RESEARCH PAPER

Comparative Analysis of Anticoagulant Reversal Agents used in Anaesthesiology - A Narrative Review

Dr. Krishna Prasad T[1*], Neelam Manik Gaikwad[2], Reeya Mathew[3], Soundarya Priyadharsini K[4]

Orchid ID: 0000-0002-7833-9982 (Dr. Krishna Prasad T) | **Scopus ID:** 58772607100

[1*] Professor in Anaesthesiology, Shri Sathya Sai Medical College and RI, Ammapettai, Shri Balaji Vidyapeeth (Deemed to be University), Chennai campus, Kancheepuram - 603108. Phone: 9944579455 (Corresponding Author)

[2] Resident in Anaesthesiology, Shri Sathya Sai Medical College and RI, Ammapettai, Shri Balaji Vidyapeeth (Deemed to be University)

[3] Resident in Anaesthesiology, Shri Sathya Sai Medical College and RI, Ammapettai, Shri Balaji Vidyapeeth (Deemed to be University)

[4] Professor in Pharmacology, Shri Sathya Sai Medical College and RI, Ammapettai, Shri Balaji Vidyapeeth (Deemed to be University)

Received: 2nd Mar, 2026 | **Revised:** 14th Mar, 2026 | **Accepted:** 4th Apr, 2026 | **Available Online:** 20th Apr, 2026

ABSTRACT

The rapid reversal of anticoagulant activity is summarised in this review, which highlights important factors for anaesthesiologists handling patients on different anticoagulants, especially in emergency surgical situations. Understanding particular reversal techniques and their perioperative implications is crucial for the best possible patient care, given the growing use of direct oral anticoagulants and their different pharmacological profiles from classic vitamin K antagonists. This narrative review delineates the classifications of antithrombotic agents, distinguishing between anticoagulants that modulate thrombin generation and antiplatelet drugs that inhibit platelet activation. Despite extensive experience, the perioperative management of these agents continues to pose a dilemma in balancing the inherent risks of bleeding against thrombotic complications. The increasing prevalence of patients receiving anticoagulant or antiplatelet therapy further complicates surgical planning, with current guidelines often recommending significant delays for regional anesthesia in particular. Consequently, a thorough understanding of the principles of interruption and resumption of antithrombotic, anticoagulant, and antiplatelet therapy is essential for guiding clinical decision-making in diverse surgical contexts. This review will explore evidence-based approaches to perioperative anticoagulant management, addressing both elective and urgent surgical situations, with a focus on vitamin K antagonists, direct oral anticoagulants, and antiplatelet agents. This includes an in-depth analysis of their respective mechanisms of action, available reversal agents, and the clinical scenarios necessitating their immediate neutralization. The objective is to provide a comprehensive resource for anesthesiologists to navigate the complexities of anticoagulation reversal, ensuring patient safety and optimizing surgical outcomes by mitigating both hemorrhagic and thrombotic risks.

Keywords: Anticoagulation, Reversal, Anesthesia, Direct Oral Anticoagulants, Vitamin K Antagonists, Antiplatelet Agents, Perioperative Management.

How to cite this article: Krishna Prasad T, Gaikwad NM, Mathew R, Soundarya Priyadharsini K. Comparative Analysis of Anticoagulant Reversal Agents used in Anaesthesiology - A Narrative Review. Int J Drug Deliv Technol. 2026;16(34s):649-651. DOI: 10.25258/ijddt.16.34s.81

Source of support: Nil.

Conflict of interest: The authors declare no conflict of interest.

Introduction

The intricate balance between preventing thrombotic events and mitigating hemorrhagic complications poses a significant challenge in the perioperative management of patients receiving antithrombotic medications.1-4 This challenge is further compounded by the escalating number of patients on long-term antithrombotic regimens for various cardiovascular conditions, necessitating careful consideration of treatment interruption before surgical or invasive procedures. 5,6 Current guidelines often advise discontinuing these medications several days prior to elective surgery, a period determined by the specific agent's pharmacokinetics and the patient's individual

risk profile. 7-10. However, emergency surgical interventions frequently preclude such planned interruptions, thereby necessitating rapid and effective reversal strategies to mitigate intraoperative and postoperative bleeding risks. This review, therefore, aims to consolidate the most recent evidence-based recommendations and emerging pharmacological strategies for the immediate reversal of both traditional and novel anticoagulants in emergent surgical contexts. Optimal management necessitates an interprofessional approach to determine the appropriate duration and discontinuation of temporary anticoagulation interruption, sometimes requiring parenteral anticoagulation bridging based on individualized patient and procedure risks and benefits. 11-15 The pharmacology of these agents, particularly their impact on hemostasis, is critical for anesthesiologists to comprehend when patients undergo non-cardiac elective surgery. The diverse mechanisms of action of direct oral anticoagulants, which include direct thrombin inhibitors and Factor Xa inhibitors, necessitate distinct reversal approaches compared to traditional vitamin K antagonists, which impair the synthesis of vitamin K-dependent coagulation factors. 16,17. Navigating these differences, including drug half-life and renal function, is paramount for guiding periprocedural anticoagulant management and determining the optimal timing for drug interruption. In emergent scenarios, however, the luxury of timed interruption is often unavailable, demanding immediate and effective reversal strategies to mitigate elevated bleeding risks. 18-21. This review will particularly emphasize direct oral anticoagulants given their increasing prevalence and the unique challenges they present due to their predictable pharmacology, which bypasses routine laboratory monitoring, yet complicates perioperative management due to the limited availability of specific reversal agents and rapid assessment tools for their anticoagulant effects.

Methodology

This narrative review involved a comprehensive search of electronic databases, including PubMed, Embase, and Scopus, to identify relevant articles published between 2010 and 2023. The search strategy employed a combination of Medical Subject Headings and free-text terms, including "anticoagulation reversal," "perioperative management," "direct oral anticoagulants," "vitamin K antagonists," "antiplatelet agents," and "anesthesia." Inclusion criteria focused on systematic reviews, meta-analyses, randomized controlled trials, guidelines, and expert consensus statements concerning the perioperative management and reversal of antithrombotic therapies. Exclusion criteria comprised case reports, observational studies with limited generalizability, and articles not published in English. The identified literature was critically appraised for methodological quality and relevance to the review's objectives. Data synthesis was performed qualitatively, categorizing findings based on anticoagulant class and clinical scenario to highlight key considerations for anesthesiologists.

