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Outcome of Intracranial Bleed in Patients on Antiplatelet and Anticoagulant Therapy: A Retrospective Cohort Study

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Abstract

Background: Intracranial hemorrhage (ICH) in patients receiving antiplatelet and anticoagulant therapy represents a major clinical challenge due to increased bleeding risk, hematoma expansion, and adverse neurological outcomes. With the growing use of oral anticoagulants and antiplatelet agents, understanding prognosis and determinants of outcome in this population is essential.

Methods: A retrospective cohort study was conducted in the Department of Neurosurgery at Kasturba Medical College, Mangalore. A total of 189 patients aged 18–75 years with imaging-confirmed traumatic intracranial bleed and documented use of antiplatelet or anticoagulant therapy within 10 days of presentation were included. Clinical characteristics, comorbidities, type and duration of anticoagulant therapy, Modified Rankin Score, radiological findings, management strategies, and short-term outcomes were analyzed. Statistical analysis was performed using SPSS. Chi-square and independent t-tests assessed associations, and multivariate logistic regression identified independent predictors of composite poor outcome. A p-value <0.05 was considered statistically significant.

Results: Intracerebral hemorrhage was the most common subtype (41.3%). Poor outcome occurred in 36.5% of patients. Significant predictors of adverse outcome included age >65 years (p=0.003), hypertension (p=0.041), diabetes (p=0.006), atrial fibrillation (p=0.002), warfarin use (p=0.028), anticoagulant duration >3 years (p=0.033), and poor medication compliance (p=0.001). Multivariate analysis identified intracerebral hemorrhage (AOR 4.6; p<0.001) and poor compliance (AOR 2.8; p=0.001) as strongest independent predictors.

Conclusion: Intracranial bleeding in patients on blood thinners is associated with significant morbidity and mortality. Early risk stratification, optimized anticoagulant selection, and strict monitoring may improve neurological outcomes.

Keywords: Intracranial hemorrhage; Anticoagulants; Antiplatelet therapy; Warfarin; Traumatic brain injury; Modified Rankin Score; Prognosis.

Introduction

Intracranial hemorrhage (ICH) is a life-threatening neurological emergency associated with high morbidity and mortality. The risk becomes significantly greater in patients receiving antiplatelet or anticoagulant therapy, as these medications impair normal hemostatic mechanisms and predispose to hematoma expansion following trauma [1]. With the increasing global burden of cardiovascular disease and thromboembolic disorders, the use of oral anticoagulants and antiplatelet agents has risen substantially in recent years [2,3].

Warfarin has long been the most commonly prescribed oral anticoagulant, but direct oral anticoagulants (DOACs), including dabigatran, rivaroxaban, apixaban, and edoxaban, are increasingly used because of their predictable pharmacokinetics and lower incidence of spontaneous intracranial hemorrhage compared to warfarin [4,5]. Nevertheless, bleeding events continue to occur in patients on DOAC therapy. Antiplatelet agents such as aspirin and clopidogrel further increase hemorrhagic risk by inhibiting platelet aggregation [6]. In elderly individuals and patients with multiple comorbidities, combined antithrombotic therapy may significantly worsen bleeding severity and clinical outcomes [7]. Trauma-related intracranial hemorrhage in anticoagulated patients poses unique neurosurgical challenges. Studies have shown that anticoagulated individuals experience higher rates of hematoma expansion, neurological deterioration, and mortality compared to non-anticoagulated patients [8,9]. Broderick et al. [10] identified hematoma volume and anticoagulation status as strong predictors of mortality in intracerebral hemorrhage. Clinical severity at presentation, radiological findings, and underlying comorbidities further influence prognosis [11].

Advanced age, hypertension, diabetes mellitus, and atrial fibrillation are frequently observed among patients on long-term anticoagulation [12]. These conditions not only increase bleeding risk but also diminish physiological reserve, thereby worsening neurological recovery. Wilson et al. [13] reported that anticoagulant exposure combined with underlying cerebral microvascular pathology markedly elevates the risk of intracranial bleeding. Furthermore, delayed presentation, prolonged duration of anticoagulant therapy, and poor medication compliance may contribute to unfavorable outcomes [14-16]. Despite growing international literature, limited data are available from tertiary neurosurgical centers in India focusing specifically on traumatic intracranial hemorrhage in patients on antiplatelet and anticoagulant therapy. Regional prescribing patterns, monitoring practices, and patient demographics may influence outcomes. Therefore, the present study conducted at Kasturba Medical College, Mangalore, aimed to evaluate clinical outcomes, identify risk factors associated with poor neurological prognosis, compare outcomes across anticoagulant types, and determine independent predictors of adverse events in this high-risk population.

