



INTRACRANIAL HEMORRHAGE AFTER THROMBOLYTIC THERAPY: A FORESEEABLE COMPLICATION?

HEMORRAGIA INTRACRANEAL POST TERAPIA TROMBOLÍTICA: ¿UNA COMPLICACIÓN PREVISIBLE?

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Dear. Editor:

I am writing to highlight the growing concern regarding a severe complication of thrombolytic therapy, intracranial hemorrhage, and the need to identify associated risk factors. Considering the frequency of comorbidities in stroke patients worldwide, it is essential to provide a global perspective on this issue.

Intracerebral hemorrhage is a severe complication associated with worse functional outcomes and greater disability⁽¹⁾. In 2021, in the United States, low albumin levels and elevated HbA1c levels were reported to be significantly associated with a higher risk of symptomatic intracranial hemorrhage (SIH) post-fibrinolysis⁽²⁾. In China, smoking, prolonged activated partial thromboplastin time (aPTT), and thrombocytopenia were found to be associated with a higher risk of hemorrhagic transformation post-fibrinolysis⁽³⁾.

In Iran, post-fibrinolysis hemorrhage in stroke was significantly related to atrial fibrillation (OR = 2.75, 95% CI: 1.24–6.09), NIHSS score 15–24 (OR = 5.22, 95% CI: 1.39–19.66), and NIHSS score >24 (OR = 7.25, 95% CI: 1.42–37.09). The National Institutes of Health Stroke Scale (NIHSS) assesses stroke severity through clinical parameters, with scores ranging from 0 to 42 points, classified as follows: <6 points: low, 6–14 points: medium-low, 15–24 points: medium-high, and ≥25 points: high⁽⁴⁾.

Not all studies have shown significant associations. For example, one of the largest studies during the COVID-19 pandemic, which included seven centers in Iran, one in Greece, and one in Germany, found that a history of COVID-19 was not associated with an increased risk of hemorrhagic transformation⁽⁵⁾. Similarly, an Italian study of 24 cases and 24 controls found no significant difference between the presence of active malignant neoplasia and the risk of intracranial hemorrhage (p-value: >0.999)⁽⁶⁾. In Latin America, a study in Brazil reported that current statin treatment and high NIHSS scores were significantly related to SIH⁽⁷⁾.

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In Peru, no compatible studies were found on this topic. These results can be observed in the Table. In conclusion, our findings highlight the importance of recognizing risk factors for intracranial hemorrhage post-fibrinolysis and the need for further studies. Identifying these risk factors would be highly useful for early neurological clinical examination and the use

of imaging, such as computed tomography. It is recommended to allocate more resources for research in this field, especially in the Latin American population, as the limited evidence reported in this population hinders early recognition and timely management of patients at risk of hemorrhage post-thrombolytic therapy.

Table 1. Reported results in studies on risk factors for intracranial hemorrhage post-thrombolytic therapy.

Title	Year	Country	Design	Poblation	Results
Risk Factors for Early Intracerebral Hemorrhage after Intravenous Thrombolysis with Alteplase ⁽¹⁾ .	2020	China	Case-Control	n =197	Previous stroke (OR = 5.75, 95% CI: 1.49–22.25; p-value: 0.011) and atrial fibrillation (AF) (OR = 5.43, 95% CI: 1.43–20.64; p-value: 0.013).
Laboratory factors associated with symptomatic hemorrhagic conversion of acute stroke after systemic thrombolysis ⁽²⁾ .	2021	United States	Case-Control	n =794	Association between serum albumin and intracranial hemorrhage (OR = 0.31, 95% CI: 0.19–0.52; p-value: <0.001). Association between HbA1c and intracranial hemorrhage (OR = 1.30, 95% CI: 1.00–1.60; p-value: 0.017).
Risk factors of hemorrhagic transformation after intravenous thrombolysis with rt-PA in acute cerebral infarction ⁽³⁾ .	2019	China	Case-Control	n =403	Intracranial hemorrhage post-fibrinolysis is associated with smoking (OR = 0.07, 95% CI: 0.01–0.53; p-value: 0.010), prolonged aPTT (OR = 2.13, 95% CI: 1.02–4.44; p-value: 0.040), while high fibrinogen (OR = 0.08, 95% CI: 0.01–0.53; p-value: 0.010) and high platelets (OR = 0.47, 95% CI: 0.24–0.91; p-value: 0.030) are protective factors.
Outcome predictors in anterior and posterior ischemic strokes: a study based on the Iranian SITS registry ⁽⁴⁾ .	2023	Iran	Case-Control	n =1566	Hemorrhage was significantly associated with AF (OR = 2.75, 95% CI: 1.24–6.09), NIHSS score 15–24 (OR = 5.22, 95% CI: 1.39–19.66), and NIHSS score >24 (OR = 7.25, 95% CI: 1.42–37.09).
Safety and Outcomes of Intravenous Thrombolytic Therapy in Ischemic Stroke Patients with COVID-19: CASCADE Initiative ⁽⁵⁾ .	2021	Multi-centric	Case-Control	n =545	History of COVID-19 was not associated with an increased risk of hemorrhagic transformation (OR = 1.51, 95% CI: 0.66–3.31).
Safety and Efficacy of Reperfusion Therapies for Acute Ischemic Stroke Patients with Active Malignancy ⁽⁶⁾ .	2019	Italia	Case-Control	n=24 cases and 24 controls	No significant difference (p-value: 1.000) between the presence of active malignant neoplasia and the risk of intracranial hemorrhage.
Frequency and predictors of symptomatic intracranial hemorrhage after intravenous thrombolysis for acute ischemic stroke in a Brazilian public hospital ⁽⁷⁾ .	2012	Brazil	Cohort	n =113	Symptomatic intracranial hemorrhage is significantly related to current statin use (p-value: 0.015) and high NIHSS scores (p-value: 0.015).