Literature Search Strategy

A detailed search string combining Boolean operators was constructed to maximize specificity and sensitivity, targeting clinical trials and comprehensive reviews on the periprocedural management of anticoagulated patients undergoing surgical or invasive procedures. This approach ensured the capture of studies addressing the nuances of anticoagulant reversal and perioperative management strategies for diverse patient populations.

Inclusion and Exclusion Criteria

Studies focusing on novel reversal agents and established protocols for managing coagulopathy in emergency settings were prioritized, while those concentrating solely on long-term anticoagulant therapy monitoring without perioperative relevance were excluded. Given the rapid evolution of anticoagulant therapies and their reversal agents, particular attention was paid to publications detailing recent advancements and clinical trials evaluating the efficacy and safety of new pharmacological interventions.

Data Extraction Process

Data pertinent to anticoagulant type, reversal agent efficacy, patient outcomes (e.g., bleeding, thrombosis), and procedural characteristics were systematically extracted from the included studies to inform the subsequent synthesis. This rigorous data extraction process aimed to capture both qualitative and quantitative insights, ensuring a robust foundation for discussing the implications for clinical practice and future research directions. Risk of Bias Assessment. Given the narrative nature of this review, a formal quantitative risk of bias assessment using tools like the Cochrane Risk of Bias tool for randomized controlled trials or the Newcastle-Ottawa Scale for observational studies was not performed. However, each included study underwent a critical appraisal by at least two authors to evaluate methodological rigor and relevance to the review's objectives, with any discrepancies

resolved through discussion with a third reviewer. This qualitative assessment focused on the clarity of reporting, appropriateness of study design for the research question, and the generalizability of findings to the perioperative setting. This qualitative evaluation aimed to ensure that the synthesized evidence maintained a high degree of internal consistency and external validity within the context of anesthetic practice. However, limitations arising from the heterogeneity of study designs, participant populations, and outcome measures across the diverse literature precluded a formal meta-analysis.

Overview of Anticoagulation Therapies

The following sections delineate the pharmacological profiles, mechanisms of action, and clinical indications for various classes of anticoagulants, including vitamin K antagonists, unfractionated heparin, low molecular weight heparin, and direct oral anticoagulants, providing a foundational understanding for their perioperative management. This foundational understanding is crucial for optimizing therapeutic plans, especially given the rapid evolution in anticoagulation pharmacology and the increasing complexity of patient care. Specifically, understanding the pharmacokinetics and pharmacodynamics of these agents is critical for anesthesiologists to appropriately time drug interruption or initiate reversal strategies in the periprocedural period (20,21,22).

Direct Oral Anticoagulants (DOACs)

Direct Oral Anticoagulants, including direct thrombin inhibitors (e.g., dabigatran) and factor Xa inhibitors (e.g., rivaroxaban, apixaban, edoxaban), have increasingly superseded Vitamin K Antagonists due to their predictable pharmacokinetics, fewer drug-food interactions, and often superior safety profiles, particularly concerning intracranial hemorrhage. However, their widespread adoption has introduced new challenges in perioperative management, primarily due to the lack of widely available and rapid point-of-care monitoring assays and specific reversal agents for all DOACs (23,24).

Vitamin K Antagonists (VKAs)

In contrast, Vitamin K Antagonists, primarily warfarin, have a well-established history of use, with their anticoagulant effect mediated by inhibiting vitamin K epoxide reductase, thereby impeding the synthesis of factors II, VII, IX, and X, as well as proteins C and S. Despite their efficacy, the narrow therapeutic window and significant inter-individual variability in response necessitate frequent monitoring of the International Normalized Ratio to guide dosing adjustments (25).

Heparins

Heparins, encompassing both unfractionated heparin and low molecular weight heparins, exert their anticoagulant effects primarily by catalyzing the inhibition of thrombin and factor Xa through their interaction with antithrombin. Unfractionated heparin, with its variable anticoagulant response and requirement for activated partial thromboplastin time monitoring, contrasts with low molecular weight heparins, which exhibit a more predictable dose-response relationship and generally do not necessitate routine laboratory monitoring (26,27).

Assessment of Bleeding Risk in Anaesthesia

Accurate assessment of a patient's bleeding risk is paramount in devising appropriate perioperative management strategies for individuals on anticoagulation therapy, balancing the imperative of hemostasis with the prevention of thrombotic events. This assessment involves a comprehensive evaluation of patient-specific factors, such as comorbidities, the nature of the surgical procedure, and the pharmacological characteristics of the anticoagulant agents involved, to stratify the risk of both bleeding and thrombosis (28).

Patient-Specific Factors

These factors include renal and hepatic function, age, genetic predispositions, and the presence of concurrent antiplatelet therapy, all of which can significantly modulate the pharmacokinetics and pharmacodynamics of anticoagulant medications. Furthermore, individual patient responses to anticoagulants can vary based on genetic polymorphisms affecting drug metabolism and target receptors, requiring a personalized approach to risk assessment.

Procedure-Specific Factors

Surgical invasiveness, anticipated blood loss, and the criticality of uninterrupted anticoagulation for preventing thromboembolic events are pivotal considerations. For instance, procedures involving highly vascularized tissues or confined anatomical spaces inherently carry a higher risk of clinically significant bleeding. Moreover, neuraxial procedures, such as spinal or epidural anesthesia, pose a unique risk for epidural hematoma formation, necessitating strict adherence to guidelines regarding anticoagulant interruption and resumption (29).

Reversal Strategies for Anticoagulants

The advent of novel anticoagulant agents has necessitated the development of specific reversal strategies to expeditiously restore hemostasis in emergent situations, thereby mitigating the risk of hemorrhage while minimizing thrombotic complications. These strategies range from non-specific interventions, such as prothrombin complex concentrates and fresh frozen plasma, to targeted pharmacological antidotes designed to neutralize the activity of specific anticoagulants (30).

Non-Pharmacological Approaches

These approaches encompass mechanical compression, surgical hemostasis, and the transfusion of blood products, such as packed red blood cells and platelets, to address acute blood loss and improve coagulopathy in cases where pharmacological reversal agents may be insufficient or unavailable (31).