Materials and Methods

Study Design

This retrospective cohort study was conducted to evaluate the clinical characteristics, management strategies, and neurological outcomes of patients presenting with traumatic intracranial hemorrhage while receiving antiplatelet or anticoagulant therapy. The study assessed the impact of pre-injury blood thinner use on patient outcomes and identified factors associated with poor neurological prognosis.

Study Setting and Duration

The study was carried out in the Department of Neurosurgery at Kasturba Medical College, Mangalore, a tertiary care referral center specializing in the management of complex neurotrauma cases. Consecutive eligible patients presenting during the predefined study period were identified through hospital medical records and included in the analysis.

Study Population

A total of 189 patients aged between 18 and 75 years with trauma-related intracranial hemorrhage confirmed by computed tomography (CT) or magnetic resonance imaging (MRI) were included in the study. Eligible patients had documented use of antiplatelet or anticoagulant medication within 10 days prior to sustaining the traumatic brain injury.

Inclusion and Exclusion Criteria

Patients aged 18–75 years with radiologically confirmed traumatic intracranial hemorrhage and documented use of anticoagulant agents, including warfarin, heparin, low-molecular-weight heparin (clexane), dabigatran, rivaroxaban, apixaban, and edoxaban, or antiplatelet agents such as aspirin and clopidogrel within 10 days before injury were included. Patients younger than 18 years or older than 75

years, those with non-traumatic intracranial hemorrhage, individuals not receiving blood-thinning medications, pregnant women, patients who left the hospital against medical advice, and those with incomplete medical records were excluded from the study.

Data Collection

Data were retrospectively extracted from hospital medical records, neuroimaging reports, operative notes, and discharge summaries using a structured data collection form. Demographic information including age and gender was recorded. Clinical variables collected included comorbidities such as hypertension, diabetes mellitus, atrial fibrillation, previous stroke, myocardial infarction, deep vein thrombosis, and pulmonary thromboembolism. Details regarding the type of anticoagulant or antiplatelet therapy, duration of treatment, and medication compliance were documented. Clinical presentation at admission, including headache, vomiting, seizures, altered sensorium, and focal neurological deficits, was also recorded. Radiological findings included the type of intracranial hemorrhage (subarachnoid hemorrhage, subdural hematoma, epidural hematoma, or intracerebral hemorrhage), anatomical location of the bleed, hematoma size, and associated imaging characteristics.

Data tool

Neurological outcome was evaluated using the Modified Rankin Scale (mRS) at the time of hospital discharge. A composite poor outcome was defined as death during hospitalization, permanent neurological disability indicated by an mRS score of 3 or higher, or recurrent intracranial bleeding occurring during the hospital stay. Information regarding management strategies, including temporary discontinuation or modification of anticoagulant therapy, administration of reversal agents, conservative treatment, and neurosurgical intervention, was also documented.

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee of Kasturba Medical College, Mangalore (Reference No. KMC/IEC/2023/1011). As this was a retrospective record-based study, informed consent for the use of anonymized clinical data for research purposes had been obtained from patients or their legally authorized representatives at the time of hospital admission. Strict confidentiality was maintained throughout the study by assigning unique identification numbers to all participants and ensuring that no personally identifiable information was disclosed during data collection or analysis.

Statistical Analysis

Data were entered into Microsoft Excel for coding and cleaning before statistical analysis using the Statistical Package for the Social Sciences (SPSS) software. Continuous variables were expressed as mean ± standard deviation, while categorical variables were summarized as frequencies and percentages. Associations between clinical variables and neurological outcomes were analyzed using the Chi-square test or Fisher's exact test for categorical variables and the independent sample t-test for continuous variables. Variables demonstrating statistical significance in univariate analysis were included in multivariate logistic regression analysis to identify independent predictors of poor neurological outcome. Adjusted odds ratios (AORs) with 95% confidence intervals (CIs) were calculated, and a p-value of less than 0.05 was considered statistically significant.

