

Dynamic Changes in Mast Cell-Derived Histamine and Tryptase Following Reperfusion Therapy in Acute Ischemic Stroke

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Abstract

Ischemic stroke (IS) is characterized by complex inflammatory mechanisms that contribute to both primary injury and reperfusion-related damage. Among inflammatory mediators, mast cell-derived histamine and tryptase have been implicated in blood–brain barrier disruption and neuroinflammation, yet their dynamics following thrombolysis remain unclear.

This study investigated plasma histamine and tryptase levels in patients with acute IS before and after intravenous thrombolytic therapy and examined their association with clinical and laboratory parameters. At admission, both mediators were significantly elevated. Following thrombolytic therapy, histamine and tryptase decreased significantly, corresponding to an approximately 1.5-fold decrease.

Correlation analysis revealed positive associations between both mediators and triglycerides, hemoglobin, and bleeding time, while post-thrombolysis tryptase levels are additionally associated with clotting time. Although mean neurological improvement was not significant, 45% of patients showed clinical improvement following treatment.

In conclusion, our findings suggest that thrombolysis may modulate mast cell-related inflammatory activity, metabolic pathways, and coagulation processes in acute IS.

Keywords: Ischemic stroke, histamine, tryptase, ELISA, thrombolysis

Introduction

Ischemic stroke (IS) is an acute cerebrovascular disease caused by occlusion of a cerebral artery, resulting in interruption of cerebral blood flow and oxygen/glucose deprivation. It is the most common type of stroke and remains a leading cause of mortality and long-term disability worldwide, imposing a substantial socioeconomic burden (1). Despite advances in acute management, the complex pathophysiological mechanisms underlying ischemic brain injury and recovery remain incompletely understood.

The pathophysiology of IS involves a complex ischemic cascade initiated by cerebral hypoperfusion. Cellular energy failure leads to disruption of ionic homeostasis, neuronal depolarization, and excessive glutamate release, resulting in excitotoxicity. Subsequent intracellular calcium overload, oxidative stress, mitochondrial dysfunction, and activation of inflammatory pathways (2). The ischemic core undergoes irreversible injury, whereas the surrounding penumbra represents potentially salvageable tissue, highly dependent on timely reperfusion (3).

Inflammation plays a central role in both primary ischemic injury and secondary damage following reperfusion. Among the various immune cells involved, mast cells have emerged as early and critical regulators of neuroinflammation. Mast cells are strategically located in the perivascular space and meninges, enabling rapid modulation of blood–brain barrier (BBB) integrity and neurovascular responses (4). Upon activation, they release a broad spectrum of mediators, including histamine and tryptase.

Histamine is a potent vasoactive amine that increases vascular permeability, promotes vasodilation, and contributes to BBB disruption and cerebral edema (4, 5). Tryptase, a mast cell-specific serine protease, activates protease-activated receptors (PARs), enhances inflammatory signaling, and contributes to extracellular matrix degradation and BBB

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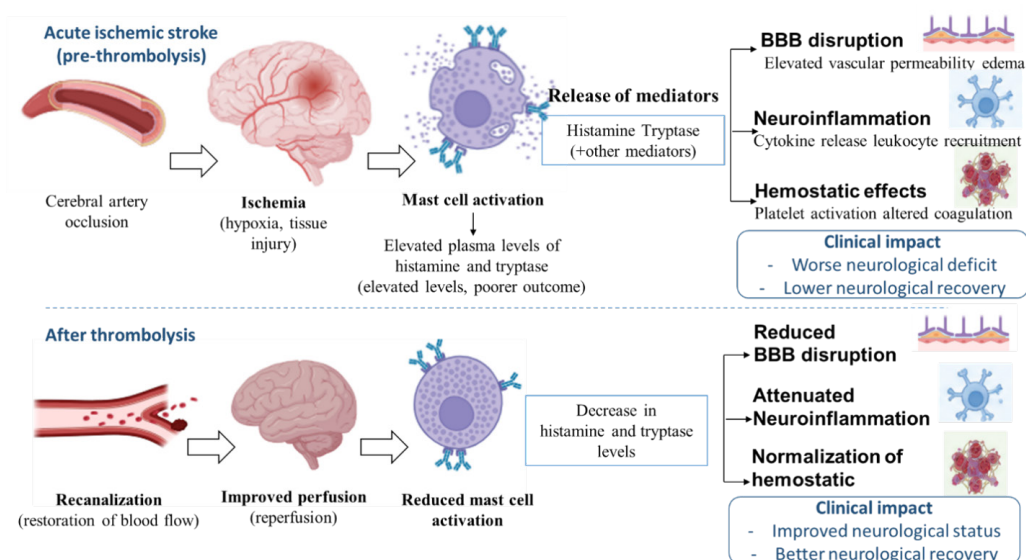


