Más Allá de la Hemostasia: Reversión Integral de la Anticoagulación, Optimización Hemodinámica y Toma de Decisiones Neuroquirúrgicas en la Hemorragia Intracerebral

Beyond Hemostasis: Integrated Anticoagulation Reversal, Hemodynamic Optimization, and Neurosurgical Decision-Making in Intracerebral Hemorrhage

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RESUMEN

La hemorragia intracerebral asociada a anticoagulantes constituye una urgencia neurológica potencialmente mortal, caracterizada por expansión rápida del hematoma, lesión cerebral

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secundaria y un elevado riesgo de mortalidad y discapacidad funcional permanente. Su tratamiento requiere estrategias coordinadas dirigidas a controlar la actividad anticoagulante, estabilizar las condiciones hemodinámicas y prevenir las complicaciones intracraneales. Esta revisión narrativa analiza críticamente la evidencia científica internacional sobre reversión farmacológica, control de la presión arterial e intervención neuroquirúrgica, incorporando perspectivas aplicables a los sistemas sanitarios latinoamericanos. Se examinaron 20 publicaciones científicas, incluidos ensayos clínicos aleatorizados, estudios observacionales y guías clínicas, mediante un enfoque cualitativo y comparativo. Los resultados del ensayo INCH demostraron una normalización más rápida de los parámetros de coagulación mediante concentrado de complejo protrombínico de cuatro factores en comparación con plasma fresco congelado. ANNEXA-I evidenció una mayor eficacia hemostática con andexanet alfa frente al tratamiento habitual, aunque con una frecuencia superior de complicaciones trombóticas y sin beneficios funcionales demostrados. Los estudios INTERACT2 y ATACH-II identificaron diferencias en los resultados clínicos del control intensivo de la presión arterial, mientras que INTERACT3 mostró mejores desenlaces funcionales mediante el manejo coordinado de alteraciones fisiológicas. La evidencia neuroquirúrgica de MISTIE III y ENRICH indicó que la efectividad de la evacuación mínimamente invasiva depende de la técnica empleada, las características anatómicas, el momento de intervención y la selección de pacientes. En conjunto, las mejoras hemostáticas o radiológicas no se tradujeron sistemáticamente en menor mortalidad o recuperación neurológica sostenida. Los hallazgos respaldan un enfoque individualizado y multidisciplinario que integre reversión temprana de la anticoagulación, estabilización hemodinámica controlada, vigilancia neurológica continua y tratamiento neuroquirúrgico selectivo. Se requieren nuevas investigaciones para definir la secuencia terapéutica óptima, los criterios quirúrgicos específicos y las estrategias de implementación en sistemas sanitarios con recursos heterogéneos.

PALABRAS CLAVE

hemorragia intracerebral asociada a anticoagulantes, reversión de la anticoagulación, concentrado de complejo protrombínico, anticoagulantes orales directos, control de la presión arterial, expansión del hematoma, neurocirugía mínimamente invasiva, desenlaces neurológicos, cuidados neurocríticos

ABSTRACT

Anticoagulant-associated intracerebral hemorrhage represents a life-threatening neurological emergency characterized by rapid hematoma expansion, secondary cerebral injury, and substantial risks of mortality and long-term functional disability. Its management requires coordinated therapeutic strategies addressing anticoagulant activity, systemic hemodynamics, and intracranial complications. This narrative review critically examines current international evidence regarding pharmacological reversal, blood pressure management, and neurosurgical intervention, incorporating perspectives relevant to Latin American healthcare systems. Twenty scientific publications, including randomized controlled trials, observational investigations, and clinical guidelines, were analyzed through a comparative qualitative approach. Evidence from the INCH trial demonstrated more rapid normalization of coagulation parameters with four-factor prothrombin complex concentrate than with fresh frozen plasma. ANNEXA-I reported greater hemostatic efficacy with andexanet alfa compared with usual care, although thrombotic complications were more frequent and functional benefits were not established. Findings from INTERACT2 and ATACH-II highlighted differences in clinical outcomes associated with intensive blood pressure reduction, whereas INTERACT3 demonstrated improved functional outcomes through coordinated management of physiological abnormalities. Neurosurgical evidence from MISTIE III and ENRICH revealed that the effectiveness of minimally invasive hematoma evacuation depends on procedural technique, anatomical characteristics, treatment timing, and patient selection. Across the reviewed studies, improvements in hemostatic or radiological parameters did not consistently translate into reduced mortality or sustained neurological recovery. The findings support an individualized, multidisciplinary approach integrating prompt anticoagulant reversal, controlled hemodynamic stabilization, continuous neurological assessment, and selective neurosurgical treatment. Further investigations are needed to establish optimal therapeutic sequencing, anticoagulant-specific surgical criteria, and implementation strategies adapted to resource-variable healthcare environments.

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KEYWORDS

anticoagulant-associated intracerebral hemorrhage, anticoagulation reversal, prothrombin complex concentrate, direct oral anticoagulants, blood pressure management, hematoma expansion, minimally invasive neurosurgery, neurological outcomes, neurocritical care

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INTRODUCCIÓN

Anticoagulant-associated intracerebral hemorrhage (ICH) represents a critical neurological emergency associated with high mortality, severe neurological deterioration, and long-term functional disability. Its clinical significance has increased alongside the widespread use of oral anticoagulants for atrial fibrillation, mechanical heart valves, and thromboembolic disorders. Although direct oral anticoagulants (DOACs) generally exhibit a lower risk of intracranial bleeding than vitamin K antagonists in several clinical settings, hemorrhagic complications remain particularly challenging because of their potential for rapid hematoma expansion and secondary cerebral injury. Effective management requires early identification of anticoagulant exposure, immediate correction of coagulation abnormalities, hemodynamic stabilization, and timely neurosurgical assessment (Greenberg et al., 2022; Christensen et al., 2019).

The pathophysiology of anticoagulant-associated ICH involves impaired hemostasis combined with vascular injury, resulting in persistent bleeding, hematoma enlargement, perihematomal edema, and increased intracranial pressure. Hematoma expansion is a major determinant of neurological deterioration and represents an important therapeutic target during the initial hours after hemorrhage onset. Pharmacological reversal strategies have therefore become central to acute management. Evidence supports the use of four-factor prothrombin complex concentrate for vitamin K antagonist-associated bleeding, idarucizumab for dabigatran reversal, and andexanet alfa for selected cases involving factor Xa inhibitors. Nevertheless, differences in reversal efficacy, thromboembolic complications, treatment availability, and institutional resources continue to influence therapeutic decisions (Frontera et al., 2016; Kuramatsu et al., 2015; Pollack et al., 2017; Connolly et al., 2024).

Hemodynamic management constitutes another fundamental component of treatment. Elevated systolic blood pressure during acute hemorrhage may contribute to hematoma expansion, whereas excessive or abrupt reduction may compromise cerebral perfusion in vulnerable patients. The INTERACT2 and ATACH-II trials established important evidence regarding intensive blood pressure reduction, although differences in their findings highlight the importance of individualized therapeutic targets. More recently, INTERACT3 demonstrated the clinical relevance of coordinated care bundles incorporating blood pressure control, correction of coagulation abnormalities, glucose regulation, and temperature management. Latin American initiatives have additionally emphasized the need to adapt these strategies to regional healthcare infrastructure, resource availability, and institutional capabilities (Anderson et al., 2013; Qureshi et al., 2016; Ma et al., 2023; Allende et al., 2025).

Neurosurgical intervention introduces further complexity, particularly when determining whether hematoma evacuation, minimally invasive techniques, decompressive craniectomy, or ventricular drainage may improve outcomes. Evidence from STICH II, MISTIE III, and subsequent randomized trials suggests that surgical benefits depend on hematoma location, volume, neurological severity, procedural timing, and patient selection. Consequently, surgical decision-making cannot be separated from anticoagulant reversal and hemodynamic optimization, especially when perioperative bleeding risks remain elevated (Mendelow et al., 2013; Hanley et al., 2019; Pradilla et al., 2024; Beck et al., 2024).

Despite substantial advances, uncertainty persists regarding the optimal sequence of reversal, blood pressure management, and neurosurgical intervention. This narrative review examines contemporary evidence on these three therapeutic domains, focusing on their effectiveness, limitations, and clinical integration. Particular attention is given to international guidelines, randomized clinical trials, and Latin American perspectives. The central question is how coordinated pharmacological, hemodynamic, and neurosurgical strategies can optimize acute management and neurological outcomes in patients with anticoagulant-associated intracerebral hemorrhage.

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DESARROLLO

Anticoagulant-associated intracerebral hemorrhage represents a multifactorial condition in which coagulation abnormalities, cerebrovascular injury, and intracranial pressure disturbances interact to determine neurological prognosis. The initial therapeutic priority is to prevent hematoma expansion while preserving cerebral perfusion and minimizing secondary injury. Clinical assessment should integrate neurological status, anticoagulant exposure, hemorrhage volume, anatomical location, and intraventricular extension. Noncontrast computed tomography remains essential for confirming hemorrhage and establishing baseline characteristics, whereas follow-up neuroimaging allows assessment of hematoma progression and complications. The heterogeneity of clinical presentations highlights the importance of individualized treatment strategies supported by multidisciplinary evaluation (Greenberg et al., 2022; Steiner et al., 2025).

