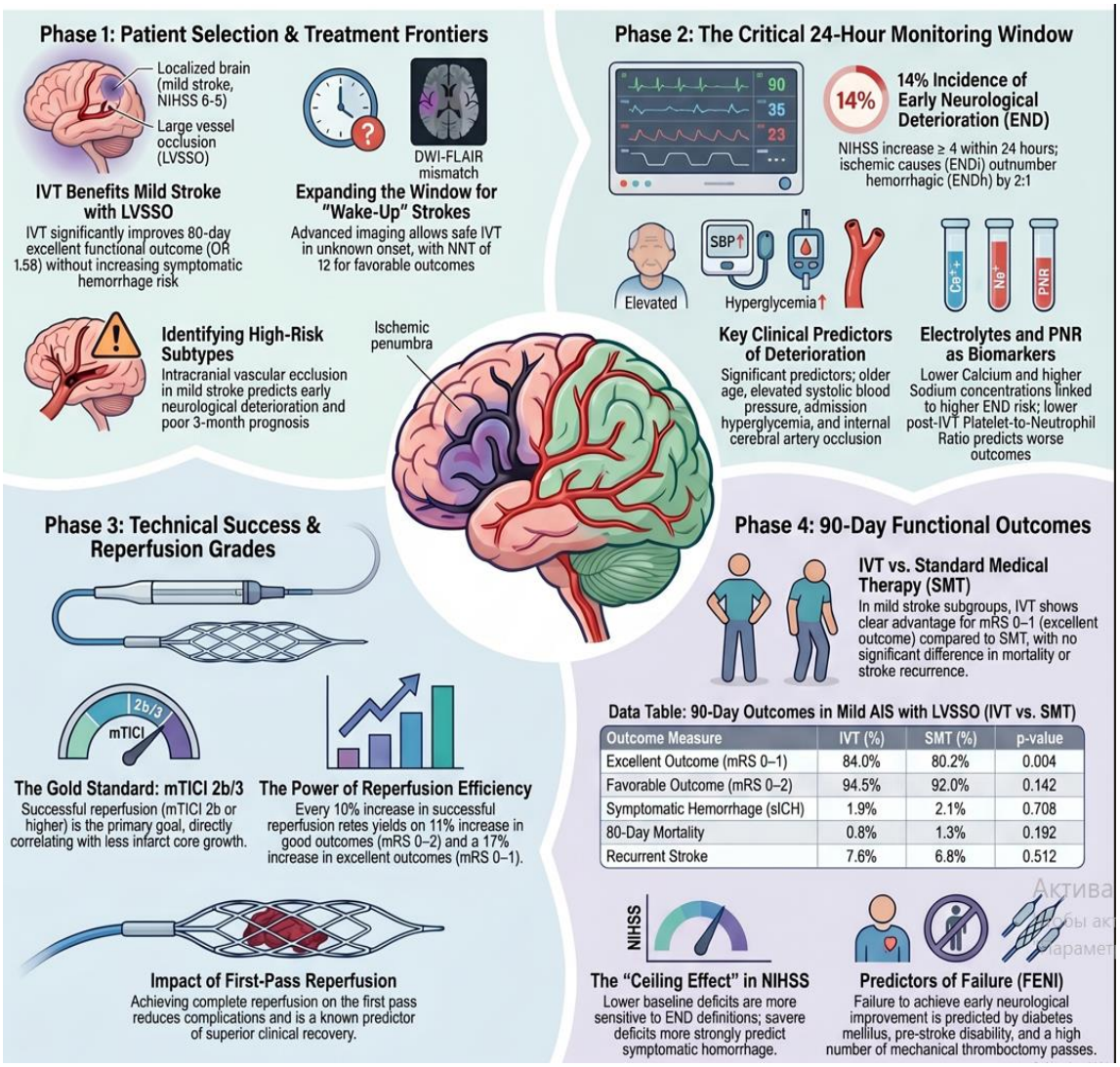


Figure 1. Optimizing Ischemic Stroke Reperfusion Outcomes

Flow Velocities and Hemodynamic Ratios: Changes in **Mean Flow Velocity (MFV)** and **End-Diastolic Velocity (EDV)** are critical indicators of vascular status. An increase in MFV of ≥

1.5 times compared to the contralateral artery is a signature of **cerebral hyperperfusion**, which may necessitate intensive blood pressure reduction to prevent injury. Furthermore, the **Peak Systolic Velocity (PSV) ratio** (recanalized artery vs. contralateral artery) is used to predict complications; an early PSV ratio increase is independently associated with an eight-fold higher risk of post-procedural intracranial hemorrhage (ICH).

Microembolic Signals (MES) and HITS: TCD can detect **High-Intensity Transient Signals (HITS)** and MES, which provide insights into the nature of the reperfusion process. While MES during thrombolysis can signal ongoing clot dissolution, their persistence after successful recanalization is correlated with a seven-fold increased risk of **recurrent stroke**, potentially prompting more aggressive antithrombotic therapy.

Intracranial Pressure (ICP) and Brain Architecture: TCD-derived **Pulsatility Index (PI)** and diastolic flow velocities allow for the non-invasive monitoring of dynamic changes in ICP. An increase in PI combined with a decrease in diastolic flow often indicates rising ICP or malignant edema. Additionally, TCCD can utilize B-mode imaging to detect **midline shift** and early hematoma growth (symptomatic ICH) at the bedside, providing an immediate explanation for clinical worsening without the need for urgent transport to a CT scanner.

