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Title: The Safety of Early Initiation of Antithrombotic Therapy Eight Hours After Intravenous Thrombolysis for Acute Ischemic Stroke

Background & Purpose: Intravenous (IV) thrombolytic therapy is standard treatment for eligible acute ischemic stroke (AIS) patients. American Heart Association / American Stroke Association Guidelines recommend brain imaging at 24 hours before initiating an antithrombotic, due to the risk of hemorrhagic transformation (HT). However, earlier antithrombotic initiation may improve outcomes. Our hospital implemented a practice change using fibrinogen testing and head computed tomography (CT) at 8 hours post-thrombolysis to guide earlier antithrombotic therapy. The purpose of this pre-post-intervention study is to assess the safety of an 8-hour screening protocol to support earlier antithrombotic use, potentially reducing the standard 24-hour post-thrombolysis window.

Methods: The option for earlier antithrombotic therapy was approved and implemented at our hospital in March 2025 for AIS patients without HT, confirmed by head CT and a fibrinogen level ≥150 mg/dL. A report generated by Discern Analytics identified patients for inclusion who received a thrombolytic agent between August 2024 and July 2025. Patients were then divided into two groups: pre- intervention and post- intervention. Additional inclusion criteria for the post-intervention group included initiation of any antithrombotic therapy within 24 hours of thrombolysis. Cases of HT following thrombolysis were identified using a stroke core quality measure defined by Joint Commission under the Certification for Comprehensive Stroke Centers (CSTK) program, known as CSTK-05a. The primary outcome was the HT rate in the pre- and post-intervention periods. Hemorrhagic transformation rates were compared using Fischer's Exact Test due to the small sample size and rare event occurrence, with $\alpha = 0.05$. Study approval was granted by our Institutional Review Board.

Results: Between August 2024 and July 2025, a total of 105 patients with AIS received IV thrombolysis and were evaluated for inclusion. Of those, 63 patients were treated during the pre- intervention period under the standard stroke protocol, and 42 patients were treated during the post- intervention period with the option of early antithrombotic pathway. Among the post-invention patients, 28 of 42 (66.7%) underwent the early antithrombotic pathway and were included in the post-intervention group for analysis. The remaining 14 patients were excluded. In our safety analysis of HT events post-thrombolysis in AIS patients, no difference was observed between the pre- and post-intervention periods ($p = 1.0$). With zero observed HT events in either group, the rule of three (3/n) estimates the upper bound of the 95% confidence interval for the true event rate as 10.7% post-intervention and 4.8% pre-intervention. This indicates that, despite observing no HT events, the true underlying event rate could still be as high as 10.7% post-intervention and 4.8% pre-intervention with 95% confidence, reflecting limited power to exclude clinically meaningful risk. During the post-intervention period, one HT event occurred prior to initiating antithrombotic therapy, corresponding to CSTK-05a rate of 12.5% in June 2025; this event was determined to be unrelated to early antithrombotic therapy and was therefore excluded from the safety analysis. These findings suggest that fibrinogen levels and head CT can be safely used as markers of bleeding risk after thrombolytic administration, supporting earlier antithrombotic initiation. However, interpretation should consider the relatively short post-intervention period, which precludes establishing non-inferiority.

Conclusion: Our findings suggest that earlier antithrombotic use, when guided by fibrinogen level and imaging at 8 hours post-thrombolysis, appears to be safe and suggests no signal of harm. Continued monitoring is warranted to further validate the findings of this study.