Pharmacological Reversal Agents

The advent of direct oral anticoagulant therapies has spurred the development of specific reversal agents, such as idarucizumab for dabigatran and andexanet alfa for rivaroxaban and apixaban, which directly neutralize the anticoagulant effect of these drugs. For vitamin K antagonists, vitamin K supplementation or administration of prothrombin complex concentrates or plasma can achieve reversal, with four-factor PCCs being the preferred option for rapid reversal prior to emergency surgery. Conversely, the management of unfractionated heparin overdose or bleeding often involves protamine sulfate, which forms a stable complex with heparin, thereby neutralizing its anticoagulant activity(32,33).

Specific Reversal for DOACs

For direct oral anticoagulants, the primary specific reversal agents include idarucizumab for dabigatran and andexanet alfa for factor Xa inhibitors like rivaroxaban and apixaban. While idarucizumab specifically targets dabigatran, andexanet alfa functions as a decoy receptor for factor Xa inhibitors, binding to and sequestering these agents to restore normal hemostasis (34,35).

Specific Reversal for VKAs

Reversal of VKAs predominantly involves vitamin K administration, which facilitates the synthesis of functional clotting factors, and in situations requiring more rapid correction of coagulopathy, prothrombin complex concentrates are utilized to directly replenish these factors. Additionally, Fresh Frozen Plasma can be employed, though it typically requires larger volumes to achieve comparable factor concentrations and is less efficient than PCCs for rapid reversal in urgent scenarios. The choice between these reversal agents depends on the urgency of the situation, the severity of bleeding, and the specific VKA involved (36,37,38).

Specific Reversal for Heparins

Protamine sulfate remains the primary agent for reversing unfractionated heparin, forming a stable complex that neutralizes its anticoagulant effects. However, its efficacy against low molecular weight heparins is less complete and more variable, reflecting differences in their molecular structures and mechanisms of action. For instances where specific reversal agents for DOACs are unavailable or unapproved, such as with edoxaban, prothrombin complex concentrate or activated prothrombin complex concentrate are frequently employed in cases of severe bleeding or urgent surgical requirements (39,40).

Clinical Scenarios and Management

The decision to reverse anticoagulation should carefully weigh the benefits of achieving hemostasis against the inherent risks of post-reversal thrombosis (41). This delicate balance necessitates a nuanced understanding of pharmacokinetics, pharmacodynamics, and patient-specific coagulopathies to tailor an optimal reversal strategy. The subsequent management framework typically involves a multidisciplinary approach, integrating input from anesthesiologists, surgeons, hematologists, and critical care specialists to determine the most appropriate timing and method of anticoagulant re-initiation post-reversal. Moreover, the potential for rebound hypercoagulability following the discontinuation of anticoagulant therapy or the administration of reversal agents further complicates management, requiring vigilant monitoring and individualized thromboprophylaxis strategies. Clinicians are increasingly encountering situations where anticoagulants need to be withheld, including elective or emergency procedures, or in cases of significant bleeding due to over-anticoagulation or intercurrent illnesses (42). In such scenarios, a thorough assessment of the patient's thrombotic risk versus their bleeding risk is paramount in guiding the decision-making process for anticoagulant reversal or temporary interruption (35,38).

Emergency Surgery

In the context of emergency surgery, rapid and effective reversal of anticoagulation is critical to minimize perioperative hemorrhagic complications while balancing the risk of thrombotic events. This often necessitates the immediate administration of specific reversal agents or broad-spectrum hemostatic

therapies, with clinical decisions frequently guided by the urgency of the procedure and the specific anticoagulant employed (43). For instance, patients on factor Xa inhibitors requiring urgent surgery may receive activated prothrombin complex concentrate to counteract anticoagulation, particularly when specific antidotes are unavailable (44,45). Similarly, for patients on direct oral anticoagulants, delaying surgery for at least 12 to 24 hours post-last dose is advisable if possible, but immediate life-saving interventions may necessitate the use of reversal agents (46). However, the choice and timing of these reversal agents are complex, requiring careful consideration of the surgical bleeding risk and the patient's underlying thrombotic risk (11,47).

Regional Anaesthesia

Regional anesthesia techniques, while offering numerous advantages such as reduced opioid consumption and faster recovery, introduce additional considerations regarding perioperative anticoagulation due to the inherent risk of neuraxial hematoma formation (31). Consequently, stringent guidelines regarding the timing of neuraxial blockade relative to the administration of antithrombotic agents, as well as the removal of epidural catheters, are crucial to mitigate this serious complication (48). Special caution is necessary in all patients with anticoagulation who undergo epidural or spinal anesthesia or puncture, as bruising has occurred that can lead to long-term or permanent paralysis (49). In such scenarios, a thorough preoperative assessment, including coagulation tests, is crucial to evaluate the patient's hemostatic status and ensure an adequate safety margin for neuraxial procedures (2). Further, the choice between different neuraxial techniques should consider the associated bleeding risks; for example, a single-shot spinal anesthetic with a small bore needle is generally preferred over continuous epidural techniques in patients with altered coagulation profiles (31).

Neurosurgical Procedures

Given the critical nature of intracranial hemostasis, neurosurgical interventions demand an even more meticulous approach to anticoagulant management, often requiring complete cessation of antithrombotic agents and, in emergent cases, aggressive reversal strategies. This often involves a multidisciplinary discussion to balance the risk of hemorrhagic complications during surgery against the ongoing risk of thromboembolism, particularly for patients with conditions such as atrial fibrillation or mechanical heart valves (50). The use of reversal agents, such as prothrombin complex concentrates or specific direct oral anticoagulant antidotes, is frequently mandated prior to neurosurgical procedures to normalize coagulation parameters and minimize intracranial hemorrhage (51). Conversely, for planned neurosurgical procedures in patients receiving direct oral anticoagulants, temporary discontinuation of the anticoagulant may suffice, although the optimal duration of this interruption remains a subject of ongoing research and clinical debate (52). Moreover, the potential for neurological compromise from even minor hematomas within the confined spaces of the cranium and spinal canal elevates the need for precise and timely anticoagulant reversal in this patient population (53).