Figure 1. Proposed role of mast cell activation in acute IS and modulation by thrombolysis. Schematic representation of the pathophysiological mechanisms in IS and the role of mast cell–derived mediators during thrombolysis.

breakdown (5). Accumulating evidence suggests that mast cell activation may exacerbate ischemic injury and contribute to reperfusion-induced neurovascular damage (4, 5).

Reperfusion therapies are the cornerstone of acute IS treatment, aiming to restore cerebral blood flow, preserve the ischemic penumbra, and improve neurological outcomes. Intravenous thrombolysis with recombinant tissue plasminogen activator (rtPA) is an established therapeutic approach when administered within a defined time window. rtPA promotes fibrinolysis through conversion of plasminogen to plasmin, leading to thrombus dissolution (6). However, reperfusion may paradoxically induce additional injury, known as reperfusion injury, characterized by oxidative stress, neuroinflammation, and BBB breakdown (2, 4, 6).

The mast cell–mediated neuroinflammation and reperfusion injury in IS are presented schematically on the original Figure 1.

Cerebral ischemia leads to energy failure, excitotoxicity, calcium overload, oxidative stress, and irreversible damage in the ischemic core, while the penumbra remains potentially salvageable. Activated mast cells release histamine and tryptase, promoting BBB disruption, vascular permeability, and neuroinflammation.

Intravenous thrombolysis with rtPA restores blood flow but may also induce reperfusion injury characterized by oxidative stress, inflammation, and further mast cell activation. Elevated levels of histamine and tryptase may be associated with clinical outcomes.

Mast cells are known as key immune sensors of the tissue microenvironment. They are capable of rapidly releasing various preformed biologically active molecules, while also synthesizing inflammatory mediators *de novo* following activation (7). Mast cells show transcriptional profiles that differ markedly from other cell types of the immune system (8). It is also

accepted that mast cells are evolutionarily ancient and function as first-line sentinels of the immune system against pathogens and tissue injury (9). Consequently, mast cells and their secreted mediators play pivotal roles in the initiation and amplification of immune-inflammatory responses.

Despite increasing evidence implicating inflammation in reperfusion injury, data regarding mast cell activation and the dynamics of their mediators - particularly histamine and tryptase - following intravenous thrombolysis remain limited. Moreover, the relationship between these biomarkers, thrombolytic therapy, and clinical outcomes in acute IS has not yet been fully elucidated.

The aim of the present study was to investigate the effects of intravenous thrombolysis on plasma levels of mast cell–derived mediators—tryptase and histamine—in patients with acute IS, and to assess their association with clinical parameters.

To our knowledge, this is one of the first clinical studies evaluating the dynamic changes in circulating histamine and tryptase before and after intravenous thrombolysis in patients with acute IS while simultaneously examining their associations with neurological outcome, coagulation parameters, and metabolic markers.

Materials and Methods

Patients

This was a prospective observational single-center study conducted at the Neurology Department of University Hospital Pulmed from May 2024 till May 2026. A total of 31 patients with acute IS treated with intravenous thrombolysis were included in the study. The cohort comprised both male ($n=18$) and female ($n=13$) patients and was characterized by an overall advanced age (mean age of 74.2 ± 9.19 years), consistent with the known epidemiological profile of IS. Baseline neurologi-

cal status was assessed at admission and at discharge using the National Institutes of Health Stroke Scale (NIHSS) and by the Glasgow Liege Coma Scale (GLCS). Cerebral CT scans were performed at admission and after thrombolysis. The mean body weight was 78.8 ± 15.1 kg. Basic hematological and biochemical clinical laboratory parameters were examined. The study was approved by the Ethics Committee at the Medical University of Plovdiv (Protocol No 2/07.02.2024).

Intravenous thrombolysis

All patients underwent intravenous thrombolysis with recombinant tissue plasminogen activator (rtPA) within 4.5 hours from symptom onset or last time known well. The rtPA dose was weight-adjusted, with a maximum of 90 mg. Their eligibility for IVT was assessed according to the inclusion and exclusion criteria defined in the current National Protocol of the Republic of Bulgaria.

