

## Review

# Acute Management of Intracerebral Hemorrhage in Patients with Anticoagulation Therapy

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## Abstract

Anticoagulation-associated intracerebral hemorrhage is a complex clinical emergency with high rates of morbidity and mortality. The increasing use of anticoagulants, particularly in elderly populations with conditions like atrial fibrillation or mechanical heart valves, has contributed to a growing number of spontaneous ICH cases. Management in the acute phase requires rapid identification of the anticoagulant involved, immediate reversal of its effects, and stabilization of the patient's neurological condition. Prothrombin complex concentrates, vitamin K, idarucizumab, and andexanet alfa are among the primary agents used, with selection depending on drug class and availability. Delays in reversal therapy are associated with increased hematoma expansion and worse functional outcomes. Clinical judgment is critical in balancing the urgency of reversal with the potential risks of thrombosis, especially in patients with significant cardiovascular comorbidities. The decision to resume anticoagulation following AAICH remains one of the most challenging aspects of long-term management. Observational studies suggest that resuming anticoagulation between 7 and 14 days after the initial event may offer protection against thromboembolism without significantly increasing the risk of recurrent bleeding. Timing often depends on hematoma location, radiographic stability, and the indication for anticoagulation. Predictors of poor outcome include low Glasgow Coma Scale scores, large hematoma volume, intraventricular extension, and lobar location. Post-discharge recovery is influenced by age, comorbidities, and access to rehabilitation services. Patients who receive early follow-up and structured care show better functional independence and reduced readmission rates. Optimizing both acute interventions and long-term planning is essential for improving survival and quality of life in this high-risk population.

**Keywords:** *intracerebral hemorrhage, anticoagulation reversal, hematoma expansion, stroke management, anticoagulant resumption*

## Introduction

Intracerebral hemorrhage (ICH) is a severe subtype of stroke resulting from bleeding directly into the brain tissue. Though it accounts for a smaller proportion of total strokes, it carries a much higher risk of early mortality and long-term disability. Among the many risk factors for ICH, anticoagulation therapy has emerged as a significant contributor, particularly in elderly patients with comorbidities such as atrial fibrillation and mechanical heart valves. Warfarin, a vitamin K antagonist, has long been associated with an increased risk of spontaneous ICH, especially in those with supratherapeutic international normalized ratio (INR) levels (1).

Management of anticoagulant-associated ICH (AAICH) begins with stabilizing the patient and halting hematoma expansion. Rapid reversal of anticoagulation is the cornerstone of early intervention, with the choice of reversal agent depending on the type of anticoagulant involved. For patients on warfarin, vitamin K and prothrombin complex concentrates (PCCs) are commonly used. In contrast, idarucizumab and andexanet alfa have been developed for reversal of dabigatran and factor Xa inhibitors, respectively. The administration of these agents must be guided by the urgency of reversal and the patient's bleeding risk profile (2).

Despite advances in treatment, AAICH continues to be associated with high morbidity and mortality. Hematoma expansion within the first 24 hours is a leading predictor of poor neurological outcome. Delays in reversing anticoagulation can significantly increase this risk. In one study, patients with oral anticoagulant-related ICH experienced worse outcomes compared to non-anticoagulated individuals, even when reversal therapies were implemented promptly. This underscores the need for early diagnosis and a standardized, protocol-driven approach to management (3).

A persistent clinical dilemma is deciding when to resume anticoagulation following an ICH event. While premature reinitiation may elevate the risk of recurrent bleeding, prolonged discontinuation increases the risk of thromboembolism, particularly

in high-risk cardiac patients. Studies suggest that this decision should be tailored based on individual stroke and bleeding risks, imaging findings, and the underlying indication for anticoagulation. In a multicenter study, early reversal and careful follow-up were associated with improved survival, yet the long-term risk-benefit balance remains an area requiring further research and clearer guidelines (4).

## Review

AAICH remains a critical medical emergency, where timely management significantly affects outcomes. The reversal of anticoagulation is the primary therapeutic goal in the acute setting. Rapid administration of reversal agents, such as PCCs or specific antidotes for direct oral anticoagulants (DOACs), has been shown to improve hemostasis and reduce hematoma expansion. However, access to these agents and variability in their clinical use continue to challenge standardized care. In particular, reversal strategies must be tailored to the pharmacodynamics of the anticoagulant involved and the severity of the hemorrhage. One study emphasized the effectiveness of ultra-rapid reversal protocols using PCCs in achieving prompt coagulation correction in surgical ICH settings, highlighting the importance of minimizing time to treatment (5).