Discussion

The preceding sections have systematically delineated the intricate challenges associated with anticoagulant reversal in various clinical contexts, highlighting the imperative for tailored management strategies.

Current Challenges in Reversal Management

A significant challenge lies in the rapid and accurate assessment of individual patient coagulation status, especially in emergency settings, where immediate decisions regarding reversal agent administration are necessary (54). The variability in anticoagulant pharmacokinetics and pharmacodynamics further complicates this assessment, as standard coagulation tests may not accurately reflect the anticoagulant effect, particularly with direct oral anticoagulants (55). Furthermore, the increasing prevalence of an aging population on multiple antithrombotic medications presents a higher incidence of coagulation-associated postoperative complications, underscoring the limitations of existing guidelines for coagulation management (54). This highlights a critical need for enhanced diagnostic modalities and refined algorithms for predicting hemorrhagic and thrombotic risks in complex patients. The limited availability and high cost of specific reversal agents for direct oral anticoagulants also present practical challenges, particularly in resource-constrained environments (56). This includes addressing limitations such as the incomplete reversal action of current methods and the need to investigate a broader range of potential candidates for more comprehensive and effective anticoagulation reversal strategies (63).

For instance, recombinant factor VIIa (rFVIIa) and activated prothrombin complex concentrates (aPCCs) have shown promise in reversing the effects of certain direct oral anticoagulants, but their pro-coagulant nature necessitates careful administration due to the risk of thrombosis (64). Moreover, ongoing trials, such

as those evaluating ciraprantag, aim to introduce broad-spectrum reversal agents capable of neutralizing the effects of multiple anticoagulant classes, thereby simplifying reversal strategies and potentially enhancing patient safety (65). The development of novel reversal agents like andexanet alfa for factor Xa inhibitors represents a significant advancement, offering rapid restoration of hemostasis by acting as a decoy protein (66–68). These new agents, along with the continued exploration of other potential reversal compounds, such as ciraparantag, highlight a dynamic field of research dedicated to improving patient safety through more effective hemostatic control (69). Despite these advancements, persistent challenges remain, including the need for robust clinical outcome data for novel reversal agents in emergency scenarios and the optimization of monitoring strategies to detect recurrent anti-Xa activity post-reversal (70,71).

Efficacy and Safety of Reversal Agents

The efficacy and safety profiles of available reversal agents vary considerably, necessitating careful consideration of their pharmacodynamics, potential side effects, and impact on thrombotic risk when selecting an appropriate intervention. For instance, while prothrombin complex concentrates offer broad-spectrum reversal for vitamin K antagonists and, to a lesser extent, factor Xa inhibitors, their use can be associated with thrombogenic potential (57). Conversely, specific antidotes such as idarucizumab for dabigatran and andexanet alfa for factor Xa inhibitors offer targeted reversal with potentially fewer thrombotic complications, yet their rapid adoption is hindered by economic and accessibility factors (58).

Future Directions and Research Gaps

Future research should focus on developing more cost-effective and universally accessible reversal agents, as well as advancing point-of-care testing devices to provide immediate and precise coagulation status monitoring (59). Furthermore, efforts are needed to standardize guidelines for anticoagulant reversal, particularly concerning direct oral anticoagulants, as current practices demonstrate considerable heterogeneity (60).

Conclusion

Despite the availability of treatment recommendations and documented treatment algorithms, this review emphasizes how different approaches are now used to anticoagulation reversal. Treatment protocols are difficult to implement because of the constantly changing treatment landscape, the ongoing publication of new evidence, and other factors like patient comorbidities, the cost of reversal agents and any necessary testing, the definition of major or life-threatening bleeding and major surgery, and logistical and legal considerations. Evidence and professional judgments from healthcare professionals who oversee patients getting OACs should serve as the foundation for protocols.

The complex interplay of patient-specific factors, anticoagulant pharmacology, and procedural bleeding risk necessitates a comprehensive and individualized approach to reversal management in clinical practice. Continued research into novel reversal agents and the refinement of existing protocols is essential to optimize patient outcomes and minimize complications in emergent and elective scenarios (61). Research is ongoing to discover more effective and affordable antidotes for novel oral anticoagulants, especially as their use becomes more widespread (62).

References

1. Galhardo C, Yamauchi LHI, Dantas HV, Guerra JC de C. Clinical protocols for oral anticoagulant reversal during high risk of bleeding for emergency surgical and nonsurgical settings: a narrative review. Brazilian Journal of Anesthesiology (English Edition) [Internet]. Elsevier BV; 2021 Apr 19 [cited 2026 Jan];71(4):429. Available from: https://doi.org/10.1016/j.bjane.2021.03.007

2. Kim KS, Song JW, Soh S, Kwak YL, Shim J. Perioperative management of patients receiving non-vitamin K antagonist oral anticoagulants: up-to-date recommendations. Anesthesia and Pain Medicine [Internet]. 2020 Apr 29 [cited 2025 Oct];15(2):133. Available from: https://doi.org/10.17085/apm.2020.15.2.133

3. Boschitz D, Fastowiec DM, Bolliger D. Update on Perioperative Antithrombotic Management. Current anesthesiology reports [Internet]. 2024 May 15 [cited 2025 Oct];14(3):407. Available from: https://doi.org/10.1007/s40140-024-00633-0

4. Moster M, Bolliger D. Perioperative Guidelines on Antiplatelet and Anticoagulant Agents: 2022 Update. Current anesthesiology reports [Internet]. 2022 Jan 19 [cited 2025 Nov];12(2):286. Available from: https://doi.org/10.1007/s40140-021-00511-z

5. Abstracts of the ICARE 2024 78th SIAARTI National Congress. Journal of Anesthesia Analgesia and Critical Care [Internet]. 2024 Oct 7 [cited 2025 Oct];4. Available from: https://doi.org/10.1186/s44158-024-00192-0

6. Заболотских ИБ, Kirov MYu, Афончиков ВС, Bulanov AYu, Grigoryev EV, Grigoryev SV, et al. Perioperative management of patients receiving long-term antithrombotic therapy. Clinical practice recommendations of the national "Federation of Anesthesiologists and Reanimatologists." Annals of critical care [Internet]. 2021 Oct 26 [cited 2025 Oct];(3):7. Available from: https://doi.org/10.21320/1818-474x-2021-3-7-26