Pharmacological reversal constitutes a fundamental intervention because persistent anticoagulant activity may facilitate continued bleeding and hematoma enlargement. In vitamin K antagonist-associated hemorrhage, four-factor prothrombin complex concentrate combined with intravenous vitamin K provides rapid correction of coagulation abnormalities. The INCH trial demonstrated that 67% of patients receiving prothrombin complex concentrate achieved an international normalized ratio of 1.2 or lower within three hours, compared with 9% receiving fresh frozen plasma. These findings support rapid reversal, although normalization of coagulation parameters does not necessarily guarantee improved functional recovery (Steiner et al., 2016). For dabigatran-associated bleeding, idarucizumab provides targeted reversal, while factor Xa inhibitor-associated hemorrhage presents additional therapeutic challenges. In ANNEXA-I, andexanet alfa achieved hemostatic efficacy in 67.0% of patients compared with 53.1% receiving usual care, but thrombotic events were more frequent in the intervention group (10.3% versus 5.6%). Subsequent safety concerns led to the withdrawal of andexanet alfa from the United States market in December 2025, underscoring the need to reassess reversal strategies according to current regulatory status, drug availability, and individual thromboembolic risk (Pollack et al., 2017; Connolly et al., 2024; U.S. Food and Drug Administration, 2025).

Hemodynamic control is equally important because acute elevations in blood pressure may promote hematoma expansion and worsen neurological injury. Nevertheless, excessively aggressive reductions can introduce additional risks, particularly in patients with impaired cerebral autoregulation or significant intracranial hypertension. INTERACT2 suggested improved functional outcomes through early intensive blood pressure management, whereas ATACH-II found no significant reduction in death or disability with more aggressive systolic pressure targets. Furthermore, renal adverse events occurred in 9.0% of patients receiving intensive treatment compared with 4.0% receiving standard treatment in ATACH-II. These findings support controlled, sustained blood pressure reduction rather than abrupt or excessively intensive interventions. In selected patients with mild to moderate hemorrhage, maintaining systolic pressure near 140 mmHg may be reasonable, provided cerebral perfusion and systemic stability are preserved (Anderson et al., 2013; Qureshi et al., 2016; Greenberg et al., 2022).

The integration of hemostatic and hemodynamic interventions has gained importance following evidence supporting standardized acute care bundles. INTERACT3 evaluated 7,036 patients across 121 hospitals and demonstrated improved functional outcomes through coordinated management of blood pressure, coagulation abnormalities, glucose concentrations, and body temperature. The intervention was associated with reduced odds of poorer functional outcomes compared with usual care (common odds ratio, 0.86; 95% confidence interval, 0.76–0.97). Although this trial included patients with intracerebral hemorrhage regardless of anticoagulant exposure, its findings support the broader principle that simultaneous correction of modifiable physiological abnormalities may be more effective than isolated therapeutic interventions. Latin American recommendations have emphasized adapting these protocols to regional healthcare systems, particularly where access to specialized reversal agents, neurocritical care services, and emergency neurosurgical facilities remains limited (Ma et al., 2023; Allende et al., 2025).

Neurosurgical management represents another critical dimension, particularly in patients with substantial mass effect, progressive neurological deterioration, obstructive hydrocephalus, or selected surgically accessible hematomas. Decisions regarding intervention must consider hemorrhage location, hematoma volume, neurological severity, anticipated functional recovery, and the feasibility of timely coagulation correction. The STICH II and MISTIE III trials demonstrated the complexity of identifying patients who benefit from surgical evacuation. In MISTIE III, favorable functional outcomes were observed in an estimated 45% of surgically treated patients compared with 41%

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receiving standard medical management, without a statistically significant difference in the primary outcome. Conversely, the ENRICH trial demonstrated improved functional outcomes at 180 days following early minimally invasive evacuation, with benefits predominantly associated with lobar hemorrhages. These findings indicate that surgical effectiveness depends substantially on anatomical selection, procedural technique, and intervention timing rather than hematoma evacuation alone (Mendelow et al., 2013; Hanley et al., 2019; Pradilla et al., 2024).

Finally, anticoagulant-associated hemorrhage requires balancing immediate hemorrhagic control against the subsequent risk of thromboembolism. This consideration is particularly relevant in patients with mechanical heart valves or high-risk cardiovascular conditions, for whom prolonged interruption of anticoagulation may produce serious complications. Decisions regarding anticoagulation resumption should incorporate hemorrhage stability, neuroimaging findings, thromboembolic risk, and the underlying indication for treatment (Kuramatsu et al., 2018). Overall, contemporary evidence supports a coordinated therapeutic framework in which rapid anticoagulant reversal, controlled hemodynamic management, continuous neurological surveillance, and selective neurosurgical intervention are integrated according to individual clinical characteristics. However, uncertainties concerning optimal treatment sequencing, reversal-associated thrombosis, and surgical eligibility reinforce the need for further comparative research and regionally applicable management strategies.

OBJETIVO GENERAL Y OBJETIVOS ESPECÍFICOS

General Objective

To critically analyze and synthesize current scientific evidence regarding pharmacological anticoagulant reversal, hemodynamic stabilization, and neurosurgical intervention in anticoagulant-associated intracerebral hemorrhage, with the purpose of identifying effective therapeutic strategies, establishing evidence-based clinical decision criteria, and examining their applicability across international and Latin American healthcare settings.

Specific Objectives

Cognitive Domain

- To identify and explain the principal pathophysiological mechanisms underlying anticoagulant-associated intracerebral hemorrhage, emphasizing hematoma expansion, secondary brain injury, and coagulation abnormalities.
- To analyze and compare the efficacy, safety, and clinical limitations of pharmacological reversal strategies according to anticoagulant class, available reversal agents, and associated thromboembolic risks.
- To evaluate current evidence regarding blood pressure targets, hemodynamic monitoring, and neuroprotective management, distinguishing interventions supported by randomized clinical trials from those requiring further investigation.
- To critically assess the indications, timing, and neurological outcomes of conventional and minimally invasive neurosurgical procedures, considering hematoma characteristics and patient-specific prognostic factors.

Psychomotor and Procedural Domain

- To develop a structured clinical decision-making framework integrating anticoagulant identification, emergency neuroimaging, reversal selection, blood pressure management, and neurosurgical referral criteria.
- To organize evidence-based diagnostic and therapeutic sequences into reproducible clinical algorithms that may support procedural training, interdisciplinary coordination, and standardized emergency management.

Affective Domain

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- To promote critical awareness of the ethical and clinical implications associated with therapeutic decisions involving hemorrhagic progression, thromboembolic complications, neurological disability, and anticipated quality of life.
- To recognize the importance of equitable access to reversal agents, specialized neurocritical care, and timely neurosurgical treatment, particularly in Latin American healthcare environments with heterogeneous resources.
- To encourage patient-centered and multidisciplinary decision-making, emphasizing clinical responsibility, evidence-based judgment, and individualized assessment of therapeutic benefits and risks.

OBJETO DE ESTUDIO

The object of this study is anticoagulant-associated intracerebral hemorrhage, defined as acute bleeding within the brain parenchyma occurring in patients receiving anticoagulant therapy, particularly vitamin K antagonists and direct oral anticoagulants. This condition represents a neurological emergency characterized by impaired hemostasis, potential hematoma expansion, secondary cerebral injury, and substantial risks of mortality and long-term disability. Its clinical management requires coordinated interventions involving neurology, neurosurgery, cardiology, and critical care medicine (Greenberg et al., 2022; Steiner et al., 2025).

The population of interest comprises adult patients presenting with nontraumatic intracerebral hemorrhage during anticoagulant treatment, including individuals receiving warfarin, dabigatran, apixaban, rivaroxaban, or edoxaban for cardiovascular and thromboembolic indications. Particular consideration is given to patients with atrial fibrillation, mechanical heart valves, and other conditions requiring sustained anticoagulation, in whom the immediate need for hemorrhagic control must be balanced against the potential consequences of treatment interruption (Kuramatsu et al., 2018).

The phenomenon under investigation encompasses three interconnected therapeutic dimensions: pharmacological reversal of anticoagulant activity, hemodynamic stabilization during the acute hemorrhagic phase, and selection criteria for neurosurgical intervention. These dimensions are examined in relation to hematoma characteristics, neurological severity, treatment timing, therapeutic safety, and clinical outcomes. Principal outcomes of interest include hematoma expansion, hemostatic effectiveness, neurological deterioration, functional recovery, mortality, and thromboembolic complications (Connolly et al., 2024; Ma et al., 2023; Pradilla et al., 2024).

The study focuses on published clinical evidence rather than direct patient recruitment or experimental interventions. International findings are examined alongside Latin American contributions to identify similarities, limitations, and opportunities for adapting therapeutic recommendations to healthcare systems with different levels of specialized resources. Through this approach, the review seeks to establish an integrated understanding of the factors influencing clinical decisions and treatment outcomes in anticoagulant-associated intracerebral hemorrhage (Allende et al., 2025).