Ultimately, the integration of these sonographic signatures—**TIBI grades, flow velocity ratios, and MES detection**—enables a proactive management strategy. By guiding blood pressure control and predicting three-month functional outcomes, TCD monitoring significantly reduces the likelihood of early neurological deterioration and mortality in the post-reperfusion period[14].

Finally, the integration of these clinical, laboratory, and imaging variables into combined prognostic models offers the highest accuracy for outcome prediction. The IScore is a validated scoring system that utilizes variables such as age, stroke severity, and admission glucose to identify patients at high risk for death or END. Complications like sICH are frequently predicted by uncontrolled high blood pressure and elevated post-thrombolytic D-dimer levels. Despite the robustness of current indicators, limitations remain, such as the retrospective nature of many studies and the need for personalized models that can account for individual collateral circulation.

Future directions

Future research should move beyond isolated markers and focus on integrated, multimodal models that combine clinical, laboratory, and imaging data. Emerging biomarkers reflecting inflammation, endothelial dysfunction, and oxidative stress may improve risk stratification, but require validation in large, diverse cohorts. In parallel, artificial intelligence–based predictive tools offer promise for real-time decision support, particularly in selecting patients for reperfusion therapy beyond traditional time windows. A shift toward personalized treatment strategies, tailored to individual pathophysiological profiles, is likely to define the next stage of stroke care.

Conclusion

Reperfusion therapy has reshaped the management of acute ischemic stroke, yet its outcomes remain heterogeneous. Evidence indicates that changes in clinical and neurological status before and after treatment provide essential insight into disease trajectory, especially when interpreted alongside laboratory and imaging findings. No single parameter adequately reflects recovery or risk. A structured, integrated assessment offers a more reliable basis for monitoring therapy and anticipating complications. Strengthening this approach may improve both clinical decision-making and long-term patient outcomes.The systematic monitoring of clinical, laboratory, and instrumental indicators is the key to reducing disability and mortality by enabling early intervention and informed prognostic assessments.

References

1. Li, X.-y., et al., *Global, regional, and national burden of ischemic stroke, 1990–2021: an analysis of data from the global burden of disease study 2021.* eClinicalMedicine, 2024. **75**.
2. Albers, G.W., et al., *Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging.* N Engl J Med, 2018. **378**(8): p. 708-718.

3. Bai, J. and P.D. Lyden, *Revisiting cerebral postischemic reperfusion injury: new insights in understanding reperfusion failure, hemorrhage, and edema.* Int J Stroke, 2015. **10**(2): p. 143-52.
4. Rehman, S., et al., *Molecular Mechanisms of Ischemic Stroke: A Review Integrating Clinical Imaging and Therapeutic Perspectives.* Biomedicines, 2024. **12**(4).
5. Ronaldson, P.T. and T.P. Davis, *Targeting transporters: promoting blood-brain barrier repair in response to oxidative stress injury.* Brain Res, 2015. **1623**: p. 39-52.
6. Man, S., et al., *Association Between Thrombolytic Door-to-Needle Time and 1-Year Mortality and Readmission in Patients With Acute Ischemic Stroke.* Jama, 2020. **323**(21): p. 2170-2184.
7. McInerney, A., et al., *From clock to outcomes: Time to thrombolytics and functional outcomes in acute ischemic stroke.* The American Journal of Emergency Medicine, 2025. **96**: p. 161-165.
8. Kidwell, C.S., J.R. Alger, and J.L. Saver, *Beyond mismatch: evolving paradigms in imaging the ischemic penumbra with multimodal magnetic resonance imaging.* Stroke, 2003. **34**(11): p. 2729-35.
9. Cao, X., et al., *Development of a prediction model for poor outcomes after thrombolysis in mild non-disabling ischemic stroke.* Front Neurol, 2026. **17**: p. 1754895.
10. Cheng, J., et al., *Factors affecting the early efficacy of intravenous thrombolysis using alteplase in acute ischemic stroke: A retrospective analysis of 255 cases.* Medicine (Baltimore), 2025. **104**(42): p. e45176.
11. Çetiner, M., et al., *Predictive Factors for Functional Outcomes After Intravenous Thrombolytic Therapy in Acute Ischemic Stroke.* Clin Appl Thromb Hemost, 2018. **24**(9_suppl): p. 171s-177s.
12. Ringleb, P.A., et al., *Thrombolytic Therapy Within 3 to 6 Hours After Onset of Ischemic Stroke.* Stroke, 2002. **33**(5): p. 1437-1441.
13. Scheldeman, L., A. Wouters, and R. Lemmens, *Imaging selection for reperfusion therapy in acute ischemic stroke beyond the conventional time window.* J Neurol, 2022. **269**(3): p. 1715-1723.
14. Kargiotis, O., et al., *Transcranial Doppler Monitoring of Acute Reperfusion Therapies in Acute Ischemic Stroke Patients with Underlying Large Vessel Occlusions.* J Neurosonol Neuroimag, 2020. **12**(1): p. 10-25.