Inclusion criteria: 1. Acute ischemic stroke within 4.5 hours from symptom onset; 2. Neurological deficit with NIHSS score ≤ 22 ; 3. Normal non-contrast brain CT or early ischemic changes involving no more than one-third of the cerebral hemisphere; 4. Age ≥ 18 years; 5. The patient and/or relatives have been informed about the potential risks and benefits of treatment and have signed informed consent. The patient must meet all the above inclusion criteria simultaneously.

Exclusion criteria: 1. Symptom onset >4.5 hours; 2. Transient, minor, or isolated neurological deficits (isolated distal motor weakness, isolated aphasia, dysarthria, ataxia, hemianopia, postictal paresis) or NIHSS score >22 ; 3. Intracranial hemorrhage of any location; 4. Increased risk of bleeding, including: • Systolic BP >185 mmHg or diastolic BP >110 mmHg, • History of intracranial hemorrhage, • Known bleeding diathesis, • Anticoagulant therapy with INR ≥ 1.5 , • Prothrombin activity $<60\%$, • Heparin treatment with prolonged aPTT, • Platelet count $<100,000/\mu\text{L}$, • Traumatic brain injury or ischemic stroke within the previous 3 months; • Intracranial neoplasm, arteriovenous malformation, or aneurysm, • Hemorrhagic retinopathy (e.g., diabetic retinopathy), • Uncontrolled severe hypertension, • Esophageal varices, • Documented gastric ulcer within the previous 3 months, • Severe malignancy or severe liver disease, including cirrhosis or active hepatitis, • Major surgery or severe trauma within the previous 14 days, • Gastrointestinal or urinary tract bleeding within the previous 21 days, • Evidence of active bleeding or acute trauma (fracture), • Arterial puncture within the previous 7 days; 5. Severe traumatic brain injury (brain contusion or skull fracture) within the previous 3 months; 6. Blood glucose <2.7 mmol/L; 7. Children, pregnant women, or breastfeeding women; 8. Seizure with persistent postictal neurological deficit; 9. Myocardial infarction within the previous 3 months; 10. Bacterial endocarditis, pericarditis, or acute pancreatitis. The presence of any of the above constitutes an exclusion criterion. For intravenous thrombolytic therapy, the patient must meet all inclusion criteria and none of the exclusion criteria.

Additional exclusions were hypoglycemia (<2.7 mmol/L), pregnancy or breastfeeding, postictal neurological deficit, recent myocardial infarction ≤ 3 months, and bacterial endocarditis, pericarditis, or acute pancreatitis.

Post-thrombolysis management

Following intravenous thrombolysis, all patients received standard supportive and intensive care management, including blood pressure control, vasoactive therapy when indicated, and symptomatic treatment.

A follow-up non-contrast brain CT was performed 24 hours after thrombolysis in all patients, and subsequent antithrombotic therapy was determined accordingly. Treatment strategies included single or dual antiplatelet therapy, combined antiplatelet therapy with low-molecular-weight heparin, or oral anticoagulation.

All patients remained hospitalized for at least 4 days following thrombolytic treatment.

Plasma extraction

Venous blood was collected in standard vacutainers containing anticoagulant (K-EDTA). The samples were centrifuged for 10 min at 1800 rpm to separate the plasma and subsequently aliquoted to avoid multiple freeze-thaw cycles and stored at -80°C until analysis.

Before performing the tests, the samples were thawed on ice and tempered to room temperature, avoiding prolonged exposure to elevated temperature to preserve the biological activity of the analyzed molecules.

Protein levels (ELISA)

Plasma tryptase and histamine levels were quantified by enzyme-linked immunosorbent assay (ELISA), according to the manufacturer's instructions.

For the determination of tryptase, a Human TPSAB1 (Tryptase alpha/beta-1) ELISA Kit (cat. no. EH1204) was used. Histamine levels were measured via the Human Histamine ELISA Kit (cat. no. EK711054).

All samples and standards were analyzed in duplicate and the mean value was used for statistical analysis. Optical density was measured with a microplate spectrophotometer at the appropriate wavelength 450 nm (Tecan Sunrise Remote Microplate Reader - Elisa Assay Absorbance 96 plate, Austria), and concentrations were calculated by constructing standard curves. Results are presented in ng/ml.