Another major area of clinical uncertainty lies in the timing of anticoagulation reinitiation following an ICH event. While delaying anticoagulation may prevent recurrent bleeding, it also increases the risk of ischemic complications, especially in patients with atrial fibrillation or mechanical heart valves. Evidence suggests that careful risk stratification and individualized decision-making are essential to minimize both thromboembolic and hemorrhagic risks. Findings from a cohort study suggest that patients with stable clinical and imaging profiles may safely resume anticoagulation within several weeks post-ICH (6).

### ***Reversal Strategies and Hemostatic Interventions***

The initial hours following the onset of ICH in anticoagulated patients are marked by high risk for hematoma growth and neurological deterioration.

Speed and accuracy in reversing the anticoagulant effect are critical for reducing further bleeding and stabilizing the patient. The challenge begins with identifying the specific anticoagulant in use and determining the most appropriate reversal agent based on pharmacologic profile and availability. In vitamin K antagonist-related ICH, PCCs are currently favored over fresh frozen plasma due to faster INR correction and lower volume load, which is important in patients at risk for elevated intracranial pressure (7).

Patients treated with direct oral anticoagulants (DOACs) such as apixaban, rivaroxaban, or dabigatran require more targeted strategies. Idarucizumab has shown rapid neutralization of dabigatran, while andexanet alfa is approved for reversal of factor Xa inhibitors. These agents, though effective, come with concerns related to high cost, restricted availability in some centers, and limited post-marketing safety data. Some institutions have adopted off-label use of PCCs for DOAC reversal in emergency settings, supported by observational data suggesting clinical benefit despite the lack of direct antagonism (8). The variation in practice patterns reflects ongoing uncertainty about the comparative efficacy of specific versus non-specific reversal agents in this context.

Timing is a determinant of outcome. In a multicenter registry, delayed administration of reversal therapy was associated with significantly larger hematoma volumes and worse functional scores at discharge. The sooner anticoagulation is neutralized, the more likely hematoma expansion can be contained. This is especially relevant in patients who require surgical intervention or external ventricular drainage. In many facilities, reversal agents are now stocked in emergency departments or intensive care units to reduce door-to-needle time for these cases (9). The integration of point-of-care coagulation testing has also improved the decision-making process, allowing faster differentiation between warfarin-associated and DOAC-related hemorrhages.

Despite advances in pharmacologic interventions, hemostatic strategies remain inconsistent across institutions. Protocols vary depending on the local availability of reversal agents, familiarity among staff, and institutional guidelines. Some centers use weight-based dosing, others fixed-dose PCC regimens. Variability in outcome reporting adds another layer of complexity when interpreting the effectiveness of these strategies. Research involving standardized reversal protocols demonstrated reduced rates of hematoma growth and better early neurologic outcomes in ICH patients treated with PCCs compared to historical controls (10).

### ***Timing and Safety of Anticoagulation Reinitiation***

The decision to resume anticoagulation therapy after ICH presents a high-stakes balance between preventing thromboembolic events and avoiding recurrent bleeding. Clinical reasoning in this context often begins with a careful evaluation of the initial cause of the hemorrhage, the underlying indication for anticoagulation, and the stability of the hemorrhagic site. While international guidelines remain cautious, growing evidence has begun to clarify certain scenarios in which reinitiation may reduce long-term risks without significantly increasing adverse outcomes. A population-based analysis demonstrated that patients with atrial fibrillation who resumed warfarin within 7 to 8 weeks after ICH had lower rates of ischemic stroke and mortality compared to those who did not restart anticoagulation at all (11).

Several observational studies and meta-analyses have attempted to define optimal time frames for restarting anticoagulation. Across these works, a consistent finding emerges: delaying therapy for too long exposes patients to preventable thromboembolic complications, particularly in those with mechanical heart valves or atrial fibrillation. One systematic review found that restarting anticoagulation between 7 and 14 days after ICH minimized the risks of both ischemia and recurrent bleeding when compared to earlier or later reinitiation windows (12). While heterogeneity in study populations and treatment protocols complicates direct comparisons, there appears to be

a general preference among neurologists and cardiologists to wait at least one week before reintroducing therapy, assuming radiological stability and no signs of expansion.

