

Reperfusion Injury Of The Brain In Ischemic Stroke: From Pathophysiology To Clinical Manifestation

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Abstract: A prospective study was conducted on 67 patients with ischemic stroke who underwent systemic intravenous thromboembolism (SILT). Depending on the course of the postreperfusion period, the patients were divided into two groups: the first group consisted of 48 patients who did not develop reperfusion syndrome, and the second group consisted of 19 patients with clinical manifestations of SILT.

In patients without SILT, significant improvement in neurological status was observed as early as 24 hours after SILT: the level of consciousness according to the GCS increased from 10.3 ± 1.2 to 13.8 ± 1.2 points, reaching 14.1 ± 0.9 points by day 7 ($p < 0.005$), while the NIHSS decreased from 14.2 ± 1.8 to 6.3 ± 1.5 points after 24 hours and to 5.2 ± 2.1 points by day 7 ($p < 0.005$). In contrast, patients with ischemic stroke experienced early clinical deterioration, accompanied by hyperthermia, worsening neurological deficit, impaired consciousness, seizures, and hemodynamic and respiratory distress. The GCS decreased from 10.6 ± 2.4 to 9.3 ± 3.5 points after 24 hours and reached 10.1 ± 4.5 points on day 7, while the NIHSS increased from 14.9 ± 3.5 to 18.3 ± 4.1 points after 24 hours and remained high (16.1 ± 4.5 points) on day 7. The development of reperfusion syndrome after systemic thrombolytic therapy is associated with early neurological deterioration and unfavorable dynamics of clinical parameters, reflecting the progression of ischemia-reperfusion brain injury.

Keywords: ischemic stroke; systemic intravenous thrombolytic therapy; reperfusion syndrome, neurological deficit.

Introduction

The modern strategy of care is based on the earliest possible restoration of cerebral blood flow through systemic intravenous thrombolytic therapy and mechanical thrombectomy. The results of large randomized clinical trials have convincingly demonstrated that timely reperfusion therapy significantly increases the likelihood of functional recovery, reduces disability and mortality, while the introduction of modern neuroimaging techniques makes it possible to substantially extend the therapeutic window through patient selection [1].

The central concept underlying the pathophysiological progression of ischemic stroke is the existence of the “ischemic penumbra.” This region refers to brain tissue surrounding the infarct core, where blood flow is reduced but energy metabolism is preserved [2].

In clinical practice, achieving rapid recanalization to preserve the peripheral ischemic zone is the primary goal of all reperfusion strategies, including endovascular therapy and intravenous systemic thrombolysis, which is currently the first-line reperfusion therapy recommended by international guidelines [3].

At the same time, although reperfusion therapy has significantly improved vascular recanalization rates, subsequent reperfusion injury and inflammatory cascade reactions continue to adversely affect the patient’s recovery outcome. Despite the obvious advances in reperfusion therapy, accumulated clinical experience indicates that achieving angiographically successful

recanalization of an occluded cerebral artery does not always result in a favorable clinical outcome [4].

In a substantial proportion of patients, despite complete or near-complete restoration of blood flow (mTICI 2b–3), the expected regression of neurological deficits is not observed, or secondary deterioration develops. This phenomenon has been termed “futile reperfusion” and is largely associated with the development of reperfusion syndrome (RS), which represents a complex of interconnected molecular, immune, cellular, and vascular disorders occurring after restoration of blood flow in previously ischemic brain tissue [5].

In the contemporary English-language literature, the term ischemic reperfusion injury of the brain is increasingly used to describe the spectrum of pathological processes developing after restoration of cerebral perfusion. This concept reflects the multifactorial nature of the injury and encompasses oxidative stress, mitochondrial dysfunction, activation of innate immunity, neuroinflammation, endothelial dysfunction, disruption of the blood–brain barrier, the phenomenon of microvascular obstruction, as well as the development of cytotoxic and vasogenic edema and hemorrhagic transformation of the ischemic lesion [6].

It is now becoming evident that reperfusion is not only a necessary condition for preserving viable brain tissue but may also be a potential factor contributing to secondary injury. Rapid oxygen delivery to ischemic tissues is accompanied by intensive generation of reactive oxygen species, activation of NADPH oxidase, xanthine oxidase, and the mitochondrial electron transport chain. This results in marked oxidative stress, activation of lipid peroxidation, damage to cellular membranes, protein denaturation, and DNA fragmentation, thereby contributing to the death of neurons, endothelial cells, astrocytes, and other components of the neurovascular unit [7].