Statistical analysis

Statistical analyses were performed using GraphPad Prism version 10.2.3 (GraphPad Software LLC, San Diego, CA, USA). Normality of continuous variables was assessed using the Shapiro–Wilk test. Data are presented as mean $\pm$ standard deviation (SD) for normally distributed variables or as median with interquartile range (IQR) for non-normally distributed variables. Categorical variables are presented as counts and percentages.

Within-subject comparisons between baseline and post-treatment measurements were performed using paired Student's t-test for normally distributed variables and Wilcoxon signed-rank test for non-normally distributed variables. Post-treatment NIHSS values were non-normally distributed and were therefore analyzed using the Wilcoxon signed-rank test.

Associations between plasma histamine and tryptase levels and clinical or laboratory parameters were assessed using Spearman's rank correlation coefficient due to small sample size and non-normal distribution of variables. Given the exploratory nature of the analysis and the large number of comparisons, no formal correction for multiple testing was applied; therefore, results should be interpreted cautiously.

Multiple linear regression analysis was performed to evaluate independent predictors of neurological outcome. NIHSS score at discharge was used as the primary dependent variable. Independent variables included baseline histamine, baseline tryptase, age, sex, body weight, and baseline NIHSS score.

Multicollinearity was assessed using variance inflation factor (VIF), with no evidence of significant collinearity (all VIF < 2.5). Model assumptions, including normality of residuals and homoscedasticity, were evaluated by visual inspection of residual plots and were found to be acceptable.

Results

We present original data based on histamine and tryptase levels in IS patients in association with thrombolytic therapy.

The included cohort reflects the inherent heterogeneity of acute IS, encompassing variability in demographic characteristics, baseline neurological impairment, metabolic status, and inflammatory profile. Such diversity is representative of real-world clinical practice and provides a relevant context for evaluating the interplay between inflammatory mediators and therapeutic response. Body weight varied across patients, generally ranging within typical adult values, reflecting diversity in anthropometric profiles. Baseline neurological status, assessed using the NIHSS, covered a broad spectrum of stroke severity, including patients with mild, moderate, and more severe neurological deficits at admission. Although no significant change in mean NIHSS score was observed at the group level, a substantial proportion of patients (approximately 45%) exhibited clinically meaningful improvement (Table 1).

Laboratory parameters revealed variability in metabolic and inflammatory status among patients. Lipid profile components, including total cholesterol (mean±SD 4.9 ± 1.7 mmol/l) and triglycerides (mean±SD 1.5 ± 0.68 mmol/l), as well as blood glucose levels, exhibited a wide distribution, suggesting differing degrees of vascular risk burden within the cohort.

Hematological parameters such as hemoglobin, along with hemostatic measures including clotting time and bleeding time, also varied, indicating heterogeneity in baseline physiological and coagulation status. In addition, inflammatory markers such as C-reactive protein (CRP) showed inter-individual variability, further supporting the presence of diverse inflammato-

Table 1. Clinical evaluation of patients with IS before and after thrombolytic therapy

Parameters	Before therapy (n=31 mean±SD)	After therapy (n=31 mean±SD)
NIHSS	8.5 ± 4.1	7.5 ± 5.8
GLCS	18.3 ± 2.1	18.2 ± 4.6

ry responses among patients with acute IS.

The ELISA assay revealed that plasma levels of both mast cell mediators, histamine and tryptase, were elevated at admission. Mean tryptase levels prior to thrombolysis were 6.9 ± 0.6 ng/ml, while histamine levels reached 69 ± 6.9 ng/ml. Following thrombolytic therapy, a significant reduction was observed in both parameters, with tryptase decreasing to 4.6 ± 0.6 ng/ml and histamine to 45.9 ± 6.3 ng/ml.

Quantitatively, tryptase levels decreased approximately 33% (1.5-fold reduction), and histamine levels showed a comparable 1.5-fold decrease. These reductions were highly statistically significant for both mediators ($p < 0.0001$) (Figure 2).

