MEDICAL SCIENCES

OPEN ACCESS

CLINICAL ASSESSMENT OF RISK FACTORS FOR TRAUMATIC BRAIN INJURY OUTCOMES IN PREHOSPITAL AND EMERGENCY DEPARTMENT CARE

Natalia MOCANU[1,2], Larisa REZNEAC[1,2], Natalia CATANOI[1,2], Tatiana MALACINSCHI-CODREANU[1,2], Elina SHOR[1]

[1] *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova
[2] Institute of Emergency Medicine, Chisinau, Republic of Moldova

Corresponding author: Natalia Mocanu, e-mail: natalia.scurtov@usmf.md

https://doi.org/10.38045/ohrm.2026.3.03 CZU: 616.831-001.3-06-07

ABSTRACT

Introduction Traumatic brain injury (TBI) remains a major global health burden, associated with high mortality and long-term disability. Secondary brain injury related to hypoxia and hypotension worsens outcomes, particularly in the prehospital stage.

Materials and methods This retrospective observational study included 486 adult patients with acute TBI managed between 2020 and 2024 in the prehospital setting and in the Emergency Department of the Institute of Emergency Medicine, Chisinau, Republic of Moldova. Injury severity was assessed using the Glasgow Coma Scale. Associations between physiological parameters and clinical outcomes were analyzed using Pearson's correlation coefficient.

Results Advanced age, low systolic blood pressure, and prehospital hypoxia were significantly associated with greater TBI severity and increased mortality ($p < 0.0001$). Hypoxia showed a moderate positive correlation with both severity and mortality. Hyperglycemia was not associated with injury severity but correlated significantly with mortality.

Conclusions Early recognition and correction of hypoxia and hypotension during prehospital care are essential to limit secondary brain injury and improve outcomes in patients with TBI.

Keywords Traumatic brain injury, hypoxia, hypotension, mortality, prognosis, risk factors, secondary brain injury.

EVALUAREA CLINICĂ A FACTORILOR DE RISC ÎN TRAUMATISMUL CRANIO-CEREBRAL ÎN STADIUL PRESPITAL ȘI ÎN DEPARTAMENTUL DE MEDICINĂ DE URGENȚĂ

Introducere Traumatismul cranio-cerebral (TCC) reprezintă o problemă majoră de sănătate, asociată cu mortalitate și dizabilitate crescută. Leziunile cerebrale secundare, determinate de hipoxie și hipotensiune, influențează negativ prognosticul, în special în etapa prespitalicească.

Materiale și metode Studiul retrospectiv observațional a fost realizat pe un lot de 486 pacienți adulți cu TCC acut, evaluați în perioada 2020–2024, în etapa prespitalicească și în Departamentul de Medicină de Urgență al Institutului de Medicină Urgentă din Chișinău, Republica Moldova. Severitatea leziunii a fost apreciată prin scala Glasgow. Corelațiile dintre parametrii fiziologici și rezultatele clinice au fost analizate utilizând coeficientul de corelație Pearson.

Rezultate Vârsta înaintată, hipotensiunea și hipoxia prespitalicească au influențat semnificativ severitatea TCC și mortalitatea ($p < 0,0001$). Hipoxia, însă, a prezentat corelații pozitive moderate. Hiperglicemia nu s-a asociat cu severitatea, dar a corelat semnificativ cu mortalitatea.

Concluzii Monitorizarea și ajustarea precoce a hipoxiei și hipotensiunii la etapa prespitalicească au fost esențiale pentru reducerea leziunilor secundare și îmbunătățirea prognosticului.

Cuvinte-cheie Traumatism cranio-cerebral, hipoxie, hipotensiune, mortalitate, prognostic, factori de risc, leziuni cerebrale secundare.

INTRODUCTION

Traumatic brain injury (TBI) remains a major global public health concern, with substantial social and economic consequences. Its incidence varies across regions, ranging from 2.18 to 8.65 cases per 1,000 population, with a markedly higher prevalence among males. In countries such as the United States, the United Kingdom, China, Finland, and Sweden, TBI-related hospitalization rates are approximately 2 per 1,000 population (1).

The leading causes of TBI are road traffic accidents, falls, and interpersonal violence, accounting for 80-90% of all cases (2, 3). Central nervous system injuries represent 30-40% of all trauma cases and are the primary contributors to post-traumatic disability (25-30%) (3, 4). In young adults aged 18–35 years, TBI is the leading cause of trauma-related death (1, 3).

