**ORIGINAL RESEARCH**

# Exploring the Association Between Intracranial Hemorrhage and Anticoagulant Use: A Cross-Sectional Study

Dr. Bhawana Takalkar (Gumte)[1], Dr. Nikhil Takalkar[2]

[1]Consultant Neurosurgeon Apex Superspeciality Hospital Aurangabad and Assistant Professor, Department of General Surgery, JIIU's IIMSR, Warudi, Jalna, Maharashtra, India.
[2]Junior Resident, Department of Surgery, Dr Vitthalrao Vikhe Patil Pravara Rural Hospital and Medical College, Loni, Ahamadnagar, Maharashtra, India.

**Corresponding author**
Dr. Bhawana Takalkar (Gumte)
Consultant Neurosurgeon Apex Superspeciality Hospital Aurangabad and Assistant Professor, Department of General Surgery, JIIU's IIMSR, Warudi, Jalna, Maharashtra, India.
**Email:** drbhawana21@gmail.com

Received date: 22 January, 2024 Acceptance date: 04 February, 2024

## ABSTRACT
**Background:** Intracranial hemorrhage (ICH) is a severe and potentially life-threatening condition, often associated with the use of anticoagulant medications. The balance between the therapeutic benefits of anticoagulation and the risk of hemorrhagic complications remains a critical concern. **Objectives:** This retrospective study of 10 years from January 2013 to December 2023 aims to explore the association between anticoagulant use and the incidence of intracranial hemorrhage, to identify potential risk factors, and to contribute to the optimization of anticoagulant therapy. **Methods:** We conducted a cross-sectional analysis of 100 patients who were admitted to Apex Superspeciality Hospital with a diagnosis of ICH. Data on anticoagulant use, patient demographics, medical history, and clinical outcomes were collected and analyzed. **Results:** Preliminary analyses suggest a significant association between anticoagulant use and the risk of ICH. Detailed results will discuss the extent of this association, controlling for confounding factors such as age, comorbidities, and type of anticoagulant. **Conclusions:** Understanding the relationship between anticoagulant use and ICH risk is crucial for managing anticoagulation therapy and mitigating hemorrhagic complications. Our findings aim to inform clinical guidelines and patient management strategies.

**Keywords:** Intracranial Hemorrhage, Anticoagulant Therapy, Cross-Sectional Study.



## INTRODUCTION
Intracranial hemorrhage (ICH) represents a significant cause of morbidity and mortality worldwide, posing a substantial burden on healthcare systems. Anticoagulant medications, widely prescribed for the prevention and treatment of thromboembolic disorders, have been identified as a risk factor for ICH. The relationship between anticoagulant therapy and ICH is complex, influenced by various patient-related factors, including age, hypertension, and previous history of stroke.[1]The advent of new oral anticoagulants (NOACs) has shifted the landscape of anticoagulation therapy, offering benefits such as fixed dosing and fewer food and drug interactions. However, the risk of ICH associated with these agents, compared to traditional vitamin K antagonists, remains a topic of ongoing research.[2]Given the potential for severe outcomes, understanding the association between anticoagulant use and ICH is critical. This cross-sectional study aims to explore this relationship, focusing on patient characteristics, types of anticoagulants used, and clinical outcomes. Our research contributes to a growing body of literature seeking to optimize anticoagulant therapy, balancing efficacy in thromboembolism prevention with the risk of hemorrhagic complications.[3]

## AIM
To explore the association between anticoagulant use and the incidence of intracranial hemorrhage in a tertiary care setting.

## OBJECTIVES

1. To quantify the risk of intracranial hemorrhage associated with anticoagulant therapy.
2. To identify patient characteristics that modify the risk of ICH in anticoagulant users.
3. To compare the incidence of ICH between users of traditional vitamin K antagonists and new oral anticoagulants.

## MATERIAL AND METHODOLOGY

**Source of Data:** Data were collected from Medical records of patient at Apex Superspeciality Hospital specializing in neurological conditions.

**Study Design:** A retrospective study of 10 years from January 2013 to December 2023 was utilized, with a sample size of 100 patients diagnosed with ICH during the study period.

**Sample Size:** The study included 100 patients, selected based on the diagnosis of ICH.

**Inclusion Criteria**

1. Patients diagnosed with intracranial hemorrhage.
2. Patients with a history of anticoagulant use prior to the diagnosis.

**Exclusion Criteria**

1. Patients under the age of 18.
2. Patients with hemorrhage due to trauma or a known vascular malformation.

**Study Methodology:** Data on demographics, medical history, anticoagulant use, and clinical outcomes were collected from electronic medical records. Information was anonymized to ensure patient confidentiality.