One of the key elements in the pathogenesis of ischemic reperfusion injury of the brain is disruption of the structure and function of the blood–brain barrier. Activation of matrix metalloproteinases, primarily MMP-9, pro-inflammatory cytokines, proteolytic enzymes, and endothelial dysfunction cause degradation of tight-junction proteins between endothelial cells, accompanied by increased vascular permeability, development of vasogenic edema, and an increased risk of hemorrhagic transformation of the ischemic lesion [8].

An equally important role is played by marked activation of the neuroinflammatory response. Reperfusion is accompanied by rapid activation of microglia, astrocytes, neutrophils, monocytes, and lymphocytes, followed by the release of a broad spectrum of pro-inflammatory mediators, including interleukin-1 β (IL-1 β), interleukin-6 (IL-6), and tumor necrosis factor- α (TNF- α) [9].

The widespread implementation of systemic thrombolysis and mechanical thrombectomy has substantially changed the prognosis of patients with acute ischemic stroke. In specialized stroke centers, successful recanalization of major cerebral arteries after mechanical thrombectomy is achieved in more than 85–90% of patients. However, high technical success does not always translate into satisfactory functional recovery. According to current studies, approximately 40–50% of patients after successful recanalization continue to have significant neurological deficits or experience unfavorable functional outcomes, indicating a discrepancy between angiographic success and clinical treatment outcome [10].

The development of ischemic reperfusion injury of the brain is determined not only by the characteristics of the reperfusion therapy performed but also by major risk factors, including advanced age, duration of ischemia before restoration of blood flow, diabetes mellitus, arterial hypertension, severe atherosclerosis, atrial fibrillation, hyperglycemia on admission, a large ischemic core volume, insufficient collateral circulation, and a pronounced systemic inflammatory response. The combination of these factors determines the extent of neurovascular unit injury and largely influences the likelihood of secondary reperfusion injury [11].

Thus, current concepts of ischemic stroke treatment regard reperfusion therapy not as the final stage of care, but as the beginning of a new pathophysiological process, the outcome of which may be determined not only by the success of recanalization but also by the development of ischemic reperfusion injury of the brain (IRI).

The aim of the study: to analyze the clinical manifestations of ischemic-reperfusion brain injury following systemic intravenous thrombolytic therapy for ischemic stroke.

Materials and Methods

Clinical and instrumental examination data from 67 patients with ischemic stroke who were hospitalized in the Neurointensive Care Unit of the Bukhara Branch of the Republican Scientific Center for Emergency Medical Care between 2024 and 2026 were studied. All patients underwent systemic intravenous thrombolytic therapy in accordance with current international recommendations. The mean age of the patients was 56.2 ± 2 years; women accounted for 45% ($n=30$) and men for 55% ($n=37$). Standard examination methods in all patients included assessment by a neurologist and a neurointensivist, with clarification of the patient's neurological status, electrocardiography, neuroimaging methods (non-contrast brain MSCT, MSCT angiography, and brain MRI), duplex scanning of the major vessels of the head, clinical and biochemical blood tests, and coagulation studies.

A thorough analysis of the medical history and somatic status, as well as instrumental examinations, revealed concomitant pathologies, including obesity of varying degrees in 23 patients (34%), cardiac rhythm disorders in 12 patients (18%), atherosclerosis of the major vessels in 24 patients (36%), and diabetes mellitus in 8 patients (12%). It should be noted that among all patients in whom diabetes mellitus was identified, 17 patients (25%) were admitted with marked hyperglycemia (blood glucose level >16.6 mmol/L), 36 patients (54%) with moderate hyperglycemia (blood glucose level 7.8–11.0 mmol/L), and only 13 patients (19.5%) with normoglycemia (blood glucose level 3.8–7.7 mmol/L); additionally, 1 patient (1.5%) was diagnosed with relative hypoglycemia on admission (blood glucose level 2.8 mmol/L).

During native non-contrast computed tomography, the brain structure, cerebrospinal fluid pathways, ventricles, and cisterns were assessed. In the absence of a formed ischemic lesion despite an evident neurological deficit, brain MRI was performed to assess signs of impaired perfusion. Detailed assessment of cerebral perfusion using DWI and FLAIR-mismatch techniques made it possible to identify hypoperfused areas from the first minutes of the vascular event and to determine the “age of ischemia” in doubtful cases when the exact time of stroke onset could not be established and a decision regarding systemic thrombolysis had to be made.