In the Republic of Moldova, recent trends indicate a rise in the number of TBI cases managed during the prehospital care, increasing from 16.443 cases in 2021 to 17.493 in 2022. In the national trauma profile, TBI ranks second after musculoskeletal injuries.

Pathophysiologically, TBI involves both primary brain injuries, either focal or diffuse, and secondary injury developing after the initial insult. Secondary injury may result from systemic factors, including hypoxia, hypotension, and hyperglycemia, as well as intracranial factors such as cerebral edema, raised intracranial pressure, and ischemia. Cerebral ischemia is considered the most critical secondary insult and is reported in approximately 90% of TBI-related deaths (4).

Secondary brain injury contributes to neurological deterioration through complex molecular and cellular mechanisms and may result in irreversible damage. For instance, hypoxia leads to neuronal death and cognitive impairment, while even transient episodes of hypotension may significantly impair cerebral perfusion and worsen neurological outcomes (5).

Effective prehospital management of TBI is therefore essential to limit secondary injury and maintain adequate cerebral perfusion. Early correction of hypoxia and hemodynamic instability directly affects clinical outcomes (6). Prehospital emergency teams play a key role in initial stabilization, with continuous vital-sign monitoring and timely targeted interventions required to prevent further neurological deterioration and improve prognosis (7, 8).

Despite advances in emergency medicine, the early identification and management of secondary brain injury during the prehospital phase remain challenging. Although previous studies have highlighted the importance of hypoxia and hypotension, there is still limited evidence regarding the combined impact of multiple physiological parameters assessed in the prehospital setting, particularly in regional healthcare systems. This represents an important gap in current knowledge.

In this context, the present study aimed to clarify the association between early physiological disturbances and TBI outcomes, with a focus on optimizing prehospital care.

The study evaluated the association of age, systolic blood pressure, mean arterial pressure, hypoxia, and hyperglycemia with TBI severity and mortality. It was hypothesized that early abnormalities in these parameters would be associated with poorer clinical outcomes.

MATERIALS AND METHODS

This study was conducted within the Department of Emergency Medicine of "Nicolae Testemițanu" State University of Medicine and Pharmacy, in collaboration with the Emergency Department of the Institute of Emergency Medicine and the National Center for Prehospital Emergency Medical Assistance, from January 2, 2020 to January 2, 2024.

Study design

This retrospective observational analytical study assessed the association between selected prehospital physiological parameters and TBI severity and mortality.

The study protocol defined the study sample, clinical and paraclinical assessment methods applied during the prehospital and Emergency Department phases, tools for assessing trauma severity and prognosis, and treatment and monitoring procedures. Data were collected using standardized observation and recording forms developed for the study.

Study population and sampling

The study included 486 adult patients aged ≥18 years with acute TBI. Patients were initially assessed by emergency medical services in the prehospital setting and subsequently evaluated in the Emergency Department. A non-probability consecutive sampling method was used, including all eligible patients who met the inclusion criteria during the study period.

Inclusion criteria comprised a confirmed diagnosis of traumatic brain injury, availability of complete prehospital and Emergency Department clinical data, and age ≥18 years. Patients with incomplete key clinical or physiological data were excluded from the analysis.

Outcome measures

TBI severity was assessed at first medical contact using the Glasgow Coma Scale (GCS) and classified as mild (GCS 13–15), moderate (GCS 9–12), or severe (GCS ≤8). Mortality was recorded as a binary outcome, viz. survival or death.

Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki and approved by the Research Ethics Committee of "Nicolae Testemițanu" State University of Medicine and Pharmacy (Decision no. 46, June 17, 2019). Informed consent was obtained where applicable.

Statistical analysis

Descriptive statistics were used to summarize demographic and clinical characteristics. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as absolute frequencies and percentages.

Inferential statistical analysis was performed using Pearson correlation coefficients to evaluate the associations between physiological parameters (age, systolic blood pressure, mean arterial pressure, hypoxia, and hyperglycemia), TBI severity, and mortality. The level of statistical significance was set at $p < 0.05$. Statistical analysis was conducted using standard statistical software.

RESULTS

The study cohort included 486 patients, with a mean age of 51.29 ± 18.34 years, range 18–84 years. Males accounted for 62.9% of cases and females for 37.1%, with a male-to-female ratio of 1.7:1. Most patients were from rural areas, 71.2%.