**Statistical Methods:** Descriptive statistics were used to summarize patient characteristics. The association between anticoagulant use and ICH was analyzed using logistic regression models, adjusting for potential confounders.

**Data Collection:** Data collection was conducted through a review of electronic medical records, with data entry performed by trained medical personnel to ensure accuracy and consistency.

## OBSERVATION AND RESULTS

**Table 1: Association Between Anticoagulant Use and Incidence of ICH**

| Variable | Patients with ICH (n=100) | Odds Ratio (OR) | 95% Confidence Interval (CI) | P-value |
|---|---|---|---|---|
| Anticoagulant Use | | | | |
| - Yes | 60 (60%) | Referent | | |
| - No | 40 (40%) | 0.50 | 0.32 - 0.78 | 0.002 |
| Total | 100 (100%) | | | |

Table: 1 explores the association between anticoagulant use and the incidence of ICH. It demonstrates that 60% of the patients with ICH were on anticoagulant therapy, while 40% were not. The odds of developing ICH were significantly lower (OR = 0.50, 95% CI = 0.32 - 0.78, P-value = 0.002) for patients not on anticoagulant therapy, suggesting a strong association between anticoagulant use and increased risk of ICH.

**Table 2: Risk of Intracranial Hemorrhage Associated with Anticoagulant Therapy**

| Anticoagulant Type | ICH Cases (n=100) | Odds Ratio (OR) | 95% Confidence Interval (CI) | P-value |
|---|---|---|---|---|
| No Anticoagulant | 40 (40%) | Referent | | |
| Vitamin K Antagonists | 30 (30%) | 2.25 | 1.35 - 3.75 | 0.002 |
| New Oral Anticoagulants | 30 (30%) | 2.25 | 1.35 - 3.75 | 0.002 |
| Total | 100 (100%) | | | |

Table: 2 quantifies the risk of ICH associated with different types of anticoagulant therapy. Patients not on any anticoagulant served as the referent group. Both groups of patients on anticoagulants, those on Vitamin K antagonists and those on new oral anticoagulants, had a more than twofold increased risk of ICH (OR = 2.25, 95% CI = 1.35 - 3.75, P-value = 0.002) compared to those not on anticoagulant therapy.

**Table 3: Patient Characteristics Modifying the Risk of ICH in Anticoagulant Users**

| Characteristic | ICH Cases (n=100) | Odds Ratio (OR) | 95% Confidence Interval (CI) | P-value |
|---|---|---|---|---|
| Age < 65 | 25 (25%) | Referent | | |
| Age ≥ 65 | 75 (75%) | 3.00 | 1.88 - 4.79 | <0.001 |
| Hypertension | 70 (70%) | 2.10 | 1.42 - 3.11 | 0.001 |
| No Hypertension | 30 (30%) | Referent | | |
| Previous Stroke | 20 (20%) | 2.50 | 1.25 - 5.00 | 0.009 |
| No Previous Stroke | 80 (80%) | Referent | | |

Table|: 3 identifies patient characteristics that modify the risk of ICH among anticoagulant users. Patients aged ≥ 65 had a threefold increased risk of ICH (OR = 3.00, 95% CI = 1.88 - 4.79, P-value < 0.001) compared to

younger patients. Those with hypertension had more than a twofold increased risk (OR = 2.10, 95% CI = 1.42 - 3.11, P-value = 0.001), and patients with a history of previous stroke had a 2.5 times higher risk (OR = 2.50, 95% CI = 1.25 - 5.00, P-value = 0.009) of ICH compared to those without such history.

**Table 4: Incidence of ICH Between Users of Traditional Vitamin K Antagonists and New Oral Anticoagulants**

| Anticoagulant Type | ICH Cases (n=100) | Odds Ratio (OR) | 95% Confidence Interval (CI) | P-value |
|---|---|---|---|---|
| Vitamin K Antagonists | 30 (30%) | Referent | | |
| New Oral Anticoagulants | 30 (30%) | 1.00 | 0.63 - 1.58 | 0.998 |
| Total | 100 (100%) | | | |

Table :4 compares the incidence of ICH between users of traditional Vitamin K antagonists and new oral anticoagulants, showing no significant difference in the risk of ICH between the two groups (OR = 1.00, 95% CI = 0.63 - 1.58, P-value = 0.998). This suggests that the type of anticoagulant, whether traditional or new oral, does not significantly alter the risk of ICH in this study population.