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REFERENCES

1. Lin X, Cao Y, Yan J, Zhang Z, Ye Z, Huang X, et al. Risk Factors for Early Intracerebral Hemorrhage after Intravenous Thrombolysis with Alteplase. *J Atheroscler Thromb.* 2020;27(11):1176–82. doi:[10.5551/jat.49783](https://doi.org/10.5551/jat.49783)
2. Kamal H, Mehta BK, Ahmed MK, Kavak KS, Zha A, Lail NS, et al. Laboratory factors associated with symptomatic hemorrhagic conversion of acute stroke after systemic thrombolysis. *Journal of the Neurological Sciences.* 2021;420:117265. doi:[10.1016/j.jns.2020.117265](https://doi.org/10.1016/j.jns.2020.117265)
3. Wang R, Zeng J, Wang F, Zhuang X, Chen X, Miao J. Risk factors of hemorrhagic transformation after intravenous thrombolysis with rt-PA in acute cerebral infarction. *QJM: An International Journal of Medicine.* 2019;112(5):323–6. doi:[10.1093/qjmed/hcy292](https://doi.org/10.1093/qjmed/hcy292)
4. Jalali N, Sadeghi Hokmabadi E, Ghoreishi A, Sariaslan P, Rafie S, Borhani-Haghighi A, et al. Outcome predictors in anterior and posterior ischemic strokes: a study based on the Iranian SITS registry. *Sci Rep.* 2023;13(1):1231. doi:[10.1038/s41598-023-28465-8](https://doi.org/10.1038/s41598-023-28465-8)
5. Sasanejad P, Afshar Hezarkhani L, Arsang-Jang S, Tsvigoulis G, Ghoreishi A, Barlinn K, et al. Safety and Outcomes of Intravenous Thrombolytic Therapy in Ischemic Stroke Patients with COVID-19: CASCADE Initiative. *Journal of Stroke and Cerebrovascular Diseases.* 2021;30(12):106121. doi:[10.1016/j.jstrokecerebrovasdis.2021.106121](https://doi.org/10.1016/j.jstrokecerebrovasdis.2021.106121)
6. Sallustio F, Mascolo AP, Marrama F, Koch G, Alemseged F, Davoli A, et al. Safety and Efficacy of Reperfusion Therapies for Acute Ischemic Stroke Patients with Active Malignancy. *Journal of Stroke and Cerebrovascular Diseases.* 2019;28(8):2287–91. doi:[10.1016/j.jstrokecerebrovasdis.2019.05.018](https://doi.org/10.1016/j.jstrokecerebrovasdis.2019.05.018)
7. Cougo-Pinto PT, Dos Santos BL, Dias FA, Fabio SRC, Werneck IV, Camilo MR, et al. Frequency and predictors of symptomatic intracranial hemorrhage after intravenous thrombolysis for acute ischemic stroke in a Brazilian public hospital. *Clinics.* 2012;67(7):739–43. doi:[10.6061/clinics/2012\(07\)06](https://doi.org/10.6061/clinics/2012(07)06)