METODOLOGÍA

This study was structured as a narrative literature review using the scientific method as its methodological framework, with an analytical and comparative approach to the management of anticoagulant-associated intracerebral hemorrhage. The investigation focused on three therapeutic dimensions: pharmacological reversal of anticoagulation, acute hemodynamic management, and neurosurgical intervention. This design was selected to integrate evidence from international clinical guidelines, randomized controlled trials, observational investigations, and expert consensus documents, while identifying areas of agreement, clinical uncertainty, and potential applicability to Latin American healthcare settings.

The literature review was organized around 20 selected scientific publications from 2013 to October 2026, with PubMed/MEDLINE serving as the principal bibliographic reference source. To facilitate reproducibility, the search

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strategy was defined using combinations of the terms *intracerebral hemorrhage*, *anticoagulant-associated hemorrhage*, *anticoagulation reversal*, *prothrombin complex concentrate*, *idarucizumab*, *factor Xa inhibitors*, *blood pressure management*, *hematoma evacuation*, and *minimally invasive neurosurgery*. Boolean operators (AND, OR) were incorporated to combine the neurological condition with specific therapeutic interventions.

Eligible publications included peer-reviewed clinical investigations, randomized trials, observational studies, and evidence-based guidelines addressing adult patients with spontaneous intracerebral hemorrhage, with particular emphasis on anticoagulant exposure. Studies focused exclusively on traumatic intracranial injuries, pediatric populations, or unrelated hemorrhagic conditions were excluded from the principal analysis. Priority was assigned to methodological quality, clinical relevance, publication recency, and the availability of measurable therapeutic outcomes. Evidence from Latin American populations and regional recommendations was incorporated when relevant to treatment implementation and healthcare accessibility.

Information was organized into a comparative evidence framework containing publication characteristics, study design, patient population, therapeutic intervention, principal outcomes, and reported limitations. Pharmacological reversal was examined according to anticoagulant type, hemostatic effectiveness, and thromboembolic safety. Hemodynamic interventions were evaluated through blood pressure targets, hematoma progression, and neurological outcomes. Neurosurgical approaches were compared according to procedural indications, anatomical characteristics, timing, functional recovery, and mortality.

Evidence interpretation followed the principles of critical scientific analysis, prioritizing randomized clinical trials and established guidelines while recognizing the complementary contributions of observational studies and expert consensus. Findings were synthesized qualitatively to identify therapeutic patterns, conflicting results, and unresolved clinical questions. Because this investigation constitutes a narrative rather than a systematic review, neither exhaustive study identification nor quantitative meta-analysis was assumed.

The methodological framework enables structured comparison of existing evidence without direct patient recruitment or experimental intervention. Its final purpose is to establish an academically reproducible basis for understanding integrated therapeutic decision-making in anticoagulant-associated intracerebral hemorrhage, considering both international standards and the practical limitations of resource-variable healthcare environments.

FASES DEL DESARROLLO

Identification and Delimitation of the Research Problem

The initial phase focused on recognizing anticoagulant-associated intracerebral hemorrhage as a major neurological emergency requiring rapid and coordinated therapeutic intervention. Particular attention was directed toward the clinical consequences of delayed anticoagulation reversal, inadequate blood pressure regulation, and uncertainty regarding surgical eligibility. The research problem was delimited to adult patients with spontaneous intracerebral hemorrhage receiving oral anticoagulants, excluding traumatic hemorrhage and unrelated intracranial bleeding conditions. This delimitation allowed the review to concentrate on potentially modifiable therapeutic factors influencing hematoma expansion, neurological deterioration, and clinical prognosis (Greenberg et al., 2022; Steiner et al., 2025).

Formulation of Research Questions and Working Hypothesis

The second phase established the central research question: How can pharmacological reversal, hemodynamic stabilization, and neurosurgical intervention be integrated to optimize clinical management and neurological outcomes in anticoagulant-associated intracerebral hemorrhage?

The guiding hypothesis proposed that early, coordinated, and individualized management of these therapeutic components may improve hemorrhage control and reduce preventable secondary neurological injury compared with delayed or fragmented treatment. This hypothesis served as an interpretative framework for examining published

evidence rather than as a proposition subjected to experimental testing within the present review (Kuramatsu et al., 2015; Ma et al., 2023).

Identification and Organization of Scientific Evidence

The bibliographic phase was structured around 20 selected publications covering anticoagulation reversal, blood pressure management, neurocritical care, and neurosurgical treatment. Evidence was organized according to study design, therapeutic approach, patient characteristics, and reported clinical outcomes. Randomized controlled trials and international clinical guidelines formed the principal evidentiary foundation, complemented by observational investigations and regional consensus recommendations.

Particular attention was assigned to studies addressing vitamin K antagonist reversal, direct oral anticoagulant-related hemorrhage, intensive blood pressure reduction, minimally invasive hematoma evacuation, and decompressive surgical approaches (Steiner et al., 2016; Connolly et al., 2024; Qureshi et al., 2016; Pradilla et al., 2024).

Critical Evaluation and Comparative Analysis

The analytical phase examined the consistency, clinical relevance, and limitations of the selected evidence. Pharmacological interventions were compared according to hemostatic effectiveness, reversal speed, and thromboembolic complications. Hemodynamic strategies were assessed through their influence on hematoma expansion, neurological outcomes, and treatment-related adverse events. Neurosurgical studies were evaluated according to anatomical eligibility, procedural timing, hematoma reduction, functional recovery, and mortality.

Differences between study populations, therapeutic protocols, and outcome measurements were considered to avoid inappropriate generalization. Greater interpretative weight was assigned to randomized evidence when available, while observational findings were evaluated within their methodological limitations (Anderson et al., 2013; Hanley et al., 2019; Beck et al., 2024).

Integration and Synthesis of Findings

The synthesis phase brought together the three therapeutic dimensions to identify clinically relevant relationships and areas of uncertainty. The evidence was examined within a multidisciplinary framework emphasizing early neurological assessment, anticoagulant-specific reversal, controlled blood pressure management, repeated neuroimaging, and timely neurosurgical evaluation.

International recommendations were also considered in relation to Latin American healthcare environments, particularly regarding differences in access to specialized medications, neurocritical care resources, and surgical infrastructure (Allende et al., 2025). The resulting synthesis provides the conceptual foundation for discussing integrated management strategies, without assuming that their combined effectiveness has been directly established in every anticoagulant-specific clinical subgroup.

Interpretation and Scientific Consolidation

The final phase focused on organizing the principal findings into clinically meaningful conclusions, identifying therapeutic uncertainties, and establishing priorities for future investigation. Particular emphasis was placed on individualized treatment selection, prevention of secondary cerebral injury, and the balance between hemorrhagic control and thromboembolic risk. This process allowed the review to connect existing scientific evidence with practical clinical considerations while acknowledging the limitations inherent to narrative synthesis and differences among healthcare settings.

RESULTADOS Y DISCUSIÓN

Figure 1.

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Early Anticoagulation Reversal: Comparison of Four-Factor Prothrombin Complex Concentrate and Fresh Frozen Plasma in the INCH Trial

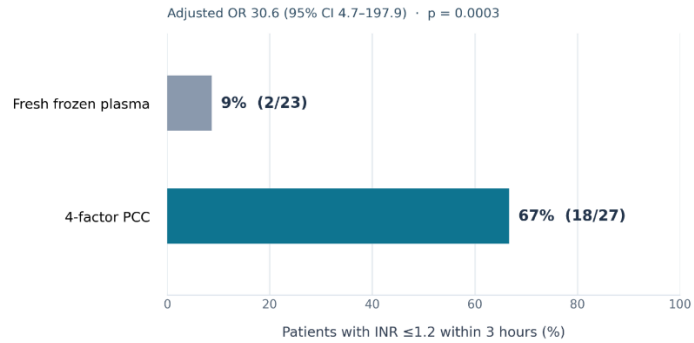


Figure 1 illustrates the comparative effectiveness of four-factor prothrombin complex concentrate (4F-PCC) and fresh frozen plasma (FFP) in achieving rapid anticoagulation reversal among patients with vitamin K antagonist-associated intracranial hemorrhage. Data derived from the randomized INCH trial demonstrate a substantial difference in early international normalized ratio (INR) correction between the two therapeutic strategies. Among 50 treated participants, 18 of 27 patients (67%) receiving 4F-PCC achieved an INR of 1.2 or lower within three hours of treatment initiation, compared with only 2 of 23 patients (9%) treated with FFP. This represented an absolute difference of approximately 58 percentage points, with an adjusted odds ratio of 30.6 (95% CI: 4.7–197.9; p = 0.0003), demonstrating a statistically significant difference in the primary hemostatic endpoint (Steiner et al., 2016).

The observed difference was accompanied by distinct patterns of hematoma progression. At the three-hour assessment, hematoma expansion of at least 33% was reported in 59% of evaluable patients receiving FFP compared with 44% receiving 4F-PCC (p = 0.048). At 24 hours, the corresponding proportions were 60% and 30%, respectively (p = 0.024). These findings demonstrate that the treatment groups differed not only in the rate of laboratory-defined anticoagulation reversal but also in radiologically documented hematoma enlargement during the early observation period. Nevertheless, these secondary findings should be interpreted in relation to the limited sample size and the trial's early termination (Steiner et al., 2016).