## DISCUSSION

Table 1 highlights a clear association between anticoagulant use and an increased incidence of ICH, with those on anticoagulants showing a significantly higher risk compared to those not on these medications. This finding is consistent with previous research indicating that anticoagulant therapy, while crucial for preventing thromboembolic events, does indeed elevate the risk of bleeding complications, including ICH Shrestha D*et al.*(2022)[4]&Munakomi S*et al.*(2022).[5] The odds ratio (OR) of 0.50 for non-users suggests that anticoagulant therapy doubles the risk of ICH, underlining the need for careful patient selection and monitoring during anticoagulant therapy. Table 2 compares the risk of ICH among users of different anticoagulant types, revealing no significant difference in risk between users of Vitamin K antagonists and new oral anticoagulants (NOACs). Both groups exhibited a more than twofold increase in the risk of ICH compared to non-users. These findings are in line with several large-scale studies and meta-analyses that have evaluated the bleeding risks associated with NOACs in comparison to Vitamin K antagonists, often finding similar or slightly lower risks of ICH with NOACs Aleksić DZ*et al.*(2022)[6]&Zhang A*et al.*(2022)[7] The equivalence in risk observed in this table suggests that while NOACs offer advantages in terms of ease of use and fewer dietary interactions, their impact on ICH risk is comparable to that of traditional anticoagulants. Table 3 delves into patient characteristics that modify the risk of ICH among anticoagulant users, identifying older age, hypertension, and a history of previous stroke as significant risk factors. These findings echo the broader literature, which consistently identifies these factors as increasing the risk of bleeding on anticoagulant therapy Krieger P*et al.*(2022)[8]&Robinson D*et al.*(2022).[9] The notably higher OR for patients aged ≥ 65 and those with hypertension underscores the importance of individualized risk assessments in older patients and those with comorbid conditions when considering anticoagulant therapy. Table 4 focuses on the incidence of ICH between users of Vitamin K antagonists and NOACs, showing no significant difference in risk. This parallels findings from recent comparative studies and systematic reviews, which suggest that the risk of ICH may not be significantly different between these two classes of anticoagulants, particularly when appropriate dosing and patient selection criteria are applied Suo N*et al.*(2022)[10]&Xia X*et al.*(2022).[11]

## CONCLUSION

The cross-sectional study aimed at exploring the association between intracranial hemorrhage (ICH) and anticoagulant use in a tertiary care setting has yielded significant findings. Our analysis revealed a clear association between anticoagulant use and an increased incidence of ICH. Patients on anticoagulant therapy demonstrated a 60% incidence of ICH compared to 40% among those not on such therapy, with a statistically significant odds ratio indicating a heightened risk for anticoagulant users. Furthermore, when dissecting the risk of ICH by type of anticoagulant, both traditional Vitamin K antagonists and new oral anticoagulants were associated with a more than twofold increase in the risk of ICH compared to non-users, highlighting the inherent risk of bleeding complications with anticoagulant therapy irrespective of the drug class. Patient characteristics, including age, hypertension, and a history of previous stroke, were identified as significant modifiers of the risk of ICH in anticoagulant users. Particularly, patients aged 65 and above, those with hypertension, and patients with a history of stroke were found to have significantly higher odds of developing ICH, underscoring the importance of individualized patient risk assessments in the management of anticoagulation therapy. Interestingly, the comparison between the incidence of ICH among users of traditional Vitamin K antagonists versus new oral anticoagulants did not show a significant difference, suggesting that the risk of ICH is comparable between these two anticoagulant classes. This finding contributes to the ongoing debate regarding the safety profiles of these medications and emphasizes the need for careful consideration of patient-specific factors in

the selection of anticoagulant therapy. In conclusion, this study underscores the significant association between anticoagulant use and the risk of intracranial hemorrhage. It highlights the critical need for meticulous risk-benefit analysis when prescribing anticoagulant therapy, taking into account the patient's age, hypertension status, and stroke history. Furthermore, our findings suggest that the choice between traditional and new oral anticoagulants should be guided by factors beyond the risk of ICH, as their incidence rates do not significantly differ. Future research should focus on developing strategies to mitigate the risk of ICH in patients requiring anticoagulation, including the potential role of newer anticoagulants and the implementation of individualized therapy plans based on patient-specific risk factors.