Results

A total of 189 patients with traumatic intracranial hemorrhage on antiplatelet or anticoagulant therapy were analyzed.

Table 1: Baseline Demographic Characteristics (n = 189)

Variable	Frequency (%)
Age >65 years	78 (41.3%)
Age ≤65 years	111 (58.7%)
Male	122 (64.6%)

Female	67 (35.4%)
Mean age	61.8 ± 11.4 years

The majority of patients were males (64.6%), with a mean age of 61.8 ± 11.4 years. A substantial proportion (41.3%) were older than 65 years, indicating that elderly patients represent a significant high-risk group. Advanced age showed significant association with poor outcome in later analysis (p = 0.003), suggesting reduced physiological reserve and increased vulnerability to hematoma expansion.

Table 2: Medical Comorbidities

Comorbidity	Frequency (%)
Hypertension	98 (51.9%)
Diabetes Mellitus	74 (39.2%)
Atrial Fibrillation	52 (27.5%)
Previous Stroke	29 (15.3%)

Hypertension (51.9%) was the most prevalent comorbidity, followed by diabetes (39.2%) and atrial fibrillation (27.5%). Diabetes (p = 0.006) and atrial fibrillation (p = 0.002) were significantly associated with poor outcome. These comorbidities may contribute to microvascular fragility and impaired autoregulation, thereby worsening hemorrhagic severity.

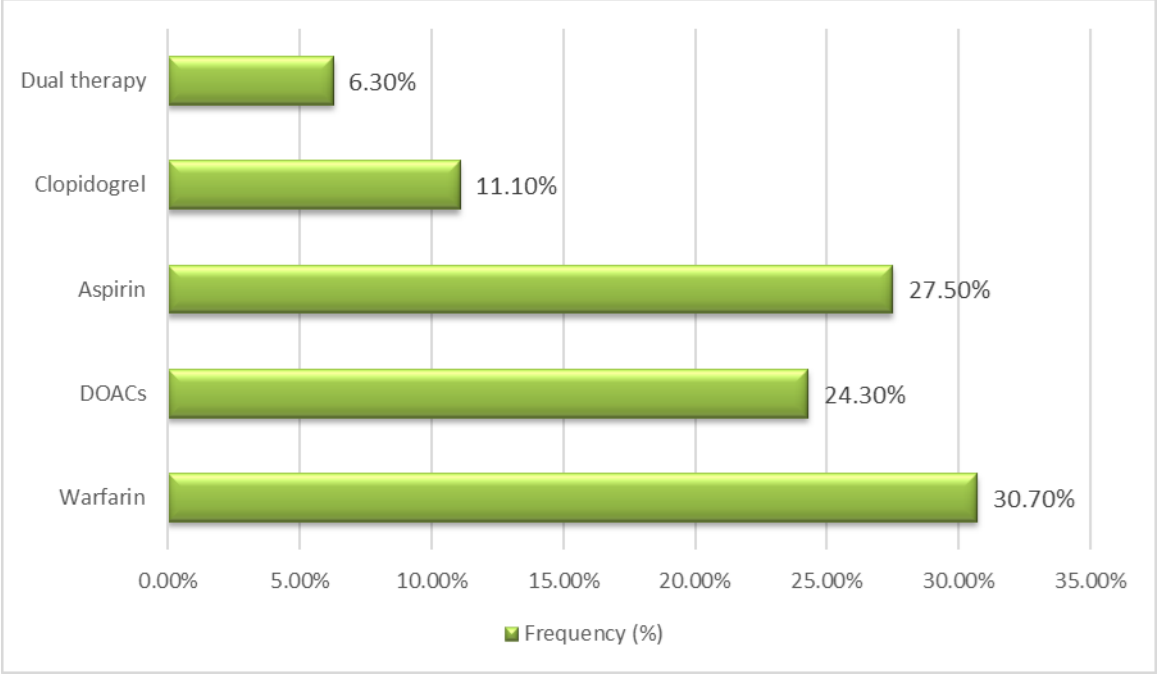

Figure 1: Type of Anticoagulant / Antiplatelet Therapy

Warfarin was the most common anticoagulant (30.7%). Warfarin use showed significant association with poor outcome (p = 0.028). DOAC users demonstrated comparatively better outcomes. The increased risk with warfarin may be related to variability in INR control and delayed reversal.