Of all patients included in the study, 2 patients (3%) were mechanically ventilated due to coma and signs of respiratory failure on admission ($\text{SpO}_2 < 90\%$, $\text{PaO}_2 < 60$ mmHg, $\text{PaCO}_2 > 45$ mmHg at $\text{FiO}_2 40\%$). Of these, 1 patient (1.5%) was weaned from mechanical ventilation 12 hours after systemic thrombolysis because of complete recovery of adequate spontaneous respiration, normalization of blood gas parameters, and complete regression of the neurological deficit. The other patient remained on mechanical ventilation because of persistent neurological deficits and coma for 12 days (1.5%).

Depending on the clinical course after thrombolytic therapy (TLT) and restoration of blood flow, the patients were divided into two groups: Group I — without signs of IRI, and Group II — with development of IRI.

Neurological status in all patients was assessed using the Glasgow Coma Scale and the NIHSS for neurological deficit. On admission, patients in Group I had a Glasgow Coma Scale score of 10.3 ± 1.2 points and an NIHSS score of 14.2 ± 1.8 points. In Group II, the total Glasgow Coma Scale score was 9.8 ± 1.4 points, while the neurological deficit according to the NIHSS was 14.9 ± 1.7 points.

The presence of a neurological deficit in the absence of an ischemic zone on MSCT was an indication for systemic thrombolysis. In the absence of contraindications, systemic thrombolysis was performed using intravenous infusion of Actilyse at a dose of 0.9 mg/kg (maximum dose, 90 mg). Initially, 10% of the drug solution was administered, followed by infusion of the remaining dose over 60 minutes.

Results and Discussion

Analysis of the results demonstrated that among the 67 patients who received systemic intravenous thrombolytic therapy, signs of IRI were identified in 19 (28.3%) patients, whereas RS did not develop in 48 (71.7%) patients. After systemic intravenous TLT, patients without IRI (Group I) demonstrated a significant reduction in the severity of neurological deficits as early as 24 hours after treatment. This was reflected by an increase in the total Glasgow Coma Scale

score to 13.8 ± 1.2 points compared with the baseline value of 10.3 ± 1.2 points, while on day 7 of observation the level of consciousness according to the Glasgow Coma Scale was 14.1 ± 0.9 points ($p < 0.005$). On day 2, the mean NIHSS score decreased by almost 2.5-fold, from 14.2 ± 1.8 to 6.3 ± 1.5 points; on day 7, the neurological deficit was 5.2 ± 2.1 points, indicating effective functional recovery of the brain tissue ($p < 0.005$).

In contrast, after systemic TLT, patients with IRI (Group II) experienced clinical deterioration during the first 24 hours. This manifested as hyperthermia, increased neurological deficit (progression of pyramidal disorders, worsening of coma, onset of seizures, and hemodynamic and respiratory disturbances) [12]. At 24 hours, neurological assessment demonstrated a decrease in the total Glasgow Coma Scale score from 10.6 ± 2.4 to 9.3 ± 3.5 points, while on day 7 the score was 10.1 ± 4.5 points. In patients with RS, the NIHSS score increased from 14.9 ± 3.5 points on admission to 18.3 ± 4.1 points or higher after 24 hours, and on day 7 was 16.1 ± 4.5 points. These changes reflected the progression of IRI [13]. Despite intensive therapy, by the time of discharge the neurological deficit according to the modified Rankin Scale remained significantly more pronounced in patients with IRI compared with patients without IRI (4–5 points versus 0–1 point, respectively) ($p < 0.001$). The obtained data indicate that the development of IRI substantially limits the beneficial effect of thrombolytic therapy. Comparative assessment of the outcomes of thrombolytic therapy versus standard therapy and in patients with IRI demonstrated a significant difference in neurological status and outcomes in patients with ischemic stroke, as shown in table 1.

Comparative Clinical Assessment of the Outcomes of Standard and Thrombolytic Therapy in Patients with Ischemic Stroke Depending on the Development of IRI

Table 1.