Correlation analysis before thrombolysis

Correlation analysis was performed to evaluate potential associations between plasma levels before thrombolysis of histamine and tryptase and a wide range of clinical and laboratory parameters, including sex, age (mean ± SD 74.2 ± 9.19), body weight (mean ± SD 77.3 ± 14.8 kg), NIHSS score at admission (mean ± SD 7.8 ± 4.1) and discharge (mean ± SD 7.5 ± 10.6), GLCS score at admission (mean ± SD 18.3 ± 2.1) and discharge (mean ± SD 18.2 ± 4.6), hemoglobin (HGB) (mean±SD 144.2 ± 16.5 g/L), clotting time (mean ± SD 275.8 ± 25.8 sec), bleeding time (mean ± SD 79.8 ± 13.7 sec), fibrinogen (mean ± SD 3.1 ± 0.5 g/l), sodium (mean ± SD 138.4 ± 10.2 mmol/l), potassium (mean ± SD 4.2 ± 0.3 mmol/l), chloride (mean ± SD 101.4 ± 8.7 mmol/l), total cholesterol (mean±SD 4.9 ± 1.6 mmol/l), triglycerides (mean ± SD 1.5 ± 0.6 mmol/l), and C-reactive protein (CRP) (mean ± SD 7.4 ± 2.9 mg/l).

Statistically significant correlations were identified only for triglycerides, hemoglobin (HGB), and bleeding time (Table 2).

A positive correlation was found between histamine levels before thrombolysis and triglycerides ($r = 0.48$; $p = 0.013$). A trend towards a significant correlation was observed between histamine before thrombolysis and hemoglobin (HGB) ($r = 0.41$; $p = 0.05$). In addition, a statistically significant positive correlation was found between histamine levels and bleeding time ($r = 0.45$; $p = 0.036$).

Tryptase levels showed a moderate positive correlation with triglycerides ($r = 0.48$; $p = 0.013$), as well as with bleeding time ($r = 0.45$; $p = 0.036$). A weak correlation between tryptase and hemoglobin was also positive and borderline statistically significant ($r = 0.41$; $p = 0.05$).

Correlation analysis after thrombolysis

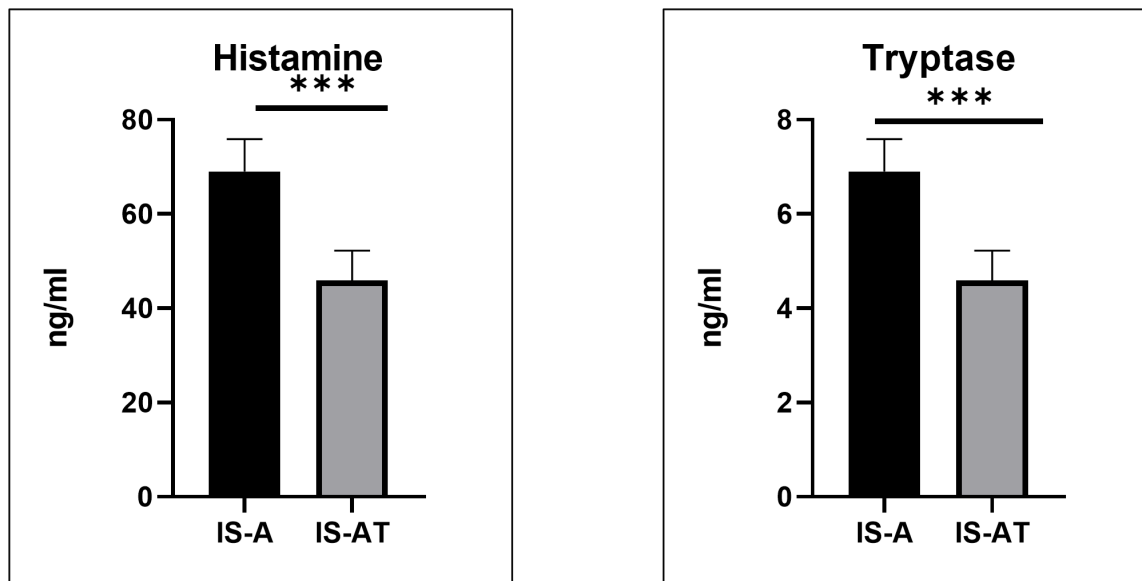


Figure 2. Histamine and tryptase levels in ischemic stroke patients at admission, before thrombolysis (IS-A) and after thrombolysis (IS-AT). Data are mean $\pm$ SD; *** $p < 0.001$.

In addition, post-thrombolysis tryptase levels were positively correlated with clotting time ($r = 0.45$; $p = 0.04$), indicating that higher tryptase concentrations were associated with prolonged coagulation time.

Table 2. Statistical correlations of histamine and tryptase levels before thrombolysis for triglycerides, hemoglobin (HGB), and bleeding time.