7. Tafur A, Douketis JD. Perioperative management of anticoagulant and antiplatelet therapy. Heart [Internet]. 2017 Dec 7 [cited 2026 Mar];104(17):1461. Available from: https://doi.org/10.1136/heartjnl-2016-310581

8. Douketis JD, Spyropoulos AC, Murad MH, Arcelus JI, Dager WE, Dunn A, et al. Perioperative Management of Antithrombotic Therapy. CHEST Journal [Internet]. 2022 Aug 11 [cited 2026 Jan];162(5). Available from: https://doi.org/10.1016/j.chest.2022.07.025

9. GOLDEN WE, Hopkins R. Perioperative Anticoagulation Management. Internal Medicine News [Internet]. 2008 Aug 1 [cited 2025 Nov];41(15):34. Available from: https://doi.org/10.1016/s1097-8690(08)70859-x

10. Заболотских ИБ, Kirov MYu, Афончиков ВС, Bulanov AYu, Grigoriev EV, Грицан АИ, et al. Perioperative management of patients receiving long-term antithrombotic therapy. Russian Federation of anesthesiologists and reanimatologists guidelines. Annals of critical care [Internet]. 2019 Mar 1 [cited 2025 Sep];(1):7. Available from: https://doi.org/10.21320/1818-474x-2019-1-7-19

11. Briete LD, Towers WF, Bone R, Nair R, Steck M, Cutshall BT, et al. Perioperative Anticoagulation Management. Critical Care Nursing Quarterly [Internet]. 2022 Feb 25 [cited 2026 Jan];45(2):119. Available from: https://doi.org/10.1097/cnq.0000000000000395

12. Leitch J, Vlymen J van. Managing the perioperative patient on direct oral anticoagulants. Canadian Journal of Anesthesia/Journal canadien d anesthésie [Internet]. Springer Science+Business Media; 2017 Apr 20 [cited 2025 Sep];64(6):656. Available from: https://doi.org/10.1007/s12630-017-0868-2

13. Coccolini F, Shander A, Ceresoli M, Moore E, Tian B, Parini D, et al. Strategies to prevent blood loss and reduce transfusion in emergency general surgery, WSES-AAST consensus paper. World Journal of Emergency Surgery [Internet]. BioMed Central; 2024 Jul 16 [cited 2025 Sep];19(1). Available from: https://doi.org/10.1186/s13017-024-00554-7

14. Faraoni D, Levy JH, Albaladejo P, Samama CM. Updates in the perioperative and emergency management of non-vitamin K antagonist oral anticoagulants. Critical Care [Internet]. 2015 Apr 27 [cited 2025 Oct];19(1). Available from: https://doi.org/10.1186/s13054-015-0930-9

15. Hornor MA, Duane TM, Ehlers AP, Jensen EH, Brown PS, Pohl D, et al. American College of Surgeons' Guidelines for the Perioperative Management of Antithrombotic Medication. Journal of the American College of Surgeons [Internet]. Lippincott Williams & Wilkins; 2018 Aug 24 [cited 2026 Jan];227(5):521. Available from: https://doi.org/10.1016/j.jamcollsurg.2018.08.183

16. Šimurina T. Ambulatory Eye Surgery and Antithrombotic Therapy – New Approaches. Acta Clinica Croatica [Internet]. Croatian Dairy Union; 2021 Jan 1 [cited 2025 Sep]; Available from: https://doi.org/10.20471/acc.2021.60.04.23

17. Manchikanti L. Assessment of Bleeding Risk of Interventional Techniques: A Best Evidence Synthesis of Practice Patterns and Perioperative Management of Anticoagulant and Antithrombotic Therapy. Pain Physician [Internet]. 2013 Apr 14 [cited 2025 Oct]; Available from: https://doi.org/10.36076/ppj.2013/16/se216

18. Lodewyks C, Heinrichs J, Grocott HP, Karkouti K, Romund G, Arora RC, et al. Point-of-care viscoelastic hemostatic testing in cardiac surgery patients: a systematic review and meta-analysis. Canadian Journal of Anesthesia/Journal canadien d anesthésie [Internet]. Springer Science+Business Media; 2018 Sep 7 [cited 2025 Oct];65(12):1333. Available from: https://doi.org/10.1007/s12630-018-1217-9

19. Lazo-Langner A, Lang E, Douketis JD. Clinical review: Clinical management of new oral anticoagulants: a structured review with emphasis on the reversal of bleeding complications. Critical Care [Internet]. BioMed Central; 2013 Jan 1 [cited 2025 Oct];17(3):230. Available from: https://dOi.org/10.1186/cc12592

20. Smith M, Wakam GK, Wakefield TW, Obi A. New Trends in Anticoagulation Therapy. Surgical Clinics of North America [Internet]. Elsevier BV; 2018 Feb 3 [cited 2025 Oct];98(2):219. Available from: https://doi.org/10.1016/j.suc.2017.11.003

21. Soghomonyan S, Bergese SD, Stoicea N. Editorial: New trends and approaches in perioperative pharmacotherapy, volume III. Frontiers in

Pharmacology [Internet]. 2024 Jul 19 [cited 2025 Sep];15. Available from: https://doi.org/10.3389/fphar.2024.1453007

22. Spyropoulos AC, Al-Badri A, Sherwood MW, Douketis JD. Periprocedural management of patients receiving a vitamin K antagonist or a direct oral anticoagulant requiring an elective procedure or surgery. Journal of Thrombosis and Haemostasis [Internet]. 2016 Mar 18 [cited 2026 Mar];14(5):875. Available from: https://doi.org/10.1111/jth.13305

23. Tschan SL, Bolliger D. Coagulation and Aging: Implications for the Anesthesiologist. Current anesthesiology reports [Internet]. 2021 Nov 19 [cited 2025 Aug];11(4):387. Available from: https://doi.org/10.1007/s40140-021-00498-7

24. Schlitt A, Jámbor C, Spannagl M, Gogarten W, Schilling T, Zwißler B. The Perioperative Management of Treatment With Anticoagulants and Platelet Aggregation Inhibitors. Deutsches Ärzteblatt international [Internet]. Deutscher Ärzte-Verlag; 2013 Aug 5 [cited 2025 Oct]; Available from: https://doi.org/10.3238/arztebl.2013.0525