Differences were also observed in mortality during follow-up. Death occurred in 8 of 23 patients (35%) assigned to FFP and 5 of 27 patients (19%) assigned to 4F-PCC. Although mortality was numerically lower in the 4F-PCC group, the between-group difference was not statistically significant (p = 0.14). Five deaths associated with hematoma expansion were reported in the FFP group, whereas no deaths attributed to hematoma expansion were reported in the 4F-PCC group. These observations provide additional descriptive information regarding the clinical course but do not establish a definitive survival benefit attributable to either intervention (Steiner et al., 2016).

Regarding treatment safety, thromboembolic complications were documented during follow-up in both groups. Three thromboembolic events occurred within the first three days, including one in the FFP group and two in the 4F-PCC group. An additional six events were reported after day 12, distributed as one in the FFP group and five in the 4F-PCC group. The study also documented serious adverse events in both treatment arms. The limited number of participants and events restricts the precision of comparisons concerning thromboembolic safety and other uncommon complications (Steiner et al., 2016).

An important methodological consideration is that the INCH trial enrolled patients with vitamin K antagonist-associated intracranial hemorrhage rather than exclusively patients with intraparenchymal bleeding. Furthermore, although 54 participants were randomized, only 50 received the assigned study treatment, and recruitment was discontinued prematurely following a safety assessment. Consequently, the statistical precision of secondary clinical outcomes was limited, as reflected by the broad confidence interval surrounding the primary treatment effect. The available results therefore provide stronger evidence for rapid INR normalization than for long-term functional improvement or mortality reduction.

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Figure 2.

Hemostatic Efficacy and Thrombotic Complications of Andexanet Alfa Versus Usual Care in Factor Xa Inhibitor-Associated Intracerebral Hemorrhage: Results From the ANNEXA-I Trial

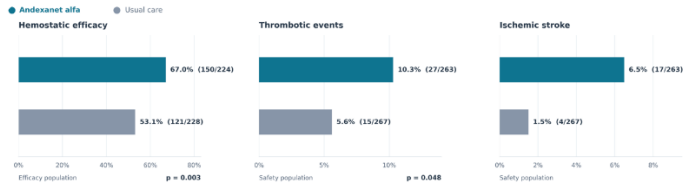


Figure 2 presents the comparative hemostatic efficacy and thrombotic safety outcomes reported in the ANNEXA-I randomized clinical trial, which evaluated andexanet alfa against usual care in patients with acute intracerebral hemorrhage associated with factor Xa inhibitors. The study included 530 participants, of whom 263 were assigned to andexanet alfa and 267 to usual care. Hemostatic efficacy was evaluated in an interim analysis involving 452 patients, whereas safety outcomes were assessed in the complete randomized population. Within the usual-care group, 85.5% of patients received prothrombin complex concentrate, providing an active-treatment context for the comparison (Connolly et al., 2024).

The primary outcome demonstrated greater hemostatic efficacy among patients receiving andexanet alfa. Successful hemostasis was achieved in 150 of 224 patients (67.0%) in the andexanet group, compared with 121 of 228 patients (53.1%) receiving usual care. The adjusted between-group difference was 13.4 percentage points (95% CI: 4.6–22.2; $p = 0.003$), indicating a statistically significant difference. Hemostatic efficacy was defined through a composite endpoint incorporating hematoma volume expansion of no more than 35% at 12 hours, neurological deterioration of fewer than seven points on the National Institutes of Health Stroke Scale, and absence of rescue treatment within the protocol-defined observation period (Connolly et al., 2024).

Analysis of the individual components of the primary endpoint demonstrated differences in early hematoma behavior. Hematoma expansion of 35% or less was observed in 76.7% of patients treated with andexanet alfa compared with 64.6% receiving usual care. The proportion without substantial neurological deterioration was 87.9% and 83.0%, respectively, while avoidance of rescue therapy was reported in 97.3% and 93.4% of patients. These findings indicate that the overall difference in composite hemostatic efficacy was accompanied by a greater proportion of patients meeting the hematoma expansion criterion in the andexanet group (Connolly et al., 2024).

Biochemical measurements further distinguished the two treatment strategies. The median reduction in anti-factor Xa activity from baseline to the lowest recorded value within one to two hours was 94.5% in the andexanet group, compared with 26.9% among patients receiving usual care ($p < 0.001$). This difference was statistically significant and corresponded with the greater hemostatic efficacy observed in the primary analysis. However, biochemical anticoagulant reversal and clinical hemostatic outcomes represent distinct measurements and were therefore evaluated separately (Connolly et al., 2024).

Regarding safety, thrombotic complications occurred more frequently among patients assigned to andexanet alfa. At least one thrombotic event was reported in 27 of 263 patients (10.3%) receiving andexanet, compared with 15 of 267 patients (5.6%) receiving usual care. The estimated between-group difference was 4.6 percentage points (95% CI: 0.1–9.2; $p = 0.048$), representing a statistically significant increase in thrombotic events in the andexanet group. Ischemic stroke was documented in 17 patients (6.5%) receiving andexanet alfa and four patients (1.5%) receiving usual care, demonstrating a numerical difference of approximately five percentage points between treatment groups (Connolly et al., 2024).

The analysis of longer-term outcomes showed no appreciable differences in functional disability, measured using the modified Rankin Scale, or mortality within 30 days. Mortality was reported in 27.8% of patients receiving andexanet alfa and 25.5% receiving usual care, without a statistically significant difference ($p = 0.51$). Consequently, the statistically significant findings observed for hemostatic efficacy and overall thrombotic complications were not

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accompanied by a demonstrated improvement in short-term survival or functional outcomes within the study's follow-up period (Connolly et al., 2024).

An important methodological distinction concerns the different populations used for the efficacy and safety analyses. The primary efficacy endpoint was calculated among 452 evaluable participants, while thrombotic complications were assessed among all 530 randomized patients. Accordingly, percentages presented in Figure 2 correspond to their respective analysis populations and should not be interpreted as having identical denominators. Additionally, the trial was stopped following the interim analysis, an aspect relevant to the precision and interpretation of its reported clinical endpoints (Connolly et al., 2024).

Figure 3.

Intensive Blood Pressure Management in Acute Intracerebral Hemorrhage: Comparative Findings From INTERACT2 and ATACH-II

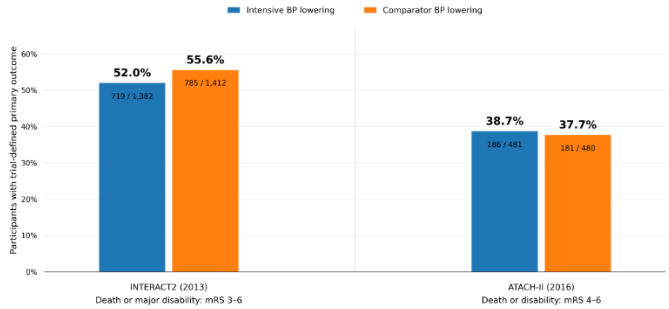


Figure 3 illustrates the primary clinical outcomes reported in two major randomized controlled trials evaluating intensive blood pressure reduction in acute spontaneous intracerebral hemorrhage: INTERACT2 and ATACH-II. Together, these investigations enrolled 3,839 participants and assessed whether more aggressive systolic blood pressure management could reduce mortality and neurological disability. Although both trials examined early antihypertensive interventions, their treatment targets, baseline characteristics, and definitions of unfavorable functional outcomes differed. Consequently, the findings are presented as separate within-trial comparisons rather than as directly comparable estimates of treatment effectiveness (Anderson et al., 2013; Qureshi et al., 2016).

In INTERACT2, 2,839 patients presenting within six hours of spontaneous intracerebral hemorrhage were randomized to intensive systolic blood pressure reduction, targeting values below 140 mmHg within one hour, or guideline-recommended treatment targeting values below 180 mmHg. The primary outcome, defined as death or major disability corresponding to modified Rankin Scale (mRS) scores of 3–6 at 90 days, occurred in 719 of 1,382 evaluable patients (52.0%) receiving intensive treatment compared with 785 of 1,412 patients (55.6%) receiving guideline-recommended treatment. The absolute difference was 3.6 percentage points, with an odds ratio of 0.87 (95% CI: 0.75–1.01; $p = 0.06$). Although the primary comparison did not reach conventional statistical significance, the numerical difference favored intensive blood pressure reduction (Anderson et al., 2013).

A prespecified ordinal analysis of functional outcomes in INTERACT2 provided additional information regarding disability distribution. Intensive treatment was associated with lower modified Rankin Scale scores across the full ordinal range, with an odds ratio of 0.87 (95% CI: 0.77–1.00; $p = 0.04$). However, mortality was nearly identical between treatment groups, occurring in 11.9% of patients receiving intensive treatment and 12.0% receiving guideline-recommended treatment. These findings demonstrate differences between the dichotomized primary endpoint, the ordinal assessment of disability, and mortality considered independently. Accordingly, the statistical significance observed in the ordinal analysis should not be interpreted as evidence of a significant reduction in the primary composite outcome or mortality (Anderson et al., 2013).

