Intracranial Hemorrhage Associated with Rivaroxaban

- Non-vitamin K antagonist oral anticoagulants (NOACs) and risk of spontaneous intracranial hemorrhage in patients with ischemic stroke: An analysis using Taiwan's National Health Insurance Research Database
- Newly identified cerebral microbleeds in patients on anticoagulation for secondary stroke prevention
- Reduced dose direct oral anticoagulants and time-in-therapeutic-range defined warfarin in new-onset atrial fibrillation: a report from the nationwide FinACAF study
- Association of Biomarkers With Intracerebral Hematoma Expansion and Arterial Thromboembolic Events in Patients With Acute Intracranial Hemorrhage: The ANNEXA-I Biomarker Substudy
- Optimizing Anticoagulation Strategies in Patients With Atrial Fibrillation and Valvular Heart Disease: A Comprehensive Evidence-Based Review
- Efficacy of pro-haemostatic agents in the management of factor Xa inhibitor-associated intracranial haemorrhages
- Reversal of Factor Xa Inhibitor-Related Intracranial Hemorrhage: A Multicenter, Retrospective, Observational Study Comparing the Efficacy and Safety of Andexanet and Prothrombin Complex Concentrates
- Andexanet alfa in patients with factor Xa inhibitor-associated intracranial hemorrhage: The prospective observational multicenter ASTRO-DE study

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Intracranial hemorrhage (ICH) is a serious and potentially life-threatening condition that can occur in patients taking anticoagulants like rivaroxaban.

Here's a concise overview of the association between rivaroxaban and intracranial hemorrhage:

Rivaroxaban, by inhibiting factor Xa, reduces the blood’s ability to clot, which increases the risk of bleeding as Rivaroxaban complications, including intracranial hemorrhage.

Incidence: The risk of ICH with rivaroxaban is generally considered to be lower compared to some other anticoagulants like warfarin, but it is still a notable risk. The incidence of ICH in patients taking rivaroxaban has been reported in clinical trials and observational studies.

Risk Factors Several factors can increase the risk of ICH in patients on rivaroxaban:

Older Age: Elderly patients are at a higher risk due to decreased renal function and increased vulnerability to bleeding. Renal Impairment: Rivaroxaban is primarily excreted through the kidneys, so impaired renal function can lead to higher drug levels and increased bleeding risk. Concomitant Medications: Use of other medications that affect bleeding, such as antiplatelet agents or other anticoagulants, can enhance the risk. Trauma or Falls: Patients who experience trauma or falls while on rivaroxaban are at higher risk for ICH. Management and Prevention Monitoring: Regular monitoring of renal function and adherence to dosing recommendations is crucial. Rivaroxaban dosing may need to be adjusted based on renal function. Reversal: In the event of significant bleeding, including ICH, specific reversal agents are available. For rivaroxaban, the antidote is andexanet alfa, though its

availability and use can vary by location. Supportive Care: Immediate management of ICH involves supportive care, including blood pressure control and neurosurgical interventions if necessary. Clinical Implications Risk-Benefit Analysis: The benefits of rivaroxaban in preventing thromboembolic events must be weighed against the risk of bleeding complications. This is particularly important in high-risk populations. Patient Education: Patients on rivaroxaban should be educated about the signs of bleeding and the importance of adhering to their prescribed regimen.

A 15-mg to 20-mg dose of rivaroxaban once daily is associated with substantially increased risks of intracranial hemorrhage, while smaller daily doses of rivaroxaban and apixaban were not, implying that risk increase is dose dependent. It may be worthwhile to conduct randomized clinical trials comparing specific NOACs in specific doses (eg, apixaban, 5 mg twice daily) and aspirin in patients without atrial fibrillation, but with potential sources of cardiac emboli that could cause stroke [1)]

Retrospective cohort studies

Rivaroxaban is associated with ICH in patients at high risk for bleeding, the outcomes are comparatively favorable (smaller hematoma, less expansion, and lower mortality) than those associated with warfarin. This comparison provides insight into the relative safety and outcomes of these anticoagulants in the context of ICH [2)].

Retrospective case series

A study assessed the real-time rate of rivaroxaban-associated ICH in Saudi patients.We retrospectively reviewed patients with ICH during rivaroxaban therapy, assessing clinical features and outcomes.Four cases out of 690 patients were identified in total, indicating an incidence of ICH during rivaroxaban therapy of 0.58%. Hematoma expansion developed in 1 case. Three out of four patients were discharged after ICH, and 1 patient died.The incidence of rivaroxaban-related ICH was similar to that previously reported, and the risk of hematoma expansion was low. Further studies are required to validate the results [3)]

Case reports

One of the first case reports of severe intracranial hemorrhage associated with rivaroxaban in an elderly patient with decreased renal function. We aim to alert emergency medicine providers regarding the likelihood of encountering these patient as newer anticoagulants rise in popularity [4)]

1)
Huang WY, Singer DE, Wu YL, Chiang CE, Weng HH, Lee M, Ovbiagele B. Association of Intracranial Hemorrhage Risk With Non-Vitamin K Antagonist Oral Anticoagulant Use vs Aspirin Use: A Systematic Review and Meta-analysis. JAMA Neurol. 2018 Dec 1;75(12):1511-1518. doi: 10.1001/jamaneurol.2018.2215. PMID: 30105396; PMCID: PMC6583193.
2)

Hagii J, Tomita H, Metoki N, Saito S, Shiroto H, Hitomi H, Kamada T, Seino S, Takahashi K, Baba Y, Sasaki S, Uchizawa T, Iwata M, Matsumoto S, Osanai T, Yasujima M, Okumura K. Characteristics of intracerebral hemorrhage during rivaroxaban treatment: comparison with those during warfarin. Stroke. 2014 Sep;45(9):2805-7. doi: 10.1161/STROKEAHA.114.006661. Epub 2014 Jul 31. PMID: 25082810.

3)

Alkhotani A, Alrishi N, Alharthi M, Alzahrani W. Rivaroxaban-associated intracranial hemorrhage in Saudi atrial fibrillation patients. Medicine (Baltimore). 2020 Nov 25;99(48):e23316. doi: 10.1097/MD.0000000000023316. PMID: 33235091; PMCID: PMC7710243.

4)

Lo JC, Gerona RR. A case of rivaroxaban associated intracranial hemorrhage. West J Emerg Med. 2014 Jul;15(4):375-7. doi: 10.5811/westjem.2014.2.19440. PMID: 25035736; PMCID: PMC4100836.