Parameters	Triglycerides	HGB	Bleeding time
Histamine levels before thrombolysis	0.48 ($p=0.013$)	0.41 ($p=0.050$)	0.45 ($p=0.036$)
Tryptase before thrombolysis	0.48 ($p=0.013$)	0.41 ($p=0.050$)	0.45 ($p=0.036$)

Association with neurological outcome

We evaluated the predictive outcome of histamine and tryptase levels measured prior to thrombolytic therapy in relation to clinical scores at discharge. Tryptase concentrations were approximately ten times lower than histamine concentrations. For this reason, both biomarkers exhibited identical predictive value and were therefore analyzed together in the models, or one was used as a representative of the other. The results revealed a positive correlation between the levels of both molecules before thrombolysis and NIHSS scores at discharge ($r = 0.54$, $p = 0.012$), indicating that higher biomarker levels were associated with persisting more severe clinical symptoms at the end of hospitalization.

No significant correlation was observed between baseline mast cell mediators and GLCS scores at admission. However, higher baseline levels of histamine and tryptase were associated with lower GLCS scores at discharge ($r = -0.49$, $p = 0.026$).

Regression analysis

Multiple linear regression analysis demonstrated that baseline histamine and tryptase levels were independent predictors of NIHSS score at discharge.

The model was statistically significant ($R^2 = 0.742$, $F(5,25) = 25.8$, $p < 0.001$). Both histamine ($\beta = 0.38$, $p = 0.003$) and tryptase ($\beta = 0.36$, $p = 0.004$) independently contributed to the prediction of outcome after adjustment for age, sex, body weight, and baseline NIHSS.

Baseline NIHSS was also an independent predictor of discharge NIHSS ($\beta = 0.44$, $p < 0.001$), whereas age, sex, and body weight were not statistically significant predictors in the model.

Discussion

This investigation provides the first prospective clinical study evaluating changes in circulating mast cell mediators (histamine and tryptase) before and after intravenous thrombolysis in patients with acute IS, together with their association with neurological outcome and their potential prognostic significance.

The present study demonstrates that mast cell-derived mediators, histamine and tryptase, are elevated in the acute phase of IS and significantly decrease following intravenous thrombolysis. Interestingly, the statistical analyses performed to predict the outcome of histamine/tryptase complement each other in a perfect and logical way. It was found that high levels correlate with high NIHSS at discharge. This corresponds to a more pronounced neurological deficit. On the other hand, in-

creased levels of the studied molecules correlate with low GLCS at discharge. This reflects a limited neurological recovery. The results indicate that high levels of histamine and tryptase at admission can successfully predict a worse clinical outcome.

These findings support the involvement of mast cell activation in the pathophysiology of IS and suggest that reperfusion therapy may attenuate mast cell-associated inflammatory responses. Moreover, our results suggest that mast cell activation may be integrated within a broader pathophysiological network linking inflammation, lipid metabolism, and hemostatic regulation in acute IS.

The consistent reduction in histamine and tryptase levels following thrombolysis likely reflects attenuation of mast cell activation after restoration of cerebral blood flow. Given the established role of mast cells in BBB disruption, vascular permeability, and neuroinflammation, these findings may indicate partial normalization of the neurovascular environment following reperfusion therapy.

In contrast, clinical outcomes demonstrated considerable heterogeneity with approximately 45% of patients showing clinically meaningful improvement. This apparent dissociation between clinical and biochemical responses highlights the complex and multifactorial nature of stroke recovery, suggesting that changes in biomarkers following thrombolysis may not directly parallel short-term neurological outcomes.

The observed correlations between mast cell mediators and selected metabolic and hemostatic parameters provide further insight into the potential systemic role of mast cell activation in acute IS. The positive associations of histamine and tryptase with triglyceride levels suggest a link between mast cell activity and lipid metabolism. This finding is consistent with previous evidence implicating mast cells in metabolic dysregulation and atherosclerotic processes, where their mediators contribute to vascular inflammation and lipid accumulation (10-12).

It was shown that patients with low HDL are more likely to suffer a stroke or other cardiovascular incidents, indicating that HDL protects against acute IS (13). Maes et al. demonstrated that increased lipid peroxidation and lowered lipid-associated antioxidant defenses may independently predict stroke outcome. High lipid peroxidation and decreased activity of the PON1-HDL complex and -SH groups are suggested as therapeutic targets for the prevention of acute IS and following neurodegeneration due to ischemia-reperfusion injury (14).