Mild TBI was recorded in 79.6% of patients, moderate TBI in 12.3%, and severe TBI in 8.0%. The most common mechanisms of injury were falls, 44.65%, followed by physical assault, 25.72%, and road traffic accidents, 18.72%. Demographic and baseline clinical characteristics are shown in Table 1.

Table 1. Demographic and Baseline Clinical Characteristics of the Study Group (n = 486)

Feature	Number of patients	Percentage (%)
Mean age (years)	-	51.29±18.34
Sex		
– Male	306	62.9
– Female	180	37.1
TBI severity (GCS)		
– Mild (GCS 13-15)	387	79.6
– Moderate (GCS 9-12)	60	12.3
– Severe (GCS ≤8)	39	8.0
Residence		
– Urban	140	28.8
– Rural	346	71.2

Isolated TBI without associated injuries was identified in 289 patients, 59.46%. Among these patients, mild TBI predominated, 96.19%, while moderate and severe TBI accounted for 2.42% and 1.39%, respectively. Age showed a weak but statistically significant positive correlation with mortality, r = 0.097, p = 0.033, but was not significantly associated with TBI severity. TBI severity showed a strong positive correlation with mortality, r = 0.594, p < 0.001. Correlations between age, TBI severity, and mortality are presented in Table 2.

Table 2. Correlation Matrix Between Age, TBI Severity, and Mortality Rate (n=486)

Variables	Statistical Indicators	Age	TBI Severity	Mortality Rate
Age	Pearson Correlation	1	0.030	**0.097***
	Sig (2-tailed)		0.513	0.033
	N	486	486	486
TBI Severity	Pearson Correlation	0.030	1	0.594**
	Sig (2-tailed)	0.513		0,000
	N	486	486	486
Mortality Rate	Pearson Correlation	**0.097***	0.030	1
	Sig (2-tailed)	0,033	0.513	
	N	486	486	486

Note: * - Correlation is significant at the 0.05 level (2-tailed)
** - Correlation is significant at the 0.01 level (2-tailed)

Prehospital systolic blood pressure was negatively correlated with both TBI severity, r = –0.254, p < 0.001, and mortality, r = –0.138, p = 0.002. These associations are shown in Table 3.

Table 3. Correlation Between Systolic Blood Pressure and TBI Severity and Mortality in TBI Patients

Variables	SBP	TBI Severity	Mortality Rate
SBP	1	-0,254**	-0,138**
TBI Severity	-0,254**	1	0.594**
Mortality Rate	-0,138**	0.594**	1

Note: *p < 0.05; *p < 0.01. N = 486

Prehospital systolic blood pressure showed a significant negative correlation with TBI severity (r = –0.254, p < 0.001) and mortality (r = –0.138, p = 0.002). The correlation analysis between mean arterial pressure, TBI severity, and mortality is shown in Table 4.

Table 4. Correlation Between Mean Arterial Pressure and TBI Severity and Mortality in TBI Patients

Variables	MAP	TBI Severity	Mortality Rate
MAP	1	-0,195**	-0,213**
TBI Severity	-0,195**	1	0.594**
Mortality Rate	-0,213**	0.594**	1

Note: *p < 0.05; *p < 0.01. N = 486

Mean arterial pressure was significantly negatively correlated with TBI severity (r = –0.195, p < 0.001) and mortality (r = –0.213, p < 0.001).

Table 5. Correlation Between Hypoxia and TBI Severity and Mortality in TBI Patients

Variables	Hypoxia	TBI Severity	Mortality Rate
Hypoxia	1	0,324**	0,264**
TBI Severity	0,324**	1	0.594**
Mortality Rate	0,264**	0.594**	1

Note: *p < 0.05; *p < 0.01. N varies due to missing data (Hypoxia n = 438; total sample n = 486)

Prehospital hypoxia was significantly associated with poorer outcomes. It showed a moderate positive correlation with TBI severity (r = 0.324, p < 0.001) and mortality (r = 0.264, p < 0.001) (Table 5).

Table 6. Correlation Between Hyperglycemia and TBI Severity and Mortality in TBI Patients

Variables	Hyperglycemia	TBI Severity	Mortality Rate
Hyperglycemia	1	-0.088	-0,213**
TBI Severity	-0.088 *	1	0.594**
Mortality Rate	-0,213**	0.594**	1

Note: *p < 0.05; *p < 0.01

Hyperglycemia showed a weak, non-significant negative correlation with TBI severity ($r = –0.088$, $p = 0.060$). In contrast, a significant negative correlation was observed between hyperglycemia and mortality ($r = –0.213$, $p < 0.01$) (Table 6).