The ATACH-II trial subsequently evaluated a more intensive blood pressure reduction strategy in 1,000 patients with intracerebral hemorrhage. Participants were assigned to an intensive systolic pressure target of 110–139 mmHg or a

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standard target of 140–179 mmHg, using intravenous nicardipine initiated within 4.5 hours of symptom onset. Unlike INTERACT2, the primary endpoint was defined as death or disability corresponding to mRS scores of 4–6 at three months. Among patients with available outcome assessments, the primary endpoint occurred in 186 of 481 participants (38.7%) assigned to intensive treatment and 181 of 480 participants (37.7%) receiving standard treatment. The adjusted relative risk was 1.04 (95% CI: 0.85–1.27), demonstrating no statistically significant difference between the randomized groups (Qureshi et al., 2016).

The observed blood pressure profiles further distinguished the interventions. During the early treatment period, mean systolic pressure in INTERACT2 was approximately 150 mmHg in the intensive group and 164 mmHg in the comparator group at one hour. In ATACH-II, mean minimum systolic pressure during the first two hours was 128.9 mmHg in the intensive group and 141.1 mmHg in the standard group. Therefore, the achieved pressure values in the ATACH-II standard-treatment group approached those recorded in the INTERACT2 intensive-treatment group. These differences demonstrate that the designation of an intervention as intensive did not represent equivalent physiological exposure across the two investigations (Anderson et al., 2013; Qureshi et al., 2016).

Safety outcomes in ATACH-II revealed additional differences between treatment groups. Renal adverse events within seven days occurred in 9.0% of patients receiving intensive blood pressure reduction compared with 4.0% receiving standard treatment ($p = 0.002$). Treatment-related serious adverse events within 72 hours were reported in 1.6% and 1.2% of patients, respectively. The trial was discontinued following a prespecified interim analysis because of futility concerning the primary endpoint. These findings document a higher frequency of renal complications under the more intensive blood pressure strategy without a corresponding statistically significant improvement in death or disability at three months (Qureshi et al., 2016).

Important differences in the study populations also affect interpretation. INTERACT2 enrolled patients with presenting systolic pressures of 150–220 mmHg, whereas ATACH-II required an initial systolic pressure of at least 180 mmHg. Furthermore, ATACH-II restricted enrollment according to hematoma volume and neurological severity. Neither investigation was specifically designed to evaluate blood pressure management exclusively in anticoagulant-associated intracerebral hemorrhage. Anticoagulated patients represented a small minority in INTERACT2, while ATACH-II excluded patients receiving direct oral anticoagulants and those with substantially elevated international normalized ratios. Consequently, the reported estimates primarily characterize broader spontaneous intracerebral hemorrhage populations rather than anticoagulant-specific treatment effects.

Figure 4.

Functional Outcomes and Clinical Safety Following Multicomponent Acute Care in Intracerebral Hemorrhage: Results From the INTERACT3 Trial

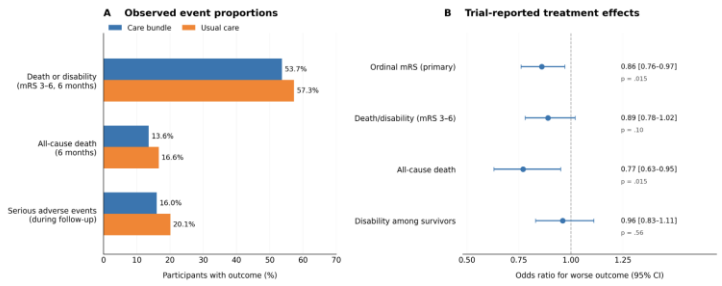


Figure 4 presents the principal functional and safety outcomes reported in the INTERACT3 trial, an international, multicenter, stepped-wedge cluster-randomized controlled study evaluating a coordinated care bundle in patients with acute spontaneous intracerebral hemorrhage. The investigation enrolled 7,036 patients across 121 hospitals in ten countries, including Brazil, Chile, Mexico, and Peru. Of these participants, 3,221 received care under the intervention protocol, whereas 3,815 received usual care. The intervention combined early intensive blood pressure reduction, glucose regulation, temperature management, and rapid correction of abnormal coagulation when indicated. The

primary outcome was the distribution of modified Rankin Scale (mRS) scores at six months, providing an assessment of neurological disability and mortality across the complete functional spectrum (Ma et al., 2023).

The primary analysis demonstrated a statistically significant difference in functional outcomes favoring the care bundle. Among 6,255 patients with available primary outcome data, the common odds ratio for worse functional status was 0.86 (95% CI: 0.76–0.97; p = 0.015). This association remained statistically significant after additional adjustment for country and patient characteristics, with an adjusted odds ratio of 0.84 (95% CI: 0.73–0.97; p = 0.017). These estimates correspond to an overall shift toward lower disability scores among patients assigned to the coordinated treatment protocol. However, the proportional-odds assumption was not fully satisfied, an important statistical consideration when interpreting a common treatment effect across the different mRS categories (Ma et al., 2023).

When functional outcomes were examined using the dichotomous endpoint of death or disability, defined as mRS scores of 3–6, events occurred in 1,553 of 2,892 patients (53.7%) receiving the care bundle and 1,927 of 3,363 patients (57.3%) receiving usual care. The corresponding odds ratio was 0.89 (95% CI: 0.78–1.02; p = 0.10). Although the observed proportion was numerically lower in the intervention group, this secondary comparison did not reach statistical significance. Similarly, major disability among survivors, defined as mRS scores of 3–5, showed no statistically significant between-group difference (OR: 0.96; 95% CI: 0.83–1.11; p = 0.56). These findings distinguish the significant shift in the overall distribution of functional outcomes from the nonsignificant results obtained using selected disability thresholds (Ma et al., 2023).

Mortality outcomes demonstrated an additional difference between treatment groups. At six months, death was documented in 407 of 2,999 patients (13.6%) assigned to the care bundle and 571 of 3,441 patients (16.6%) receiving usual care. The primary statistical model produced an odds ratio of 0.77 (95% CI: 0.63–0.95; p = 0.015). However, after further adjustment for country and individual patient characteristics, the estimated association was attenuated and no longer statistically significant (adjusted OR: 0.84; 95% CI: 0.65–1.07; p = 0.16). Accordingly, the mortality findings differed according to the statistical adjustment applied, despite the consistently lower observed death proportion in the intervention group (Ma et al., 2023).

Regarding treatment safety, serious adverse events occurred in 516 of 3,221 patients (16.0%) receiving the intervention compared with 767 of 3,815 patients (20.1%) receiving usual care. The between-group difference was statistically significant (p = 0.0098), corresponding to an absolute difference of approximately 4.1 percentage points. The safety comparison involved the entire intervention and usual-care populations, whereas functional and mortality analyses used smaller outcome-specific populations. These denominator differences were preserved in the graphical presentation to maintain consistency with the original trial reporting (Ma et al., 2023).

Analysis of early physiological management demonstrated measurable differences in treatment implementation. Mean systolic blood pressure at one hour was 148.4 mmHg in the intervention group compared with 154.7 mmHg under usual care. At 24 hours, the corresponding values were 136.1 and 139.0 mmHg. Among patients with elevated blood pressure, the median time required to reach the specified systolic pressure target was 2.3 hours with the care bundle and 4.0 hours with usual care. Glucose targets were achieved in 13.4% of eligible patients receiving the intervention and 6.5% receiving usual care. These observations document differences in physiological control during the acute treatment period (Ma et al., 2023).

With respect to anticoagulation reversal, correction of abnormal coagulation was documented in 12 of 25 eligible patients (48.0%) assigned to the care bundle and 24 of 59 eligible patients (40.7%) receiving usual care. The small number of patients contributing to this comparison limits the precision of anticoagulation-specific findings. Furthermore, INTERACT3 was not restricted to patients receiving anticoagulant therapy, and the overall functional outcomes therefore represent the broader population with spontaneous intracerebral hemorrhage rather than an anticoagulant-associated subgroup alone (Ma et al., 2023).

The international composition of the study also permitted examination of outcomes across heterogeneous healthcare environments. Participating countries included several Latin American centers, although the distribution of hospital resources and treatment practices differed among regions. The investigators reported regional heterogeneity in the primary treatment effect, particularly in analyses involving geographical location and the COVID-19 study period.

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Nevertheless, the principal overall analysis demonstrated a statistically significant improvement in the ordinal distribution of functional outcomes associated with coordinated acute care, accompanied by lower observed mortality and serious adverse event rates. These results provide the quantitative evidence presented in Figure 4 while preserving the distinctions between primary and secondary outcomes, adjustment models, and anticoagulant-specific observations (Ma et al., 2023).

Figure 5.