Parameter	Standard therapy	Thrombolytic therapy		p
		Without RS	With RS	
Age, years	$63,2 \pm 7,8$	$62,8 \pm 8,4$	$65,9 \pm 9,2$	$>0,05$
NIHSS on admission	$14,2 \pm 2,8$	$14,2 \pm 1,8$	$14,9 \pm 3,5$	$>0,05$
NIHSS at 24 hours	$13,1 \pm 3,9$	$6,3 \pm 1,5$	$18,3 \pm 4,1$	$<0,001$
NIHSS on day 7	$11,7 \pm 3,3$	$5,2 \pm 2,1$	$16,1 \pm 4,5$	$<0,001$
NIHSS at transfer	$8,7 \pm 3,3$	$3,1 \pm 1,1$	$12,3 \pm 2,6$	$<0,001$
GCS on admission	$10,2 \pm 2,5$	$10,3 \pm 1,2$	$10,6 \pm 2,4$	$>0,05$
GCS at 24 hours	$10,7 \pm 3,3$	$13,8 \pm 1,2$	$9,3 \pm 3,5$	$<0,001$
GCS on day 7	$12,4 \pm 2,6$	$14,1 \pm 0,9$	$10,1 \pm 4,5$	$<0,001$
GCS at transfer	$13,7 \pm 2,3$	$14,2 \pm 0,8$	$12,4 \pm 2,6$	$<0,05$
mRS at discharge	3-4	0-1	4-5	$<0,001$
Length of hospital stay, days	$13,4 \pm 4,6$	$4,2 \pm 2,8$	$16,5 \pm 5,2$	$<0,001$

As can be seen from the table, patients who received TLT without IRI had extremely low disability scores according to the mRS at discharge compared with patients with IRI after TLT and those receiving standard therapy. The development of IRI also had a notable effect on the duration of hospitalization. In patients without RS, the duration of hospitalization was 4.2 ± 2.8 days, compared with 16.5 ± 5.2 days in patients with RS and 13.4 ± 4.6 days in patients receiving standard therapy [14].

Thus, IRI following TLT is associated with an unfavorable clinical course, a greater extent of ischemic–reperfusion brain injury, and poorer functional outcomes.

The diagram clearly demonstrates that the neurological status parameters of patients with IRI after TLT showed some improvement during intensive therapy. However, compared with patients receiving standard therapy and those who underwent TLT without IRI, these changes remained statistically insignificant [15]. On day 7, the GCS score was 12.4 ± 2.6 in patients receiving standard therapy and 14.2 ± 0.8 in patients receiving TLT without RS, whereas in patients who developed IRI after TLT, the GCS score was 12.4 ± 2.6 , indicating the need for

continued intensive therapy (Fig. 1).