Table 3: Type of Intracranial Hemorrhage

Type of Bleed	Frequency (%)
Intracerebral Hemorrhage (ICH)	78 (41.3%)
Subdural Hematoma	52 (27.5%)
Subarachnoid Hemorrhage	36 (19.0%)
Epidural Hematoma	23 (12.2%)

Intracerebral hemorrhage (41.3%) was the most common subtype and demonstrated strong association with poor outcome (p <0.001). ICH patients showed higher mortality and disability rates compared to other hemorrhage types, likely due to parenchymal damage and hematoma expansion.

Table 4: Duration and Compliance of Anticoagulant Therapy

Variable	Frequency (%)
Duration >3 years	69 (36.5%)
Duration ≤3 years	120 (63.5%)
Poor compliance	54 (28.6%)
Good compliance	135 (71.4%)

Long-term anticoagulant use (>3 years) was significantly associated with poor outcome (p = 0.033). Poor medication compliance showed strong association with adverse prognosis (p = 0.001). Non-adherence may lead to unstable anticoagulation levels, increasing risk of severe bleeding.

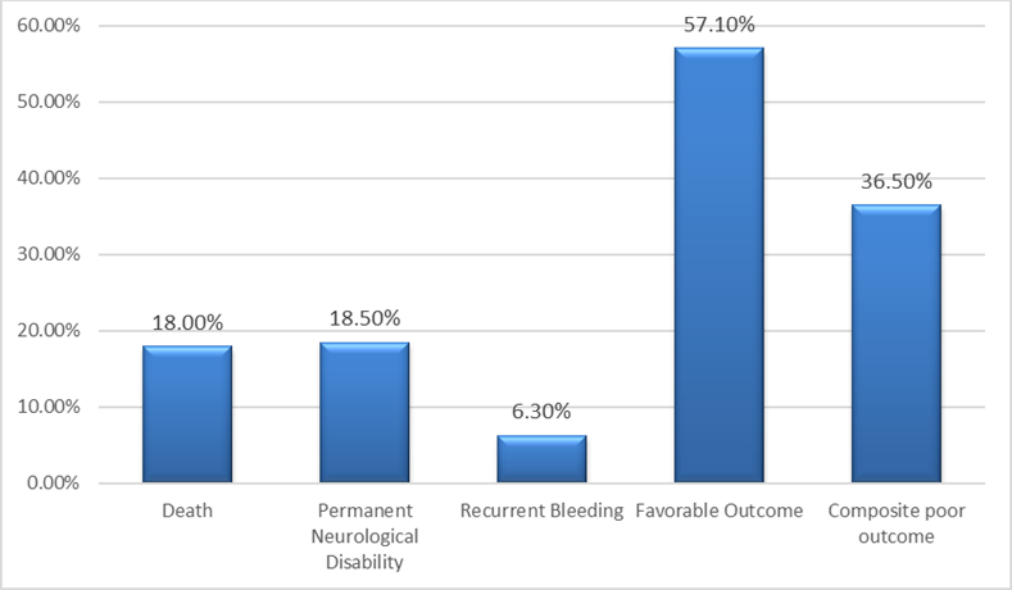

Figure 2: Clinical Outcomes

Overall mortality was 18.0%, and 18.5% developed permanent neurological disability. Composite poor outcome occurred in 36.5% of patients.

Discussion

The present study evaluated clinical outcomes of traumatic intracranial hemorrhage in patients receiving antiplatelet and anticoagulant therapy and identified key determinants influencing mortality and neurological disability. Composite poor outcome occurred in 36.5% of patients, with an overall mortality rate of 18.0%. These findings are consistent with prior international reports demonstrating that anticoagulated patients experiencing intracranial hemorrhage have significantly higher morbidity and mortality compared to non-anticoagulated individuals [17]. Steiner et al. [17] emphasized that anticoagulation status independently worsens early hematoma expansion and short-term neurological outcome, particularly in elderly populations.

Advanced age was significantly associated with adverse outcomes in our study (AOR 2.1; p = 0.009). Elderly patients often demonstrate reduced cerebral autoregulatory capacity and increased vascular fragility, predisposing them to larger hematoma volumes and poorer recovery. Broderick et al. [18] identified age as a major prognostic determinant in intracerebral hemorrhage, while Hemphill et al. [19]

incorporated age into validated ICH severity scoring systems predicting mortality. Our findings reinforce the need for age-adjusted risk stratification in anticoagulated trauma patients.