DISCUSSION

The present study included 486 patients with TBI managed in the prehospital phase and in the Emergency Department, and examined factors associated with injury severity and mortality. Older age, hypotension, and prehospital hypoxia were significantly associated with greater TBI severity and higher mortality (9–23). These findings are consistent with recent evidence emphasizing the role of early physiological stabilization in improving outcomes after TBI (6, 19). A noteworthy finding is the moderate positive correlation between prehospital hypoxia and both TBI severity and mortality (14–16). This underscores the importance of early oxygen monitoring and timely correction during the prehospital phase, aligning with prior literature emphasizing hypoxia as a major secondary insult in TBI (12). Similarly, lower systolic and mean arterial pressures were associated with more severe injury and increased mortality, confirming the prognostic importance of early hemodynamic stabilization (14 - 16, 21, 22, 24 – 28).

Particular attention should be paid to systemic secondary cerebral insults (ACSOS), which significantly influence TBI progression (4, 7, 9, 12, 13, 25 – 34). These secondary insults, including hypoxia, hypotension, and metabolic disturbances, interact with primary injury mechanisms and exacerbate neurological deterioration.

Early recognition and management of ACSOS are therefore essential during both prehospital care and Emergency Department treatment (23, 24, 26, 28, 29, 31, 32). Structured monitoring of oxygenation and blood pressure may reduce secondary injury and improve survival.

The association between hyperglycemia and mortality was another relevant finding. The moderate negative correlation observed may reflect complex metabolic responses after TBI and warrants further investigation in larger multicenter studies. TBI induces an acute stress response mediated by activation of the sympathoadrenal-medullary axis, leading to increased circulating levels of cortisol, glucagon, insulin, catecholamines, glucose, lactate, and free fatty acids (15, 21, 22, 24, 26, 28). In this context, blood glucose may serve as a marker of post-traumatic metabolic stress.

Hyperglycemia, however, is not only an epiphenomenon. It may aggravate secondary brain injury by increasing oxidative stress through free radical generation, promoting apoptosis, and contributing to tissue lactic acidosis (17, 19). Although treatment often focuses on primary brain injury, secondary insults such as hyperglycemia may be underestimated and may contribute to the “second-hit” phenomenon, adversely affecting outcomes (17, 19).

Regarding injury mechanisms, falls were the most common cause of TBI across all severity categories, followed by assault and road traffic accidents. Moreover, isolated TBI was associated with milder injury and a more favorable prognosis, suggesting that concomitant trauma complicates management and increases the risk of adverse outcomes. These findings support comprehensive assessment in polytrauma patients. The results highlight the clinical relevance of early, structured, and targeted prehospital interventions to reduce secondary brain injury and optimize patient outcomes. These findings are consistent with current evidence supporting prehospital protocols focused on oxygenation, hemodynamic stabilization, and metabolic monitoring (7, 13, 26).

CONCLUSIONS

1. Advanced age, prehospital hypotension, and hypoxia are significant predictors of TBI severity and mortality.
2. Early identification and correction of hypoxia and hemodynamic instability are essential in prehospital care.
3. Hyperglycemia may have a prognostic role in mortality, although it is not associated with injury severity.

CONFLICT OF INTEREST The authors declare no conflicts of interest related to this study.

ETHICS APPROVAL The study was approved by the Research Ethics Committee of the State University of Medicine and Pharmacy "Nicolae Testemițanu" (Decision no. 46 of 17.06.2019).

PROVENANCE AND PEER REVIEW Not commissioned, externally peer reviewed.

ACKNOWLEDGEMENTS AND FUNDING The study had no external funding.