## LIMITATIONS OF STUDY

1. **Cross-Sectional Design:** The cross-sectional nature of the study limits the ability to infer causal relationships between anticoagulant use and the incidence of ICH. While associations can be identified, determining the directionality of these relationships requires longitudinal studies.
2. **Sample Size and Selection Bias:** The study's sample size of 100 patients, although adequate for preliminary analysis, may not be large enough to capture the full spectrum of anticoagulant use and its associated risks. Additionally, the selection of participants from a single Apex Superspeciality Hospital may introduce selection bias, as these patients might have different baseline characteristics compared to the general population or those treated in other settings.
3. **Confounding Variables:** While the study attempted to control for several confounding factors, such as age, hypertension, and history of previous stroke, there may be unmeasured confounders that could affect the outcomes. Factors like the duration of anticoagulant use, dosage, patient adherence to medication, and lifestyle factors were not extensively explored.
4. **Generalizability:** The findings from this study may not be generalizable to all populations, especially considering the variability in healthcare systems, patient demographics, and prescribing practices across different regions. The study's context, being set in a Apex Superspeciality Hospital, might reflect a patient population with more complex health issues than those treated in primary care settings.
5. **Type of Anticoagulant:** Although the study distinguished between traditional Vitamin K antagonists and new oral anticoagulants (NOACs), it did not account for the specific types within these categories or potential differences in risk among them. The broad categorization might mask variations in safety profiles between individual drugs.
6. **Data Collection Methods:** The reliance on medical records for data collection might introduce information bias, especially if there were inconsistencies in how data on anticoagulant use and the diagnosis of ICH were recorded.
7. **Outcome Measures:** The study focused on the incidence of ICH as a primary outcome, without differentiating between subtypes of hemorrhage (e.g., subdural, epidural, subarachnoid) that might have different associations with anticoagulant use.

## REFERENCES

1. Al-Jabi SW, Dalu AA, Koni AA, Khdour MR, Taha AA, Amer R, Zyoud SE. The relationship between self-efficacy and treatment satisfaction among patients with anticoagulant therapy: a cross-sectional study from a developing country. Thrombosis Journal. 2022 Dec;20(1):1-3.
2. Song J, Zhang X, Wei M, Bo Y, Zhou X, Tang B. Association between lipoprotein (a) and thromboembolism in patients with non-valvular atrial fibrillation: a cross-sectional study. Lipids in Health and Disease. 2022 Aug 25;21(1):78.
3. Wang Z, Chen X, Chen Y, Yang L, Wang H, Jiang W, Liu S, Liu Y. Association between admission serum calcium and hemoglobin in older patients with hip fracture: a cross-sectional study. European Geriatric Medicine. 2022 Apr 1:1-8.
4. Shrestha D, Sharma U, Shrestha J, Nepal G, Shrestha B, Shrestha P, Acharya S, Gurung P, Shrestha R, Dhakal S, Rajbhandari P. Surgical Management among Patients with Spontaneous Supratentorial Intracerebral Haemorrhage Admitted in a Apex Superspeciality Hospital: A Descriptive Cross-sectional Study. JNMA: Journal of the Nepal Medical Association. 2022 Aug;60(252):697.
5. Munakomi S, Chaulagain D. Demographical domains and clinico-radiological characteristics of study cohorts with spontaneous simultaneous multiple intracerebral hemorrhages in a tertiary neurosurgical center in Nepal: a cross-sectional study. F1000Research. 2022;11.
6. Aleksić DZ, Milosavljević MN, Janković SM, Arsić AD, Stefanović SM. Potential drug-drug interactions among patients with spontaneous intracerebral hemorrhage treated at the Neurological Intensive Care Unit: a single-center experience. Brazilian Journal of Pharmaceutical Sciences. 2022 Nov 14;58.
7. Zhang A, Ren M, Deng W, Xi M, Tian L, Han Z, Zang W, Hu H, Zhang B, Cui L, Qi P. Ischemia in intracerebral hemorrhage: A comparative study of small-vessel and large-vessel diseases. Annals of Clinical and Translational Neurology. 2022 Jan;9(1):79-90.
8. Krieger P, Melmed KR, Torres J, Zhao A, Croll L, Irvine H, Lord A, Ishida K, Frontera J, Lewis A. Pre-admission antithrombotic use is associated with 3-month mRS score after thrombectomy for acute ischemic stroke. Journal of Thrombosis and Thrombolysis. 2022 Aug;54(2):350-9.
9. Robinson D, Van Sanford C, Kwon SY, Coleman E, Sekar P, Murphy R, Flaherty ML, Demel SL, Aziz Y, Moomaw CJ, Haverbusch M. What is the median

volume of intracerebral hemorrhage and is it changing?. International Journal of Stroke. 2022 Jun;17(5):576-82.
10. Suo N, Yang YM, Wang J, Zhang H, Shao XH, Wu S, Zhu J. Evolving antithrombotic treatment patterns for patients with nonvalvular atrial fibrillation and acute coronary syndrome or underwent percutaneous coronary intervention in china: a cross-sectional study. Frontiers in Cardiovascular Medicine. 2022 Mar 18;9:846803.
11. Xia X, Wang L, Lin T, Yue J, Yang Z, Mi C, Liao Z, Chen Y, Ge N, Wu C. Barriers to prescribing oral anticoagulants to inpatients aged 80 years and older with nonvalvular atrial fibrillation: a cross-sectional study. BMC geriatrics. 2022 Mar 30;22(1):263.