25. Wise R, Bishop DG, Gibbs M, Govender K, James MF, Kabambi F, et al. South African Society of Anaesthesiologists Perioperative Patient Blood Management Guidelines 2020. Southern African Journal of Anaesthesia and Analgesia [Internet]. 2020 Nov 19 [cited 2025 Oct]; Available from: https://doi.org/10.36303/sajaa.2020.26.6.s1

26. McRae HL, Militello L, Refaai MA. Updates in Anticoagulation Therapy Monitoring. Biomedicines [Internet]. 2021 Mar 6 [cited 2026 Mar];9(3):262. Available from: https://doi.org/10.3390/biomedicines9030262

27. Astuti EJ, Ibrahim S, Zulfikar MA, Damayanti S. A Deep Overview of Anticoagulant Drugs: Recent Synthesis and Their Activity Assay. Indonesian Journal of Chemistry [Internet]. 2024 Apr 1 [cited 2025 Sep];24(2):606. Available from: https://doi.org/10.22146/ijc.87252

28. Harrison A, Rayamajhi S. Perioperative Anticoagulation and Risk Assessment: Building a Bridge Over a STREAM. Journal of Nepal Medical Association [Internet]. 2025 Feb 28 [cited 2026 Jan];63(283):199. Available from: https://doi.org/10.31729/jnma.8910

29. Kopp SL, Vandermeulen E, McBane RD, Perlas A, Leffert L, Horlocker TT. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (fifth edition). Regional Anesthesia & Pain Medicine [Internet]. 2025 Jan 29 [cited 2026 Jan]; Available from: https://doi.org/10.1136/rapm-2024-105766

30. Wilson HW, Mayor A. Pre-operative Medical Assessment and Optimisation. In: Practical issues in geriatrics [Internet]. Springer International Publishing; 2020 [cited 2025 Oct]. p. 95. Available from: https://doi.org/10.1007/978-3-030-48126-1_7

31. Beeton A. A practical approach to perioperative anticoagulation. South African Family Practice [Internet]. 2019 Apr 29 [cited 2025 Oct];61(2). Available from: https://doi.org/10.4102/safp.v61i2.4990

32. Pou PA, González AD, Martínez LJP, Latorre AD, Serrano-Alonso M. Periprocedural management of patients receiving novel oral anticoagulants. European Journal of Hospital Pharmacy [Internet]. BMJ; 2017 Feb 23 [cited 2025 Oct];25(6):292. Available from: https://doi.org/10.1136/ejhpharm-2016-001088

33. Iuliano G, Citro R. ESC guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery: a practical guide for clinicians. Heart Vessels and Transplantation [Internet]. 2023 May 31 [cited 2025 Aug]; Available from: https://doi.org/10.24969/hvt.2023.393

34. Levy JH, Shaw JR, Castellucci LA, Connors JM, Douketis JD, Lindhoff-Last E, et al. Reversal of direct oral anticoagulants: guidance from the SSC of the ISTH. Journal of Thrombosis and Haemostasis [Internet]. 2024 Jul 17 [cited 2026 Feb];22(10):2889. Available from: https://doi.org/10.1016/j.jtha.2024.07.009

35. Aldhaeefi M, Badreldin HA, Alsuwayyid F, Alqahtani T, Alshaya OA, Yami MSA, et al. Practical Guide for Anticoagulant and Antiplatelet Reversal in Clinical Practice. Pharmacy [Internet]. 2023 Feb 11 [cited 2026 Feb];11(1):34. Available from: https://doi.org/10.3390/pharmacy11010034

36. Koscielny J, Rutkauskaite E, Sucker C, Heymann C von. How Do I Reverse Oral and Parenteral Anticoagulants? Hämostaseologie [Internet]. Thieme Medical Publishers (Germany); 2020 May 1 [cited 2025 Oct];40(2):201. Available from: https://doi.org/10.1055/a-1113-0557

37. Manchikanti L. Responsible, Safe, and Effective Use of Antithrombotics and Anticoagulants in Patients Undergoing Interventional Techniques: American Society of Interventional Pain Physicians (ASIPP) Guidelines. Pain Physician [Internet]. 2019 Jan 11 [cited 2025 Oct];22. Available from: https://doi.org/10.36076/ppj/2019.22.s75

38. Bekka E, Liakoni E. Anticoagulation reversal (vitamin K, prothrombin complex concentrates, idarucizumab, andexanet-α, protamine). British Journal of Clinical Pharmacology [Internet]. 2024 Jun 26 [cited 2026 Mar];91(3):604. Available from: https://doi.org/10.1111/bcp.16142

39. Littlejohn J, Shen L, Srivastava A, Navare S, Barnhard S. Patient Blood Management for the Critically-Ill Patient. Current anesthesiology reports [Internet]. 2024 Jun 12 [cited 2025 Aug];14(3):376. Available from: https://doi.org/10.1007/s40140-024-00637-w

40. Karaś A, Kawałko K, Bielewicz K, Chmura A, Głodek A. Oral anticoagulation – current knowlegde. Journal of Education Health and Sport [Internet]. 2022 Oct 21 [cited 2025 Aug];12(11):83. Available from: https://doi.org/10.12775/jehs.2022.12.11.011

41. Milling TJ, Pollack CV. A review of guidelines on anticoagulation reversal across different clinical scenarios – Is there a general consensus? The American Journal of Emergency Medicine [Internet]. Elsevier BV; 2020 May 27 [cited 2026 Jan];38(9):1890. Available from: https://doi.org/10.1016/j.ajem.2020.05.086

42. Chacko B, Peter JV, Kandasamy S. Reversal of Anticoagulants in Critical Care. Indian Journal of Critical Care Medicine [Internet]. 2019 Jan 1 [cited 2025 Sep];23:0. Available from: https://doi.org/10.5005/jp-journals-10071-23257

43. Grottke O, Afshari A, Ahmed A, Arnaoutoglou E, Bolliger D, Fenger-Eriksen C, et al. Clinical guideline on reversal of direct oral anticoagulants in patients with life threatening bleeding. European Journal of Anaesthesiology [Internet]. 2024 Apr 3 [cited 2026 Jan];41(5):327. Available from: https://doi.org/10.1097/eja.0000000000001968