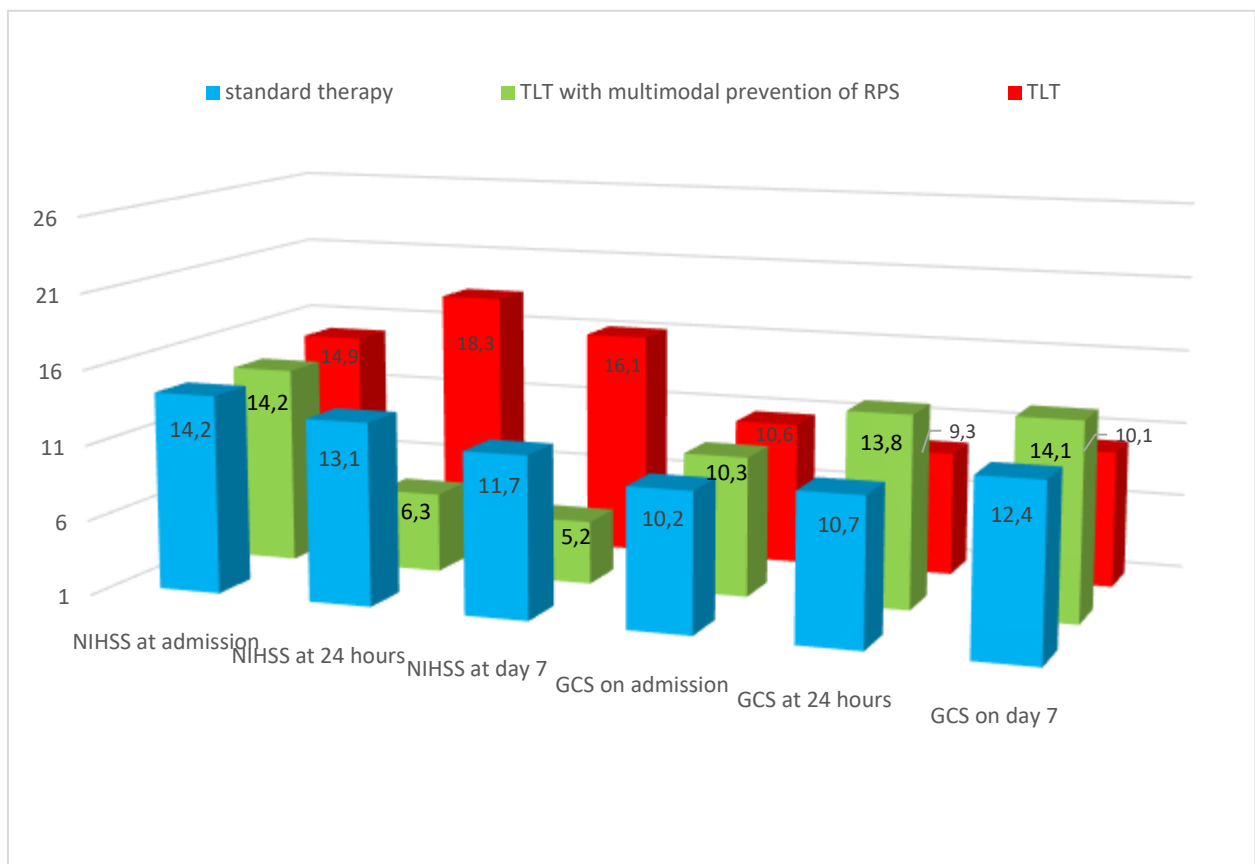


Figure 1. Comparison of neurological status parameters in patients with ischemic stroke receiving standard therapy and thrombolytic therapy without and with the development of IRI.

Instrumental examination: brain computed tomography performed 24 hours after thrombolytic therapy also revealed significant differences between the groups.

In patients without IRI, MSCT showed no formed ischemic lesion, signs of cerebral edema, or hemorrhagic transformation; the cerebral ventricles retained their normal configuration, indicating preserved normal cerebrospinal fluid dynamics [16].

In patients who developed IRI, the following findings were recorded significantly more frequently on MSCT: hemorrhagic transformation; symptomatic intracranial hemorrhage; marked vasogenic cerebral edema; an increase in infarct volume; and signs of cerebral herniation. The obtained results confirm the leading role of blood–brain barrier disruption in the development of IRI [17].

Clinical case: Patient S.S., 56 years old, was brought by relatives to the admission department with complaints of slurred speech and absence of movement and sensation in the left extremities due to ischemic stroke, which had developed 4 hours prior to hospitalization against a background of high blood pressure. According to the medical history, the patient had been suffering from persistent atrial fibrillation for several years and was taking antiarrhythmic and antithrombotic medications irregularly. BMI was 32 kg/m² (grade I obesity) [18].

On admission, the level of consciousness was stupor; the Glasgow Coma Scale score was 10 points and the NIHSS score was 14 points. Deep hemiparesis, hemihypesthesia, and hyporeflexia were noted in the left extremities. After examination by a neurologist and a neurointensivist, taking into account the medical history, the presence of clinical and neurological symptoms, the short duration from disease onset, and the absence of formed ischemic lesions on brain MSCT, systemic thrombolysis with Actilyse was performed at a dose of 0.9 mg/kg [19].

Thrombolytic therapy was not accompanied by significant hemodynamic or respiratory changes. During dynamic observation within the first 6 hours after thrombolytic therapy, an increase in body temperature to 39°C was noted, while the level of consciousness remained at the stupor

level, accompanied by a profound neurological deficit. Subsequently, a gradual worsening of neurological impairment was observed, progressing to hemiplegia, with deterioration of consciousness to grade I coma (GCS 9 points, NIHSS 16–17 points) [20].

Repeat brain MSCT performed 12 hours after TLT demonstrated signs of marked intracranial hypertension, including flattening of the cerebral gyri and cortical convolutions, narrowing of the cerebral ventricles and basal cisterns, as well as areas of hemorrhagic transformation. Fundoscopic examination revealed signs of marked optic disc edema and small petechial hemorrhages around the optic disc [21].