Functional Outcomes Following Minimally Invasive Hematoma Evacuation: Comparative Evidence From MISTIE III and ENRICH

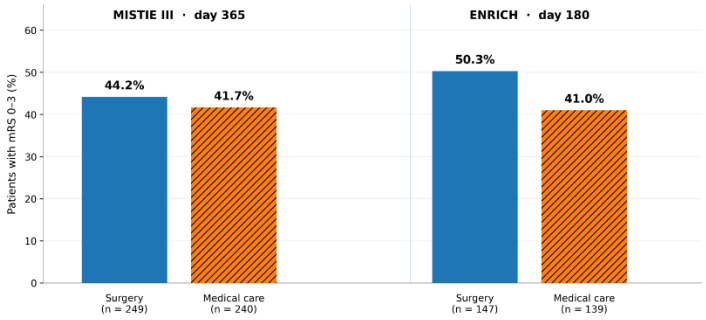


Figure 5 presents the comparative functional outcomes reported in two major randomized controlled trials evaluating minimally invasive hematoma evacuation in patients with spontaneous intracerebral hemorrhage: MISTIE III and ENRICH. Both investigations examined surgical approaches intended to reduce intracerebral hematoma volume while limiting injury to surrounding brain tissue. However, they differed in procedural technique, intervention timing, patient selection, and the assessment of neurological recovery. The graphical representation focuses on the proportion of patients achieving modified Rankin Scale (mRS) scores of 0–3, corresponding to survival with disability ranging from none to moderate. Outcomes were evaluated at 365 days in MISTIE III and 180 days in ENRICH, with each comparison maintained within its original trial population (Hanley et al., 2019; Pradilla et al., 2024).

MISTIE III was a multicenter, randomized phase III trial involving 506 patients with spontaneous supratentorial intracerebral hemorrhage measuring at least 30 mL. Participants were assigned to minimally invasive catheter-based hematoma evacuation followed by thrombolytic treatment or standard medical management. Among 489 patients with available functional assessments at 365 days, favorable neurological outcomes were documented in 110 of 249 patients (44.2%) receiving surgical treatment compared with 100 of 240 patients (41.7%) receiving standard medical care. The primary adjusted analysis estimated favorable outcomes in 45% and 41% of patients, respectively, corresponding to an adjusted absolute difference of four percentage points (95% CI: −4 to 12; p = 0.33). This difference did not reach statistical significance, indicating that the trial did not demonstrate improvement in its prespecified primary functional endpoint (Hanley et al., 2019).

Despite the absence of a statistically significant difference in the primary outcome, MISTIE III demonstrated substantial differences in hematoma evacuation. The mean reduction in hematoma volume was 69% in the surgical group compared with 3% under standard medical management. Mean residual hematoma volume at the end of treatment was 16 mL among surgically treated patients versus 47 mL in the medical group. Furthermore, 146 of 250 patients (58%) receiving the minimally invasive procedure achieved the predefined surgical objective of reducing residual hematoma volume to 15 mL or less. Exploratory analyses identified an association between more extensive hematoma removal and favorable neurological recovery; however, these analyses were not confirmatory evaluations of the primary randomized treatment effect (Hanley et al., 2019).

Mortality and procedural safety outcomes provided additional information. At 30 days, mortality occurred in 24 of 255 surgically assigned patients (9%) and 37 of 251 patients (15%) receiving standard medical treatment (p = 0.07).

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Although mortality was numerically lower in the surgical group, the difference did not achieve conventional statistical significance at this time point. Symptomatic intracranial bleeding occurred in approximately 2% of surgically treated patients and 1% of medically managed patients, while bacterial brain infections were reported in approximately 1% and 0%, respectively. These observations characterized the early safety profile of the catheter-based evacuation technique within the population selected for the trial (Hanley et al., 2019).

The ENRICH trial subsequently evaluated a different minimally invasive surgical approach involving early trans-sulcal parafascicular hematoma evacuation. The study randomized 300 patients with spontaneous supratentorial hemorrhages measuring 30–80 mL to surgery plus guideline-based medical management or medical management alone. Among patients with available 180-day assessments, favorable outcomes defined as mRS scores of 0–3 occurred in 74 of 147 patients (50.3%) receiving surgery and 57 of 139 patients (41.0%) receiving medical treatment. The estimated between-group difference was 9.2 percentage points (95% Bayesian credible interval: −2.0 to 20.3), indicating that this dichotomized secondary endpoint did not independently establish superiority (Pradilla et al., 2024).

The primary ENRICH analysis, however, used the utility-weighted modified Rankin Scale, a functional measurement incorporating preference-based weights for different disability states. At 180 days, the mean utility-weighted score was 0.458 in the surgical group compared with 0.374 in the control group. The estimated treatment difference was 0.084 (95% Bayesian credible interval: 0.005–0.163), with a posterior probability of surgical superiority of 0.981. This result exceeded the prespecified Bayesian superiority threshold of 0.975, demonstrating a favorable primary functional outcome under the statistical framework established for the trial (Pradilla et al., 2024).

Anatomical subgroup analyses in ENRICH revealed differences according to hemorrhage location. Among patients with lobar hemorrhage, the estimated treatment difference in utility-weighted functional outcomes was 0.127 (95% Bayesian credible interval: 0.035–0.219). In contrast, patients with anterior basal ganglia hemorrhage demonstrated an estimated difference of −0.013 (95% Bayesian credible interval: −0.147 to 0.116). Following a prespecified interim analysis, further enrollment of patients with anterior basal ganglia hemorrhage was discontinued because the criteria for futility had been reached, and subsequent recruitment was restricted to lobar hemorrhages. Therefore, the overall functional findings were influenced by the trial's adaptive enrollment strategy and the greater representation of patients with lobar hemorrhage (Pradilla et al., 2024).

Early mortality and postoperative complications were also evaluated in ENRICH. Mortality within 30 days occurred in 9.3% of surgically treated patients compared with 18.0% receiving standard medical management. The estimated difference was −8.7 percentage points (95% Bayesian credible interval: −16.4 to −1.0). Postoperative rebleeding accompanied by neurological deterioration occurred in five patients (3.3%) undergoing surgery. These findings provide additional quantitative evidence regarding early survival and procedural complications associated with minimally invasive evacuation (Pradilla et al., 2024).

Several methodological differences limit direct comparison between the two trials. MISTIE III required radiological hematoma stability and correction of coagulation abnormalities before intervention, whereas ENRICH investigated surgical evacuation within 24 hours of symptom onset in selected patients. Their surgical methods were also distinct, involving catheter-directed thrombolysis in MISTIE III and trans-sulcal parafascicular evacuation in ENRICH. Additionally, neither trial was specifically designed to evaluate surgical outcomes exclusively among patients with anticoagulant-associated intracerebral hemorrhage. MISTIE III required normalization of coagulation parameters before treatment, while ENRICH excluded patients with anticoagulant effects that could not be rapidly reversed or with persistent clinically significant coagulopathy.

DISCUSIÓN

The findings of this review demonstrate that anticoagulant-associated intracerebral hemorrhage requires an integrated therapeutic approach in which pharmacological reversal, hemodynamic stabilization, and neurosurgical assessment are coordinated during the early stages of neurological deterioration. Although these interventions address different aspects of hemorrhagic injury, their effectiveness is closely related to treatment timing, hematoma characteristics, anticoagulant exposure, and the patient's underlying cardiovascular condition. The analyzed evidence supports the

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importance of rapid hemorrhage control while revealing substantial differences in the strength of clinical evidence supporting individual therapeutic strategies (Greenberg et al., 2022; Steiner et al., 2025).

Pharmacological reversal remains a fundamental component of emergency management, particularly because persistent anticoagulant activity may contribute to hematoma expansion. The INCH trial demonstrated substantially faster normalization of coagulation parameters with four-factor prothrombin complex concentrate than with fresh frozen plasma. However, the limited sample size prevented definitive conclusions regarding survival and long-term functional recovery (Steiner et al., 2016). Similarly, ANNEXA-I demonstrated improved hemostatic efficacy with andexanet alfa compared with usual care, although this benefit was accompanied by a higher incidence of thrombotic complications, particularly ischemic stroke, without a demonstrated improvement in functional outcomes or mortality (Connolly et al., 2024). These findings emphasize the distinction between achieving rapid hemostasis and improving patient-centered clinical outcomes.

The therapeutic balance becomes especially complex when anticoagulation is indicated for conditions associated with substantial thromboembolic risk. Patients with mechanical heart valves, for example, may face serious cardiovascular complications following prolonged interruption of anticoagulant treatment. Observational evidence suggests that decisions regarding treatment resumption should consider hemorrhage stability, thromboembolic risk, and the underlying indication for anticoagulation rather than relying exclusively on standardized timelines (Kuramatsu et al., 2018). Consequently, the management of intracerebral hemorrhage extends beyond the immediate correction of coagulation abnormalities and requires continued collaboration between neurological and cardiovascular specialists.

The results concerning blood pressure management further demonstrate that greater treatment intensity does not necessarily produce superior neurological outcomes. INTERACT2 suggested a favorable shift in functional recovery with early intensive systolic blood pressure reduction, whereas ATACH-II failed to demonstrate additional clinical benefit from more aggressive targets and identified an increased incidence of renal adverse events (Anderson et al., 2013; Qureshi et al., 2016). These differences may be partially explained by variation in achieved blood pressure levels, inclusion criteria, treatment protocols, and baseline patient characteristics. Collectively, the findings favor prompt, sustained, and carefully monitored blood pressure reduction rather than indiscriminate pursuit of the lowest achievable systolic values.