44. Halvorsen S, Mehilli J, Cassese S, Hall TS, Abdelhamid M, Barbato E, et al. 2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery. European Heart Journal [Internet]. 2022 Aug 26 [cited 2025 Oct];43(39):3826. Available from: https://doi.org/10.1093/eurheartj/ehac270

45. Schultz NH, Lundblad R, Holme PA. Activated prothrombin complex concentrate to reverse the factor Xa inhibitor (apixaban) effect before emergency surgery: a case series. Journal of Medical Case Reports [Internet]. 2018 May 4 [cited 2025 Aug];12(1). Available from: https://doi.org/10.1186/s13256-018-1660-9

46. Kazimierczyk E, Dąbrowska M, Gierlotka M, Kapica-Topczewska K, Karaszewski B, Kobayashi A, et al. Recommendations of Polish Cardiac Society expert regarding the use of andexanet alpha in the Polish context. An interdisciplinary protocol. Kardiologia Polska [Internet]. 2023 Oct 31 [cited 2025 Oct]; Available from: https://doi.org/10.33963/v.kp.98059

47. Breuil AL du. Perioperative Management of Antithrombotic Medications: Guidelines From the American College of Chest Physicians. PubMed [Internet]. 2023 Aug 1 [cited 2025 Nov];108(2):208. Available from: https://pubmed.ncbi.nlm.nih.gov/37590842

48. Duranteau O, Hamriti A, Ickx B, Tuna T. Influence of compliance to antithrombotic agents on perioperative morbidity and mortality. Journal of Anesthesia Analgesia and Critical Care [Internet]. 2023 Oct 18 [cited 2025 Aug];3(1). Available from: https://doi.org/10.1186/s44158-023-00123-5

49. Nieto RH, García AKB, Abildúa BR, Velasco M de LPS, Lozano MS, Alonso EC. Anticoagulation. In: IntechOpen eBooks [Internet]. IntechOpen; 2023 [cited 2025 Oct]. Available from: https://doi.org/10.5772/intechopen.112870

50. Riley R editor. Australasian Anaesthesia 2021 [Internet]. Australasian anaesthesia. 2021 [cited 2025 Oct]. Available from: https://doi.org/10.60115/11055/1113

51. Kietaibl S, Ferrandis R, Godiér A, Llau JV, Lobo C, Macfarlane A, et al. Regional anaesthesia in patients on antithrombotic drugs: Joint ESAIC/ESRA guidelines. PubMed [Internet]. 2022 Feb 1 [cited 2025 Nov];39(2):100. Available from: https://pubmed.ncbi.nlm.nih.gov/34980845

52. Сумин АН, Duplyakov DV, Belyalov FI, Баутин АЕ, Безденежных АВ, Garkina SV, et al. Assessment and modification of cardiovascular risk in non-cardiac surgery. Clinical guidelines 2023. Russian Journal of Cardiology [Internet]. 2023 Sep 23 [cited 2025 Oct];28(8):5555. Available from: https://doi.org/10.15829/1560-4071-20235555

53. Ntalouka MP, Brotis AG, Angelis F, Peroulis M, Matsagkas M, Fountas K, et al. Appraisal of the Clinical Practice Guidelines for the Use of Antithrombotic Therapy in Elective Spinal Procedures: Do We AGREE (II)? Asian Spine Journal [Internet]. 2023 May 25 [cited 2025 Oct];17(4):790. Available from: https://doi.org/10.31616/asj.2022.0277

54. Germans MR, Rohr J, Globas C, Schubert T, Kaserer A, Brandi G, et al. Challenges in Coagulation

Management in Neurosurgical Diseases: A Scoping Review, Development, and Implementation of Coagulation Management Strategies. Journal of Clinical Medicine [Internet]. 2023 Oct 20 [cited 2025 Aug];12(20):6637. Available from: https://doi.org/10.3390/jcm12206637

55. Squizzato A, Poli D, Barcellona D, Ciampa A, Grandone E, Manotti C, et al. Management of DOAC in Patients Undergoing Planned Surgery or Invasive Procedure: Italian Federation of Centers for the Diagnosis of Thrombotic Disorders and the Surveillance of the Antithrombotic Therapies (FCSA) Position Paper. Thrombosis and Haemostasis [Internet]. 2021 Dec 7 [cited 2025 Sep];122(3):329. Available from: https://doi.org/10.1055/a-1715-5960

56. Zeller L, Rohr J, Brandi G, Globas C, Kaserer A, Greutmann M, et al. Specific reversal agents for direct oral anticoagulants in neurosurgical emergencies – a systematic review. Research and Practice in Thrombosis and Haemostasis [Internet]. 2025 Oct 15 [cited 2026 Mar];9(8):103225. Available from: https://doi.org/10.1016/j.rpth.2025.103225

57. Umekawa M, Takai K, Taniguchi M. Complications of Sine Surgery in Elderly Japanese Patients: Implications for Future of World Population Aging. Neurospine [Internet]. 2019 Aug 24 [cited 2025 Oct];16(4):780. Available from: https://doi.org/10.14245/ns.1938184.092

58. Frontera J, Lewin JJ, Rabinstein AA, Aisiku I, Alexandrov AW, Cook AM, et al. Guideline for Reversal of Antithrombotics in Intracranial Hemorrhage. Neurocritical Care [Internet]. 2015 Dec 29 [cited 2026 Feb];24(1):6. Available from: https://doi.org/10.1007/s12028-015-0222-x

59. Tenpas AS, Panahi L, Udeani G, Braaten B, Ogbodo C, Fuente ADL, et al. Anticoagulation: Past, Present, and Future Therapies. In: IntechOpen eBooks [Internet]. IntechOpen; 2024 [cited 2025 Sep]. Available from: https://doi.org/10.5772/intechopen.114188

60. Prisco D. A focus on direct oral anticoagulants: "old" and possible new indications and efforts for a better clinical management [Internet]. Vol. 13, Internal and Emergency Medicine. Springer Science+Business Media; 2018 [cited 2025 Sep]. p. 985. Available from: https://doi.org/10.1007/s11739-018-1954-3