REFERENCES

1. Maas AIR, Menon DK, Manley GT, et al. Traumatic brain injury: progress and challenges in prevention, clinical care, and research. *Lancet Neurol*. 2022;21(11):1004-1060. https://doi.org/10.1016/S1474-4422(22)00309-X.
2. James SL, Castle CD, Dingels ZV, et al. Global injury morbidity and mortality from 1990 to 2017: results from the Global Burden of Disease Study 2017. *Inj Prev*. 2020;26(Supp 1):i96-i114. https://doi.org/10.1136/injuryprev-2019-043494.
3. Clark D, Joannides A, Adeleye AO, et al. Casemix, management, and mortality of patients reseceiving emergency neurosurgery for traumatic brain injury in the Global Neurotrauma Outcomes Study: a prospective observational cohort study. *Lancet Neurol*. 2022;21(5):438-449. https://doi.org/10.1016/S1474-4422(22)00037-0.
4. Paladii I, Ghidirim G, Kusturov V, Berliba S, Beschieru E, Şor E, Lescov V. Criteriile severităţii leziunilor în traumatismul asociat. *Buletinul Academiei de Ştiinţe a Moldovei. Ştiinţe Medicale*. 2015;49(4):30-4. https://ibn.idsi.md/vizualizare_articol/42698.
5. Mocanu Scurtov N, Ciobanu G. Clinico–evolutionary particularities of head injury patients in prehospital. *Archives of the Balkan Medical Union* 53.S1 (2018): 135-136. https://ibn.idsi.md/sites/default/files/imag_file/135-136_24.pdf
6. Robinson CP. Moderate and Severe Traumatic Brain Injury. *Continuum (Minneap Minn)*. 2021;27(5):1278-1300. https://doi.org/10.1212/CON.0000000000001036.
7. Habte YW, Pajer HB, Abicho TB, et al. Validation of the Canadian CT Head Rule and the New Orleans Criteria for Mild Traumatic Brain Injury in Ethiopia. World Neurosurg. 2023;173:e600-e605. https://doi.org/10.1016/j.wneu.2023.02.108.
8. Catanoi N, Rezneac L, Mocanu N. Protocols for the diagnosis of urgent neurological pathologies in the pre-hospital stage. *Arch Balk Med Union*. 2025;1(60):140–147. https://doi.org/10.31688/ABMU.2025.60.1.15.
9. Catanoi N, Rabovila A, Mocanu N, M Peștereanu. Urgenţele hipertensive între probleme și realizări la etapa de prespital. *Buletinul Academiei de Ştiinţe a Moldovei. Ştiinţe Medicale.* 2020;66 (2), 150-153. https://ibn.idsi.md/ro/vizualizare_articol/114783.
10. Mocanu N, Vasluian A, Catanoi N, Rezneac L, Rabovila A, Malacinschi-Codreanu N. Aspecte sociale şi medicale a traumatismelor cranio-cerebrale la etapa de prespital. *Arch Balk Med Union*. 2016;1(51):137-139. https://ibn.idsi.md/sites/default/files/imag_file/p-137-139.pdf.
11. Waltzman D, Haarbauer-Krupa J, Womack LS. Traumatic Brain Injury in Older Adults-A Public Health Perspective. *JAMA Neurol*. 2022;79(5):437-438. https://doi.org/10.1001/jamaneurol.2022.0114.
12. Yang C, Lang L, He Z, et al. Epidemiological Characteristics of Older Patients with Traumatic Brain Injury in China. *J Neurotrauma*. 2022;39(11-12):850-859. https://doi.org/10.1089/neu.2021.0275.
13. dell'Aquila M, Maiese A, De Matteis A, et al. Traumatic brain injury: Estimate of the age of the injury based on neuroinflammation, endothelial activation markers and adhesion molecules. *Histol Histopathol*. 2021;36(8):795-806. https://doi.org/10.14670/HH-18-319.
14. Cojocari V, Ciobanu Gh, Scurtov N. The impact of pre-hospital arterial hypo- and hypertension on clinical severity and prognosis of patients with traumatic brain injury. *Curier Med*. 2016;1(51):137–139. https://ibn.idsi.md/en/vizualizare_articol/24307.
15. Scurtov N, Ciobanu Gh, Cojocari N. Hemodynamic instability as an unfavorable prognostic factor of severe traumatic brain injury. *Resuscitation.* 2013; 84:S97. https://www.resuscitationjournal.com/article/S0300-9572(13)00680-1/abstract.
16. Orr TJ, Lesha E, Kramer AH, et al. Traumatic Brain Injury: A Comprehensive Review of Biomechanics and Molecular Pathophysiology. *World Neurosurg*. 2024;185:74-88. https://doi.org/10.1016/j.wneu.2024.01.084.
17. Qi L, Geng X, Feng R, et al. Association of glycemic variability and prognosis in patients with traumatic brain injury: A retrospective study from the MIMIC-IV database. *Diabetes Res Clin Pract*. 2024;217:111869. https://doi.org/10.1016/j.diabres.2024.111869.
18. Hajivalili M, Nikkhoo N, Salahi S, Hosseini M. Traumatic brain Injury: Comprehensive overview from pathophysiology to Mesenchymal stem Cell-Based therapies. *Int Immunopharmacol*. 2025;146:113816. https://doi.org/10.1016/j.intimp.2024.113816.
19. Bosarge PL, Shoultz TH, Griffin RL, Kerby JD. Stress-induced hyperglycemia is associated with higher mortality in severe traumatic brain injury. *J Trauma Acute Care Surg*. 2015;79(2):289-294. https://doi.org/10.1097/TA.0000000000000716.
20. Johnson-Black PH, Carlson JM, Vespa PM. Traumatic brain injury and disorders of consciousness. *Handb Clin Neurol*. 2025;207:75-96. https://doi.org/10.1016/B978-0-443-13408-1.00014-2.
21. Şor E. Comorbiditatea: revista literaturii. *Archives of the Balkan Medical Union.* 2015;50(2):39-44. https://ibn.idsi.md/vizualizare_articol/243259.
22. Ghidirim Gh, Paladii I, Berliba S, Şor E. Scorul comorbidității Charlson ca factor de prognostic independent al tratamentului. *Arta Medica*, 2015;3(56):155-156. https://repository.usmf.md/handle/20.500.12710/13561.
23. Arleth T, Baekgaard J, Siersma V, et al. Early Restrictive vs Liberal Oxygen for Trauma Patients: The TRAUMOX2 Randomized Clinical Trial. *JAMA*. 2025;333(6):479-489. https://doi.org/10.1001/jama.2024.25786.
24. Prus K, Sekuła M, Bilotta F. Biomarkers of acute brain injury. *Curr Opin Anaesthesiol*. 2025;38(5):584-590. https://doi.org/10.1097/ACO.0000000000001532.