The INTERACT3 trial provides an important perspective by demonstrating that coordinated management of several physiological abnormalities can improve functional outcomes in acute intracerebral hemorrhage. Unlike studies examining isolated interventions, INTERACT3 evaluated a structured bundle addressing blood pressure, coagulation, glucose concentrations, and body temperature. Its findings support a multidisciplinary model in which treatment components are implemented simultaneously according to clinical priorities (Ma et al., 2023). Nevertheless, because the study was not restricted to anticoagulated patients, the magnitude of benefit specifically attributable to anticoagulation reversal within the care bundle remains uncertain.

Neurosurgical evidence presents a similarly heterogeneous pattern. MISTIE III demonstrated that substantial hematoma reduction through minimally invasive catheter-based evacuation did not necessarily translate into statistically significant improvement in the primary functional outcome. In contrast, ENRICH demonstrated superior utility-weighted functional outcomes following early minimally invasive surgery, particularly among patients with lobar hemorrhage (Hanley et al., 2019; Pradilla et al., 2024). These differences suggest that hematoma removal alone is insufficient to predict treatment success. Surgical timing, anatomical accessibility, surrounding tissue injury, procedural technique, and baseline neurological severity must also be considered. Importantly, neither trial established definitive anticoagulant-specific surgical selection criteria, leaving uncertainty regarding the optimal interval between pharmacological reversal and operative intervention.

The findings also highlight the importance of distinguishing radiological improvement from meaningful neurological recovery. Reductions in hematoma volume, normalization of coagulation parameters, and achievement of predefined blood pressure targets represent measurable therapeutic responses, but they are not interchangeable with improved survival, independence, or quality of life. This distinction is particularly relevant when evaluating treatments associated with procedural complications or thromboembolic events. Clinical outcomes should therefore remain central when

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interpreting the effectiveness of interventions, while physiological and radiological measures provide complementary information regarding treatment response (Connolly et al., 2024; Hanley et al., 2019).

From an international perspective, differences in healthcare infrastructure introduce additional challenges. Access to specialized reversal agents, rapid neuroimaging, intensive monitoring, and minimally invasive neurosurgical technologies varies considerably between institutions. Latin American recommendations developed following INTERACT3 emphasize the adaptation of evidence-based protocols to regional resources and organizational capabilities (Allende et al., 2025). Within resource-limited environments, early recognition, rapid referral, standardized treatment pathways, and coordinated multidisciplinary care may represent essential elements of service organization. Nevertheless, further regional research is required to determine how differences in healthcare access influence treatment delays, neurological outcomes, and mortality.

Several limitations should be acknowledged. First, the narrative design does not provide the exhaustive evidence identification or quantitative synthesis characteristic of a systematic review. Second, substantial heterogeneity exists among the included investigations regarding patient selection, hemorrhage severity, therapeutic interventions, outcome definitions, and follow-up duration. Third, several major trials enrolled broader populations with spontaneous intracerebral hemorrhage rather than exclusively anticoagulated patients, restricting direct extrapolation to anticoagulant-associated hemorrhage. Finally, evolving therapeutic recommendations and regulatory decisions affect the contemporary applicability of certain reversal strategies. In particular, the withdrawal of andexanet alfa from the United States market in December 2025, following concerns regarding thromboembolic safety, reinforces the need to evaluate emerging evidence alongside current treatment availability and regulatory restrictions (U.S. Food and Drug Administration, 2025).

Future investigations should prioritize prospective comparisons of anticoagulant-specific reversal strategies, standardized blood pressure protocols, and clearly defined criteria for neurosurgical intervention. Particular attention should be directed toward treatment sequencing, the relationship between hemostatic correction and surgical safety, thromboembolic complications, and long-term functional recovery. Studies incorporating Latin American populations would additionally help determine the feasibility, effectiveness, and equity of integrated care pathways across healthcare environments with different resource capacities.

CONCLUSIÓN

Anticoagulant-associated intracerebral hemorrhage remains a major neurological emergency requiring rapid, individualized, and multidisciplinary management. The evidence reviewed demonstrates that optimal treatment depends on the integration of pharmacological anticoagulation reversal, controlled hemodynamic stabilization, and timely neurosurgical assessment. Although each intervention addresses a distinct component of hemorrhagic injury, their coordination is essential for limiting potentially preventable complications and supporting neurological recovery.

Pharmacological reversal represents a critical priority during the acute phase, particularly in patients with persistent anticoagulant activity and elevated risk of hematoma expansion. Four-factor prothrombin complex concentrate provides rapid correction of vitamin K antagonist-associated coagulopathy, whereas anticoagulant-specific reversal strategies offer additional therapeutic options for selected patients receiving direct oral anticoagulants. Nevertheless, improvements in hemostatic parameters do not consistently translate into reductions in mortality or long-term disability, and thromboembolic complications remain an important limitation of certain reversal approaches.

Hemodynamic management should prioritize early, sustained, and carefully monitored blood pressure control, avoiding excessive reductions that may increase treatment-related complications. Evidence from major randomized trials supports individualized targets rather than uniformly aggressive antihypertensive strategies. Furthermore, the findings of INTERACT3 reinforce the importance of coordinated management protocols addressing multiple physiological abnormalities during the acute hemorrhagic period.

Neurosurgical intervention should be guided by hematoma location, volume, neurological deterioration, mass effect, and procedural feasibility. Contemporary evidence suggests that selected patients, particularly those with accessible

lobar hemorrhages, may benefit from early minimally invasive evacuation. However, surgical effectiveness remains dependent on appropriate patient selection, technical considerations, and clinical timing. The optimal relationship between anticoagulation reversal and surgical intervention requires further investigation.

From an international perspective, the implementation of evidence-based management strategies must account for differences in healthcare infrastructure, specialized treatment availability, and multidisciplinary capabilities. Strengthening standardized emergency pathways and regional clinical research is particularly relevant for Latin American healthcare systems, where timely access to advanced neurological and neurosurgical care may be heterogeneous.

In conclusion, the management of anticoagulant-associated intracerebral hemorrhage should be understood as a dynamic process requiring continuous reassessment of hemorrhagic progression, cardiovascular risk, neurological status, and therapeutic response. Future research should focus on defining optimal treatment sequences, refining anticoagulant-specific surgical criteria, and evaluating long-term functional outcomes. An integrated, patient-centered approach supported by high-quality evidence remains fundamental to improving clinical decision-making and advancing the management of this life-threatening condition.

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REFERENCIAS

- Allende, M. I., Muñoz-Venturelli, P., Gonzalez, F., Bascur, F., Anderson, C. S., Ouyang, M., Cabieses, B., Obach, A., Cano-Nigenda, V., & Arauz, A. (2025). Recommendations for implementing the INTERACT3 care bundle for intracerebral hemorrhage in Latin America: Results of a Delphi method. *Cerebrovascular Diseases, 54*(3), 363–370. DOI: 10.1159/000540038.
- Anderson, C. S., Heeley, E., Huang, Y., Wang, J., Stapf, C., Delcourt, C., Lindley, R., Robinson, T., Lavados, P., Neal, B., Hata, J., Arima, H., Parsons, M., Li, Y., Wang, J., Heritier, S., Li, Q., Woodward, M., Simes, R. J., . . . Chalmers, J. (2013). Rapid blood-pressure lowering in patients with acute intracerebral hemorrhage. *The New England Journal of Medicine, 368*(25), 2355–2365. DOI: 10.1056/NEJMoa1214609.
- Beck, J., Fung, C., Strbian, D., Bütikofer, L., Z'Graggen, W. J., Lang, M. F., Beyeler, S., Gralla, J., Ringel, F., Schaller, K., Plesnila, N., Arnold, M., Hacke, W., Jüni, P., Mendelow, A. D., Stapf, C., Al-Shahi Salman, R., Bressan, J., Lerch, S., . . . Fischer, U. (2024). Decompressive craniectomy plus best medical treatment versus best medical treatment alone for spontaneous severe deep supratentorial intracerebral haemorrhage: A randomised controlled clinical trial. *The Lancet, 403*(10442), 2395–2404. DOI: 10.1016/S0140-6736(24)00702-5.
- Christensen, H., Cordonnier, C., Kõrv, J., Lal, A., Ovesen, C., Purrucker, J. C., Toni, D., & Steiner, T. (2019). European Stroke Organisation guideline on reversal of oral anticoagulants in acute intracerebral haemorrhage. *European Stroke Journal, 4*(4), 294–306. DOI: 10.1177/2396987319849763.
- Connolly, S. J., Sharma, M., Cohen, A. T., Demchuk, A. M., Członkowska, A., Lindgren, A. G., Molina, C. A., Bereczki, D., Toni, D., Seiffge, D. J., Tanne, D., Sandset, E. C., Tsivgoulis, G., Christensen, H., Beyer-Westendorf, J., Coutinho, J. M., Crowther, M., Verhamme, P., Amarenco, P., . . . Shoamanesh, A. (2024). Andexanet for factor Xa inhibitor-associated acute intracerebral hemorrhage. *The New England Journal of Medicine, 390*(19), 1745–1755. DOI: 10.1056/NEJMoa2313040.
- Frontera, J. A., Lewin, J. J., III, Rabinstein, A. A., Aisiku, I. P., Alexandrov, A. W., Cook, A. M., Del Zoppo, G. J., Kumar, M. A., Peerschke, E. I. B., Stiefel, M. F., Teitelbaum, J. S., Wartenberg, K. E., & Zerfoss, C. L. (2016). Guideline for reversal of antithrombotics in intracranial hemorrhage: A statement for healthcare professionals from the Neurocritical Care Society and Society of Critical Care Medicine. *Neurocritical Care, 24*(1), 6–46. DOI: 10.1007/s12028-015-0222-x.
- Greenberg, S. M., Ziai, W. C., Cordonnier, C., Dowlatshahi, D., Francis, B., Goldstein, J. N., Hemphill, J. C., III, Johnson, R., Keigher, K. M., Mack, W. J., Mocco, J., Newton, E. J., Ruff, I. M., Sansing, L. H., Schulman, S., Selim, M. H., Sheth, K. N., Sprigg, N., Sunnerhagen, K. S., & American Heart Association/American Stroke Association. (2022). 2022 guideline for the management of patients with spontaneous intracerebral hemorrhage: A guideline from the American Heart Association/American Stroke Association. *Stroke, 53*(7), e282–e361. DOI: 10.1161/STR.0000000000000407.
- Hanley, D. F., Lane, K., McBee, N., Ziai, W., Tuhrim, S., Lees, K. R., Dawson, J., Gandhi, D., Ullman, N., Mould, W. A., Mayo, S. W., Mendelow, A. D., Gregson, B., Butcher, K., Vespa, P., Wright, D. W., Kase, C.