Patient stratification plays a critical role in these decisions. Variables such as hematoma location, volume, presence of intraventricular extension, and baseline functional status influence timing. Lobar hemorrhages, for instance, are associated with a higher recurrence rate and may warrant longer delays, whereas deep hemorrhages in hypertensive patients may be considered lower-risk for recurrence under close imaging surveillance. A retrospective cohort analysis found that individuals with lobar ICH had significantly better outcomes when anticoagulation was resumed after four weeks, compared to earlier time frames (9). In contrast, those with deep ICH and a strong indication for anticoagulation could benefit from earlier reintroduction, particularly if initial hemostasis was achieved with effective reversal and imaging confirmed hematoma resolution.

Reinitiation strategies are also influenced by the type of anticoagulant. In patients previously on DOACs, clinicians may be more inclined to resume therapy sooner due to the shorter half-life and lower rates of intracranial bleeding associated with these agents compared to warfarin. For warfarin-treated patients, bridging strategies involving low molecular weight heparin have sometimes been employed, although their safety in the ICH context remains less well defined. Data from a multicenter registry revealed that patients restarted on DOACs within 14 to 21 days experienced fewer ischemic events than those restarted later, with no statistically significant increase in ICH recurrence (13).

### ***Outcome Predictors and Long-Term Management Considerations***

Long-term outcomes following AAICH are shaped by a complex interplay of clinical, radiographic, and therapeutic factors. Functional recovery often depends on early neurological status, hematoma location, and size, as well as the timeliness of care provided during the acute phase. Several large-scale studies have emphasized the prognostic value of the

Glasgow Coma Scale (GCS) score at presentation. Lower GCS scores tend to correlate with higher 30-day mortality and reduced likelihood of functional independence. Patients arriving with GCS scores below 8 face markedly worse trajectories compared to those with mild to moderate impairment, even when reversal therapy is initiated promptly (14).

Hematoma volume and intraventricular extension further influence recovery profiles. Volumes greater than 30 mL are consistently associated with higher early mortality and more profound disability in survivors. Intraventricular hemorrhage often leads to hydrocephalus, requiring external ventricular drainage and prolonged intensive care. Both of these complications significantly prolong hospitalization and limit the possibility of early mobilization. Additionally, lobar hemorrhages tend to carry a greater risk of recurrence, especially when cerebral amyloid angiopathy is suspected based on imaging features and patient age. A study comparing lobar to deep hemispheric bleeds found that those with lobar location had a greater chance of delayed clinical deterioration and often required longer periods of observation before transitioning to rehabilitation settings (15).

Beyond acute care, cognitive function and physical independence are influenced by preexisting comorbidities, especially in elderly populations. Hypertension, diabetes, and chronic kidney disease are strongly associated with worse long-term neurologic recovery. These comorbidities often complicate blood pressure management and limit pharmacologic choices for secondary stroke prevention. In post-discharge follow-ups, patients with higher CHA<sub>2</sub>DS<sub>2</sub>-VASc and HAS-BLED scores not only experienced more adverse cardiovascular events but also faced increased rates of hospital readmission due to recurrent bleeding or thromboembolic complications. Predictive models incorporating both neurologic and cardiovascular risk factors have been proposed to guide care plans beyond the initial hospital stay (16).

Long-term strategies also require multidisciplinary coordination, especially in patients for whom resuming anticoagulation is medically indicated. A

structured follow-up plan involving neurology, cardiology, and primary care has been linked to improved outcomes in observational studies. Physical and cognitive rehabilitation play a central role in reducing long-term dependency, though access varies widely depending on geographic and socioeconomic factors. In a prospective cohort, patients who received early rehabilitation within two weeks of discharge had significantly higher functional independence at six months. Medication adherence and education on lifestyle modification further influence secondary prevention efforts, though these are often under-addressed during the transition from hospital to home. Registries tracking post-ICH outcomes show that consistent engagement with outpatient care providers correlates with reduced rates of both recurrent bleeding and ischemic stroke over the following year (16, 17).

## Conclusion

Effective acute management of anticoagulation-associated intracerebral hemorrhage relies on timely reversal, individualized risk assessment, and structured long-term planning. Decisions around reinitiating anticoagulation must weigh recurrence risk against thromboembolic protection. Prognostic indicators like hematoma characteristics and baseline functional status guide both immediate and future care. Coordinated follow-up and rehabilitation remain essential to improving long-term outcomes.

## Disclosure

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### *Data availability*

All data is available within the manuscript.

## *Author contribution*

All authors contributed to conceptualizing, data drafting, collection and final writing of the manuscript.

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