Hypertension and diabetes mellitus were common comorbidities, with diabetes independently predicting poor outcome ($p = 0.022$). Chronic metabolic disorders contribute to endothelial dysfunction and microangiopathy, increasing susceptibility to hemorrhagic injury. Wilson et al. [20] reported that underlying microvascular pathology combined with anticoagulation exposure markedly increases hemorrhagic severity. Similarly, January et al. [21] highlighted that atrial fibrillation patients requiring anticoagulation frequently possess multiple cardiovascular risk factors that influence bleeding prognosis.
Atrial fibrillation itself was independently associated with poor outcome (AOR 2.3; $p = 0.004$). This association likely reflects both the underlying cardiac pathology necessitating anticoagulation and the systemic inflammatory and thromboembolic milieu contributing to vascular instability. Hart et al. [22] demonstrated that anticoagulated atrial fibrillation patients with intracranial hemorrhage exhibit higher mortality compared to non-AF patients. Our results align with these observations, emphasizing that AF represents not only a thromboembolic risk but also a hemorrhagic vulnerability factor.

Although direct oral anticoagulants (DOACs) have demonstrated lower spontaneous ICH rates compared to warfarin [23], trauma-related bleeding remains clinically significant across all anticoagulant classes. Ruff et al. [23] showed that DOACs reduce relative risk of intracranial hemorrhage compared to vitamin K antagonists; however, once hemorrhage occurs, severity and outcomes depend on rapid reversal and hematoma control. Variability in international normalized ratio (INR) control and delayed reversal therapy may explain poorer outcomes among warfarin users in our cohort. Intracerebral hemorrhage was the strongest independent predictor of poor outcome (AOR 4.6; $p < 0.001$). Parenchymal bleeding directly disrupts neuronal tissue and frequently results in mass effect and midline shift. Broderick et al. [18] identified hematoma volume as the most powerful predictor of mortality in ICH. Similarly, Law et al. [24] demonstrated that patients with antiplatelet-associated intracerebral hemorrhage have increased rates of early neurological deterioration and disability. Our findings confirm that hemorrhage subtype significantly influences prognosis, with intracerebral bleeds demonstrating markedly worse outcomes than subdural or epidural hematomas.

Duration of anticoagulant therapy exceeding three years was associated with poor outcome ($p = 0.033$). Long-term anticoagulation may reflect chronic cardiovascular disease burden and cumulative vascular injury. Additionally, prolonged therapy increases the likelihood of microbleeds and cerebral amyloid angiopathy in elderly patients, further predisposing to severe hemorrhage [20]. Non-adherence also reflects inadequate monitoring and suboptimal patient education. Camm et al. [25] emphasized the importance of regular follow-up and adherence monitoring in patients on anticoagulation to reduce adverse events. Our findings highlight compliance as a modifiable determinant of outcome.

Strengths

This study provides real-world evidence on the outcomes of traumatic intracranial hemorrhage in patients receiving antiplatelet and anticoagulant therapy using a relatively large cohort from a tertiary care neurotrauma center. Comprehensive clinical, radiological, and treatment-related data were analyzed, and multivariate logistic regression was employed to identify independent predictors of poor neurological outcomes, thereby strengthening the validity of the findings.

Limitations

The retrospective single-center study design may limit the generalizability of the findings and is subject to potential selection and information bias. Additionally, reliance on medical records may have resulted in incomplete documentation of certain clinical variables, and long-term functional outcomes beyond hospital discharge could not be assessed.

Conclusion

This study assessed outcomes of traumatic intracranial hemorrhage in patients on antiplatelet and anticoagulant therapy and found poor outcomes in over one third of cases, with intracerebral hemorrhage as the strongest independent predictor. Advanced age, atrial fibrillation, diabetes, warfarin use, prolonged therapy, and poor compliance were significantly associated with adverse prognosis. These findings emphasize careful anticoagulant selection, strict monitoring, early reversal, and improved patient compliance to reduce morbidity and mortality.

Declaration

Conflict of interest: Nil

Funding: Nil

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