Several studies report mast cells can be activated by cholesterol-dependent cytolytic toxins, a class of pore-forming toxins whose membrane-disrupting activities depend on the presence of cholesterol in the plasma membrane of host cells (15). In addition, the positive correlations between mast cell mediators and bleeding time, as well as the association between post-thrombolysis tryptase levels and clotting time, support the involvement of mast cells in the regulation of hemostasis.

By protein-protein interaction (PPI) network analysis it was revealed that the backbone of the highly connective network of IS-associated death consisted of several molecules including the Von Willebrand Factor (VWF) - a key glycoprotein that

facilitates hemostasis by acting as a bridge between platelets and damaged blood vessel walls. Cluster analysis uncovered immune and hemostasis subnetworks, which were strongly interconnected through the major switches *ALB* and *VWF* (16). Therefore, IS-associated death may be prevented by targeting VWF along with some other molecules.

Tryptase has been shown to interfere with fibrin formation and modulate coagulation pathways, whereas mast cell degranulation leads to the release of multiple bioactive substances, including histamine and heparin, which exert anticoagulant and profibrinolytic effects (17, 18). Collectively, these mechanisms may contribute to the prolongation of bleeding and coagulation times observed in patients with elevated mast cell mediator levels.

Mast cell activation may affect hemostasis through effects on vascular and cellular components, as well as by clotting and fibrinolytic factors. Histamine, as a key mediator released by activated mast cells, has been implicated in hemostatic processes (19). Platelet activation may also trigger mast cell activation and mediator release, thereby contributing to disbalanced hemostasis (20).

Furthermore, the borderline association with hemoglobin may reflect underlying interactions between inflammatory activation and hematological status, although this finding requires further investigation.

Notably, the observed correlations between mast cell mediators and metabolic as well as hemostatic parameters such as triglycerides, bleeding time, and clotting time, suggest that mast cell activation may participate in a broader systemic network linking inflammation, lipid metabolism, and coagulation. Mast cell-derived mediators, particularly tryptase, have been implicated in vascular inflammation, extracellular matrix remodeling, and modulation of coagulation pathways, thereby providing a biologically plausible explanation for these associations. The lack of concordance between uniform biochemical changes and heterogeneous clinical outcomes suggests that mast cell activation may reflect a systemic inflammatory response rather than a direct determinant of short-term neurological recovery. Alternatively, the findings may indicate that multiple interacting mechanisms - including vascular, metabolic, and inflammatory pathways, collectively contribute to clinical outcomes following reperfusion therapy.

Taken together, our findings identify mast cell activation as a potential mechanistic link between inflammatory, metabolic, and hemostatic processes in acute IS and suggest that its modulation following thrombolysis may represent an important component of the systemic response to reperfusion therapy. These observations suggest a potential dissociation between inflammatory and neurological responses and highlight the need for further studies to clarify the role of mast cell activation in stroke outcomes.

However, this study has several limitations. First, the relatively small sample size limits statistical power and the generalizability of the findings. Second, the single-center observational design precludes causal inference. Only short-term biomarker

changes following thrombolysis were evaluated, without long-term clinical follow-up and no non-thrombolysis control group was included. Finally, residual confounding by comorbidities, medications, and stroke subtype cannot be excluded. Therefore, our findings require validation in larger cohorts.

Conclusion

Intravenous thrombolysis in acute IS was associated with a significant reduction in the circulating mast cell mediators histamine and tryptase, suggesting modulation of mast cell-related inflammatory responses following reperfusion. Nevertheless, neurological recovery, as assessed by the NIHSS, remained heterogeneous among patients.

Higher pre-treatment concentrations of histamine and tryptase were associated with higher NIHSS scores and lower GLCS scores at discharge, indicating a relationship between increased mast cell activation and less favorable short-term neurological outcomes. These complementary findings support the potential prognostic relevance of mast cell-derived mediators in acute IS.

If validated in larger studies, these findings consistently suggest that higher pre-treatment levels of histamine and tryptase are associated with worse clinical outcomes and may serve as promising candidate biomarkers in acute IS.

Ethical Approval

The study was approved by the Ethics Committee at the Medical University of Plovdiv (Protocol No 2/07.02.2024).

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Conflict of Interest

The authors declare that they have no conflict of interest.

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