S., Carhuapoma, J. R., Keyl, P. M., . . . Awad, I. A. (2017). Thrombolytic removal of intraventricular haemorrhage in treatment of severe stroke: Results of the randomised, multicentre, multiregion, placebo-controlled CLEAR III trial. *The Lancet, 389*(10069), 603–611. DOI: 10.1016/S0140-6736(16)32410-2.

- Hanley, D. F., Thompson, R. E., Rosenblum, M., Yenokyan, G., Lane, K., McBee, N., Mayo, S. W., Bistran-Hall, A. J., Gandhi, D., Mould, W. A., Ullman, N., Ali, H., Carhuapoma, J. R., Kase, C. S., Lees, K. R., Dawson, J., Wilson, A., Betz, J. F., Sugar, E. A., . . . Awad, I. A. (2019). Efficacy and safety of minimally invasive surgery with thrombolysis in intracerebral haemorrhage evacuation (MISTIE III): A randomised, controlled, open-label, blinded endpoint phase 3 trial. *The Lancet, 393*(10175), 1021–1032. DOI: 10.1016/S0140-6736(19)30195-3.
- Kuramatsu, J. B., Gerner, S. T., Schellinger, P. D., Glahn, J., Endres, M., Sobesky, J., Flechsenhar, J., Neugebauer, H., Jüttler, E., Grau, A., Palm, F., Röther, J., Michels, P., Hamann, G. F., Hüwel, J., Hagemann, G., Barber, B., Terborg, C., Trostdorf, F., . . . Huttner, H. B. (2015). Anticoagulant reversal, blood pressure levels, and anticoagulant resumption in patients with anticoagulation-related intracerebral hemorrhage. *JAMA, 313*(8), 824–836. DOI: 10.1001/jama.2015.0846.
- Kuramatsu, J. B., Sembill, J. A., Gerner, S. T., Sprügel, M. I., Hagen, M., Roeder, S. S., Endres, M., Haeusler, K. G., Sobesky, J., Schurig, J., Zweynert, S., Bauer, M., Vajkoczy, P., Ringleb, P. A., Purrucker, J., Rizos, T., Volkmann, J., Müllges, W., Kraft, P., . . . Huttner, H. B. (2018). Management of therapeutic anticoagulation in patients with intracerebral haemorrhage and mechanical heart valves. *European Heart Journal, 39*(19), 1709–1723. DOI: 10.1093/eurheartj/ehy056.
- Lopes, R. D., Barros e Silva, P. G. M., Furtado, R. H. M., Macedo, A. V. S., Guerra, J. C. C., Rocha, A. T. C., Bizzacch, J. M. A., & Writing Committee for the SBTH Consensus Collaboration. (2026). Brazilian consensus on the management of bleeding complications related to the use of oral anticoagulants. *Revista da Associação Médica Brasileira, 72*(6), e20252032. DOI: 10.1590/1806-9282.20252032.
- Ma, L., Hu, X., Song, L., Chen, X., Ouyang, M., Billot, L., Li, Q., Malavera, A., Li, X., Muñoz-Venturelli, P., de Silva, A., Thang, N. H., Wahab, K. W., Pandian, J. D., Wasay, M., Pontes-Neto, O. M., Abanto, C., Arauz, A., Shi, H., . . . Anderson, C. S. (2023). The third Intensive Care Bundle with Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial (INTERACT3): An international, stepped wedge cluster randomised controlled trial. *The Lancet, 402*(10395), 27–40. DOI: 10.1016/S0140-6736(23)00806-1.
- Mendelow, A. D., Gregson, B. A., Rowan, E. N., Murray, G. D., Gholkar, A., & Mitchell, P. M. (2013). Early surgery versus initial conservative treatment in patients with spontaneous supratentorial lobar intracerebral haematomas (STICH II): A randomised trial. *The Lancet, 382*(9890), 397–408. DOI: 10.1016/S0140-6736(13)60986-1.
- Milling, T. J., Jr., Middeldorp, S., Xu, L., Koch, B., Demchuk, A. M., Eikelboom, J. W., Verhamme, P., Cohen, A. T., Beyer-Westendorf, J., Gibson, C. M., Lopez-Sendon, J., Crowther, M., Shoamanesh, A., Coppens, M., Schmidt, J., Albaladejo, P., & Connolly, S. J. (2023). Final study report of andexanet alfa for major bleeding with factor Xa inhibitors. *Circulation, 147*(13), 1026–1038. DOI: 10.1161/CIRCULATIONAHA.121.057844.
- Pollack, C. V., Jr., Reilly, P. A., van Ryn, J., Eikelboom, J. W., Glund, S., Bernstein, R. A., Dubiel, R., Huisman, M. V., Hylek, E. M., Kam, C. W., Kamphuisen, P. W., Kreuzer, J., Levy, J. H., Royle, G., Sellke, F. W., Stangier, J., Steiner, T., Verhamme, P., Wang, B., . . . Weitz, J. I. (2017). Idarucizumab for dabigatran reversal—Full cohort analysis. *The New England Journal of Medicine, 377*(5), 431–441. DOI: 10.1056/NEJMoa1707278.
- Pradilla, G., Ratcliff, J. J., Hall, A. J., Saville, B. R., Allen, J. W., Paulon, G., McGlothlin, A., Lewis, R. J., Fitzgerald, M., Caveney, A. F., Li, X. T., Bain, M., Gomes, J., Jankowitz, B., Zenonos, G., Molyneaux, B. J., Davies, J., Siddiqui, A., Chicoine, M. R., . . . Barrow, D. L. (2024). Trial of early minimally invasive removal of intracerebral hemorrhage. *The New England Journal of Medicine, 390*(14), 1277–1289. DOI: 10.1056/NEJMoa2308440.
- Qureshi, A. I., Palesch, Y. Y., Barsan, W. G., Hanley, D. F., Hsu, C. Y., Martin, R. L., Moy, C. S., Silbergleit, R., Steiner, T., Suarez, J. I., Toyoda, K., Wang, Y., Yamamoto, H., & Yoon, B. W. (2016). Intensive blood-pressure lowering in patients with acute cerebral hemorrhage. *The New England Journal of Medicine, 375*(11), 1033–1043. DOI: 10.1056/NEJMoa1603460.
- Steiner, T., Poli, S., Griebe, M., Hüsing, J., Hajda, J., Freiberger, A., Bendszus, M., Bösel, J., Christensen, H., Dohmen, C., Hennerici, M., Kollmer, J., Stetefeld, H., Wartenberg, K. E., Weimar, C., Hacke, W., & Veltkamp, R. (2016). Fresh frozen plasma versus prothrombin complex concentrate in patients with

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intracranial haemorrhage related to vitamin K antagonists (INCH): A randomised trial. *The Lancet Neurology, 15*(6), 566–573. DOI: 10.1016/S1474-4422(16)00110-1.

- Steiner, T., Purrucker, J. C., Aguiar de Sousa, D., Apostolaki-Hansson, T., Beck, J., Christensen, H., Cordonnier, C., Downer, M. B., Eilertsen, H., Gartly, R., Gerner, S. T., Ho, L., Jahr, S. H., Klijn, C. J. M., Martinez-Majander, N., Orav, K., Petersson, J., Raabe, A., Sandset, E. C., . . . Al-Shahi Salman, R. (2025). European Stroke Organisation (ESO) and European Association of Neurosurgical Societies (EANS) guideline on stroke due to spontaneous intracerebral haemorrhage. *European Stroke Journal, 10*(4), 1007–1086. DOI: 10.1177/23969873251340815.

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