Due to the deterioration of the patient's condition, mechanical ventilation was initiated, and appropriate standard therapy for cerebral edema was administered. However, persistent hyperthermia ($>39^{\circ}\text{C}$), progressive neurological deficit (NIHSS >25 points), and hemodynamic instability persisted, ultimately leading to death on day 7 of the disease [22].

Brain MSCT demonstrated displacement of the midline structures from right to left. The gray and white matter of the brain were no longer differentiated. Diffuse reduction in the density of the brain parenchyma was observed in the right hemisphere. Small areas of hemorrhagic transformation were present within the brain parenchyma. The cytoarchitectonic structure of the cerebral cortex was markedly altered, with pronounced flattening of the cerebral gyri and cortical convolutions [23]. The subarachnoid spaces, cisterns, and cerebral ventricles were markedly narrowed. The lateral ventricles were deformed due to cerebral edema and displacement of the midline structures, while the third and fourth ventricles were not visualized. The cerebellar tonsils were located below the level of the foramen magnum (Fig. 2).

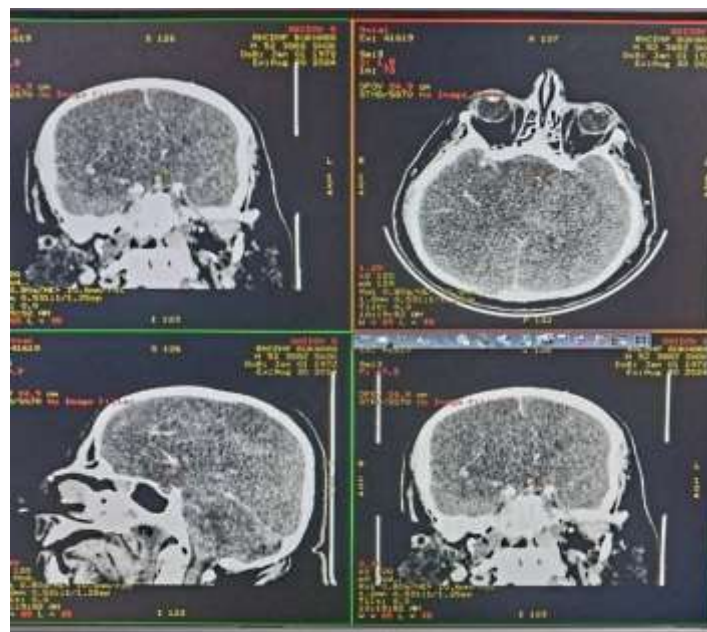


Figure 2. Brain MSCT scan of a patient with ischemic stroke following the development of IRI.

Brain MSCT performed 24 hours after TLT in the patient with IRI demonstrated displacement of the midline structures from left to right. A clearly demarcated area of ischemia was observed in the left parietotemporal region. The differentiation between the gray and white matter of the brain was indistinct. Areas of hemorrhagic transformation were visualized within the ischemic brain tissue [24]. The cerebral gyri and cortical convolutions were flattened. The subarachnoid spaces and cisterns were narrowed, and the left lateral cerebral ventricles were compressed by edematous tissue. The third and fourth ventricles were visualized. The cerebellar tonsils were positioned at the level of the foramen magnum (Fig. 3).

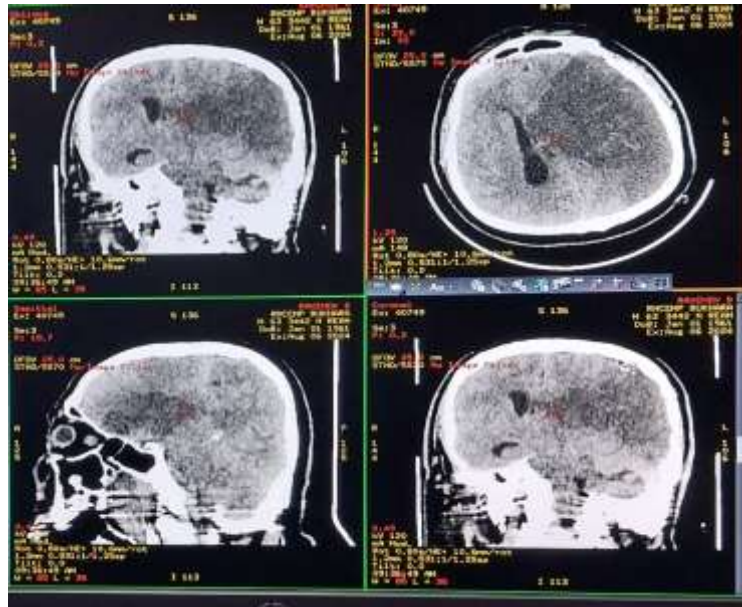


Figure 3. Brain MSCT scan of a patient with ischemic stroke following the development of IRI.