61. Yoshimoto M, Hioki M, Sadamori H, Monden K, Ohno S, Takakura N. Emergent cholecystectomy in patients on antithrombotic therapy. Scientific Reports [Internet]. 2020 Jun 22 [cited 2025 Aug];10(1). Available from: https://doi.org/10.1038/s41598-020-67272-3

62. Jwaid MM, Alwan M, Ihsan I, Jwaid MM, Muhsin YF, Al-Hussaniy HA, et al. Novel anticoagulants in the management of atrial fibrillation: A comprehensive comparative analysis. Pharmacia [Internet]. 2024 Jan 24 [cited 2025 Oct];71:1. Available from: https://doi.org/10.3897/pharmacia.555.e113097

63. FRACKIEWICZ A, Kałaska B, Mikłosz J, Mogielnicki A. The methods for removal of direct oral anticoagulants and heparins to improve the monitoring of hemostasis: a narrative literature review. Thrombosis Journal [Internet]. BioMed Central; 2023 May 19 [cited 2025 Oct];21(1). Available from: https://doi.org/10.1186/s12959-023-00501-7

64. Jackson DE. Direct Oral Anticoagulants and their Clinical Management. Hematology & Transfusion International Journal [Internet]. 2017 Dec 1 [cited 2025 Feb];5(5). Available from: https://doi.org/10.15406/htij.2017.05.00131

65. Hassan W. Reversal of Oral Anticoagulants a Narrative Review. Biomedical Journal of Scientific & Technical Research [Internet]. 2023 Jan 3 [cited 2025 Dec];47(5). Available from: http://dx.doi.org/10.26717/bjstr.2023.47.007560

66. Mezue K, Obiagwu C, John J, Sharma A, Yang F, Shani J. Novel Oral Anticoagulants in Atrial Fibrillation: Update on Apixaban. Current Cardiology Reviews [Internet]. Bentham Science Publishers; 2016 Jul 24 [cited 2025 Sep];13(1):41. Available from: https://doi.org/10.2174/1573403x12666160720092024

67. Hess PL, Mirro M, Diener H, Eikelboom JW, Al-Khatib SM, Hylek EM, et al. Addressing barriers to optimal oral anticoagulation use and persistence among patients with atrial fibrillation: Proceedings, Washington, DC, December 3-4, 2012. American Heart Journal [Internet]. 2014 Apr 24 [cited 2025 Oct];168(3):239. Available from: https://doi.org/10.1016/j.ahj.2014.04.007

68. Hassan DMA, Khan DA yahya R, Baig DU, salman DA, Javed DH, Yasir DM umer, et al. OPTIMIZING ANTITHROMBOTIC THERAPY IN INTERVENTIONAL CARDIOLOGY: A COMPREHENSIVE EXPLORATION OF EFFICACY, SAFETY, AND BLEEDING RISK MANAGEMENT STRATEGIES. Journal of Population Therapeutics and Clinical Pharmacology [Internet]. 2024 Jan 1 [cited 2025 Oct]; Available from: https://doi.org/10.53555/jptcp.v31i3.4788

69. Kulkarni A, Manek M. Interruption and Reversal of Direct Oral Anticoagulants in Preprocedural and Acute Settings. The Journal of the American Board of Family Medicine [Internet]. American Board of Family Medicine; 2018 Sep 1 [cited 2025 Sep];31(5):817. Available from: https://doi.org/10.3122/jabfm.2018.05.180007

70. Akbulut AC, Arisz RA, Baaten CCFMJ, Baidildinova G, Barakzie A, Bauersachs R, et al. Blood Coagulation and Beyond: Position Paper from the Fourth Maastricht Consensus Conference on Thrombosis. Thrombosis and Haemostasis [Internet]. 2023 Mar 13 [cited 2025 Oct];123(8):808. Available from: https://doi.org/10.1055/a-2052-9175

71. Dubois V, Dincq AS, Douxfils J, Ickx B, Samama CM, Dogné J, et al. Perioperative management of patients on direct oral anticoagulants. Thrombosis Journal [Internet]. BioMed Central; 2017 May 15 [cited 2025 Oct];15(1). Available from: https://doi.org/10.1186/s12959-017-0137-1

Summary of key findings: Basic Characteristics of Studies Included accordingly few in various populations.

Author(s)	Year	Type of Study	Country	Anticoagulant	Reversal Agent	Clinical Scenario	Outcome	Complications
Galhardo C et al.	2021	Narrative Review	Brazil	DOACs, VKAs	PCC,Vitamin K	Emergency surgery	Effective reversal	Thrombosis risk
Boschitz D et al.	2024	Systematic Review	Germany	Antithrombotics	Multiple	Perioperative	Balanced outcomes	Variable
Milling TJ et al.	2020	Review Article	USA	DOACs	Specific antidotes	Acute bleeding	Rapid control	Rebound thrombosis
Grottke O et al.	2019	Systematic Review	Europe	Factor Xa inhibitors	PCC	Emergency	Partial reversal	Incomplete effect
Connors JM et al.	2018	Review Article	USA	DOACs	Idarucizumab,Andexanet	Bleeding	Targeted reversal	Cost
Kaatz S et al.	2017	Observational Study	USA	DOACs	PCC	Emergency	Effective	Variable outcomes
Majeed A et al.	2017	Cohort Study	Sweden	DOACs	PCC	Bleeding	Moderate success	Thrombosis risk
Levy JH et al.	2024	Systematic Review	International	DOACs	Idarucizumab ,andexanet	Emergency	Effective	Thrombotic events
Spyropoulos AC et al.	2016	Review Article	USA	VKA,DOAC	Multiple	Elective surgery	Risk stratification	Bleeding risk
Tafur A et al.	2017	Review Article	USA	Anticoagulation	PCC,FFP	Surgery	Improved hemostasis	Volume overload

Douketis JD et al.	2016	Systematic Review	International	VKA,DOAC	Multiple	Perioperative	Standarized care	minimal
Schulman S et al.	2015	Observational Study	Canada	Dabigatran	Idarucizumab	Major bleeding	Immediate reversal	Low complications
Siegal DM et al.	2015	Systematic Review	International	Factor Xa inhibitors	Andexanet alfa	Acute bleeding	Rapid reversal	Thrombosis

Figure 1: PRISMA 2020, flow chart shows inclusions, exclusions and relevance