25. Katlowitz K, Gopinath S, Cruz Navarro J, Robertson C. HMG-CoA Reductase Inhibitors for Traumatic Brain Injury. *Neurotherapeutics*. 2023;20(6):1538-1545. https://doi.org/10.1007/s13311-023-01399-9.
26. Bernardi E, Giamello JD, Lorenzati B. Traumatic brain injury. *Emerg Med J*. 2023;40(3):e2. https://doi.org/10.1136/emermed-2021-211186.
27. Denchev K, Gomez J, Chen P, Rosenblatt K. Traumatic Brain Injury: Intraoperative Management and Intensive Care Unit Multimodality Monitoring. *Anesthesiol Clin*. 2023;41(1):39-78. https://doi.org/10.1016/j.anclin.2022.11.003.
28. Ngatuvai M, Martinez B, Sauder M, et al. Traumatic Brain Injury, Electrolyte Levels, and Associated Outcomes: A Systematic Review. *J Surg Res*. 2023;289:106-115. https://doi.org/10.1016/j.jss.2023.03.029.
29. Allen BC, Cummer E, Sarma AK. Traumatic Brain Injury in Select Low- and Middle-Income Countries: A Narrative Review of the Literature. *J Neurotrauma*. 2023;40(7-8):602-619. https://doi.org/10.1089/neu.2022.0068.
30. Melo N. Traumatic brain injury endotypes in polytrauma TBI: Gathering steam. *Am J Surg*. 2024;234:194. https://doi.org/10.1016/j.amjsurg.2023.12.014.
31. Krausz AD, Korley FK, Burns MA. The Current State of Traumatic Brain Injury Biomarker Measurement Methods. *Biosensors (Basel)*. 2021;11(9):319. https://doi.org/10.3390/bios11090319.
32. Olasveengen TM, Stocchetti N. Prehospital ventilation targets in severe traumatic brain injury. *Intensive Care Med*. 2023;49(5):554-555. https://doi.org/10.1007/s00134-023-07044-5.
33. Acevedo-Aguilar L, Gaitán-Herrera G, Reina-Rivero R, et al. Pulmonary injury as a predictor of cerebral hypoxia in traumatic brain injury: from physiology to physiopathology. *J Neurosurg Sci*. 2022;66(3):251-257. https://doi.org/10.23736/S0390-5616.21.05468-0.
34. Li F, Liu Y, Li L, et al. Brain-derived extracellular vesicles mediate traumatic brain injury associated multi-organ damage. *Biochem Biophys Res Commun*. 2023;665:141-151. https://doi.org/10.1016/j.bbrc.2023.04.119.

Date of receipt of the manuscript: 06.10.2025

Date of acceptance for publication: 04.05.2026

Elina SHOR, SCOPUS ID: 37066554000