After TLT, the most frequent manifestations of reperfusion syndrome were early neurological deterioration, hyperthermia ($>39^{\circ}\text{C}$), hemorrhagic transformation, cerebral edema, and seizures, table 2.

Table 2.
Types of complications of IRI

Types of complications of IRI	Frequency (%)
Early neurological deterioration	62
Hyperthermia ($>39^{\circ}\text{C}$)	58
Hemorrhagic transformation	48
Cerebral edema	44
Seizure syndrome	12

Multivariable regression analysis demonstrated that independent predictors of the development of reperfusion syndrome (RS) in 19 patients included occlusion of the proximal segments of the middle cerebral artery (M1–M2), hyperglycemia, severe arterial hypertension, cardiac rhythm disturbances (arrhythmias), and metabolic syndrome [25].

Thus, RS following IVT was associated with an unfavorable clinical course, a greater volume of ischemia–reperfusion brain injury, a pronounced neuroinflammatory response, and poorer functional outcomes [26].

Discussion of the Results

In patients who did not develop RS following systemic intravenous thrombolytic therapy, rapid recovery of neurological function was observed. The mean NIHSS score decreased from 14.2 ± 1.8 to 6.0 ± 1.5 at discharge ($p < 0.001$). A favorable functional outcome within 3–5 days was documented in 48 patients (71.7%).

In contrast, in 19 patients (28.3%), the development of RS was accompanied by early neurological deterioration, progression of focal neurological deficits, and worsening of the functional prognosis. In this group, 24 hours after IVT, the mean NIHSS score increased to 18 or higher, consistent with early neurological deterioration. Neuroimaging more frequently demonstrated hemorrhagic transformation, cerebral edema, and an increase in infarct volume [27].

The results obtained support the current concept of ischemia–reperfusion brain injury as a complex multifactorial process involving oxidative stress, inflammatory activation, endothelial dysfunction, disruption of the blood–brain barrier, and secondary neuronal injury [28].

Despite successful IVT and restoration of cerebral blood flow, reperfusion itself does not guarantee a favorable clinical outcome. In a substantial proportion of patients, reperfusion is accompanied by a cascade of pathological reactions leading to secondary injury of previously viable brain tissue [29].

The high incidence of hemorrhagic transformation and symptomatic intracranial hemorrhage in patients with RS suggests that impaired vascular permeability represents one of the central mechanisms underlying its pathogenesis.

These findings emphasize the need for early identification of patients at high risk, dynamic monitoring of clinical status, and serial assessment of neuroimaging changes following thrombolytic therapy [30].

The results indicate the potential value of developing novel preventive and neuroprotective strategies aimed at reducing the severity of ischemia–reperfusion injury and improving the efficacy of reperfusion therapy.

In contemporary English-language literature, the term ischemia–reperfusion injury (IRI) is more commonly used to describe the spectrum of pathological processes that develop following restoration of cerebral perfusion. Most recent publications use the term “reperfusion injury”, as it is widely accepted in the AHA/ASA and ESO recommendations and in contemporary English-language scientific literature [31].

This concept reflects the multifactorial nature of the injury and encompasses oxidative stress, mitochondrial dysfunction, activation of innate immunity, neuroinflammation, endothelial dysfunction, disruption of blood–brain barrier integrity, the phenomenon of microvascular obstruction, as well as the development of cytotoxic and vasogenic edema and hemorrhagic transformation of the ischemic lesion.

However, ischemia–reperfusion injury is primarily a pathophysiological concept. It describes the underlying process and mechanisms of cellular injury at the microstructural level that occur when blood flow is abruptly restored to previously ischemic brain tissue, including the generation of reactive oxygen species, cellular edema, and inflammatory activation [32].

When ischemia–reperfusion injury develops following successful restoration of cerebral blood flow, for example after thrombus dissolution, it may manifest clinically as a constellation of symptoms, including neurological deterioration (worsening paresis and speech impairment), severe headache associated with abrupt reperfusion and cerebral edema, general cerebral symptoms (depressed consciousness, nausea, and vomiting), seizures, and hemorrhagic transformation, representing a complication in which damaged vessels are unable to withstand increased intravascular pressure, resulting in extravasation of blood into the brain tissue [33].

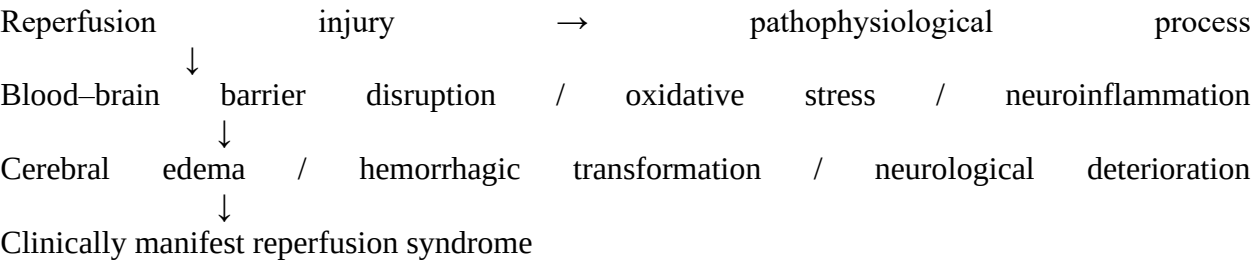
From this perspective, ischemia–reperfusion injury refers to the underlying pathological processes occurring at the cellular and tissue levels, whereas the clinically apparent result of these processes, manifested by a constellation of neurological, systemic, laboratory, and neuroimaging abnormalities, may be conceptualized as reperfusion syndrome.

Reperfusion syndrome is a clinical medicine term describing the specific constellation of manifestations observed at the bedside when the underlying pathophysiological process of ischemia–reperfusion injury becomes clinically apparent [34].

In the present study, we propose considering ischemia–reperfusion injury as the pathophysiological basis of an independent reperfusion syndrome, reflecting the combination of clinical manifestations and pathophysiological responses that develop as a consequence of reperfusion injury following successful recanalization of an occluded cerebral artery during systemic intravenous thrombolytic therapy or mechanical thrombectomy. This approach provides a logical distinction whereby reperfusion injury represents the underlying pathogenetic process, whereas reperfusion syndrome represents its clinical manifestation, integrating neurological symptoms, laboratory and immunological abnormalities, and neuroimaging findings [35].

It should be noted that the term “reperfusion syndrome” in the context of ischemic stroke following reperfusion therapy is considerably less frequently used in contemporary literature

than the term “reperfusion injury.” Nevertheless, the use of this term may be clinically justified because it integrates the clinical manifestations, instrumental findings, and immunoinflammatory changes occurring during the early post-reperfusion period. Furthermore, the term “reperfusion syndrome” directs the clinician not only toward the fact of restored cerebral blood flow but also toward the need for active prediction, early detection, and prevention of adverse consequences of reperfusion. This is of particular importance for personalized intensive care and improvement of outcomes in patients with acute ischemic stroke. In our opinion, the term “reperfusion syndrome” should not be regarded as an alternative to the established concept of “reperfusion injury”. Rather, these terms describe different levels of the same pathological process. Reperfusion injury characterizes the molecular, cellular, and tissue-level mechanisms that arise following restoration of blood flow, whereas reperfusion syndrome represents their clinical manifestation, expressed as a combination of neurological, neuroimaging, laboratory, and immunoinflammatory abnormalities.



The use of the term “reperfusion syndrome” makes it possible to integrate these manifestations into a unified clinical and pathophysiological concept, thereby facilitating early diagnosis, risk stratification, personalization of intensive care, and the development of preventive interventions in patients with ischemic stroke following reperfusion therapy.

Conclusions

Reperfusion syndrome represents one of the most clinically significant complications following systemic intravenous thrombolytic therapy and is associated with a significant deterioration in neurological status, lower Glasgow Coma Scale scores, higher NIHSS scores, and greater functional disability.

Early identification of patients at high risk of developing reperfusion syndrome, together with comprehensive clinical and instrumental assessment, enables timely prediction of an unfavorable disease course and optimization of intensive care.

A promising direction for future research is the development of preventive strategies for reperfusion syndrome based on the combination of contemporary reperfusion technologies with neuroprotective, anti-inflammatory, and endothelial-protective therapies.

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