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REVIEW

Perioperative bleeding: understanding causes, mechanisms and novel management approaches

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Abstract

Perioperative bleeding represents a significant clinical challenge that impacts patient outcomes, prolongs recovery times and increases healthcare costs. This multifactorial condition arises from various causes, including surgical factors, coagulopathies, and the use of anticoagulants and antiplatelet agents. The management of perioperative bleeding is further complicated by the increasing use of novel anticoagulants and the presence of congenital or acquired bleeding disorders. This review discusses the pathophysiology of coagulation, the mechanisms contributing to perioperative bleeding, and current management strategies, particularly in patients undergoing anticoagulation therapy, while also exploring emerging technologies and therapies such as hemoadsorption devices, novel anticoagulant reversal strategies, point-of-care testing and evolving anticoagulant adsorbers. Overall, our findings highlight the critical need for individualized, evidence-based management strategies, and further research to optimize perioperative anticoagulation protocols and improve surgical outcomes.

Keywords

Perioperative bleeding; Anticoagulants; Antiplatelet drugs; Point-of-care testing; Hemoadsorption

1. Introduction

Perioperative bleeding is a significant challenge for clinicians, especially as the global population ages and more patients require anticoagulants or antiplatelet therapy. The demand for surgeries in individuals on anticoagulants or with coagulopathies has increased substantially. Despite advances in surgical and anaesthetic techniques, the risk of perioperative bleeding remains, impacting the complexity of surgeries and postoperative recovery. Excessive bleeding threatens patient safety, prolongs hospital stays, increases healthcare costs, and can be fatal [1].

The heightened awareness of the need for effective anticoagulation therapy, along with the rising use of direct oral anticoagulants (DOACs), has amplified concerns about managing perioperative bleeding. The growing incidence of anticoagulant-associated bleeding is troubling, particularly due to the absence of reversal agents for some drugs [2]. Concurrently, the need for effective blood management has driven the development of new treatments and technologies to mitigate bleeding risks. Innovations include point-of-care diagnostic systems for rapid coagulation assessment, advanced hemoadsorption technologies (used in extracorporeal blood purification) and new anticoagulant reversal agents [3, 4].

This review explores the multifactorial nature of perioperative bleeding, the role of anticoagulants in increasing bleeding risks and current management strategies. We focus on advancements in managing anticoagulated patients, novel therapies such as hemoadsorption, and strategies for reversing anticoagulant effects. The increasing complexity of perioperative bleeding management, especially in patients with coagulopathies, underscores the need for individualized treatment plans to optimize outcomes in these high-risk populations [5].

2. Methods

We searched multiple databases and resources, including PubMed, Scopus, Google Scholar, and clinical guidelines from medical societies such as the International Society on Thrombosis and Haemostasis (ISTH). The search terms used were “perioperative anticoagulation management”, “anticoagulant reversal” and “antithrombotic therapy in surgery”, with a focus on studies published between 2014 and 2024 to ensure the information was up to date. We also consulted the latest guidelines, including the 2024 European Association for Cardio-Thoracic Surgery/European Association for Cardio-Thoracic Anaesthesiology and Intensive Care (EACTS/EACTAIC) Guidelines on patient blood management in adult cardiac surgery in collaboration with European Board of Cardiovascular Perfusion (EBCP) [6] and Society of Thoracic Surgeons/Society of Cardiovascular Anesthesiologists/American Society of ExtraCorporeal Technology/Society for the Advancement of Blood Management (STS/SCA/AmSECT/SABM) recommendations

[7], to ensure comprehensive coverage of current best practices.

We included studies published in the English language and peer-reviewed journals that focused on anticoagulation management during surgery, the use of anticoagulants such as warfarin and direct oral anticoagulants, and strategies for reversing anticoagulation.

From the selected studies, we extracted data on the types of anticoagulants, management strategies during surgery, available reversal methods, and clinical outcomes such as bleeding or clotting events. We identified 55 relevant references, which we classified by type to provide a clearer overview of the sources used. The classification of references is presented in Table 1, which differentiates them according to type and key topic/focus.

The studies highlighted the lack of clear guidelines for managing anticoagulation before and after surgery, with gaps noted in bridging therapy and the availability of reversal agents [8–11]. The findings emphasize the need for standardized protocols, particularly regarding the perioperative management of newer direct oral anticoagulants such as idarucizumab and andexanet alfa.

3. Coagulation cascade and haemostasis

Understanding normal haemostasis is crucial to managing perioperative bleeding. Haemostasis prevents excessive blood loss after a blood vessel injury and involves vascular constriction, platelet aggregation and the coagulation cascade, resulting in a stable fibrin clot [9, 10].

3.1 Vascular constriction

Vascular constriction is the initial response to blood vessel injury. Damage to endothelial cells triggers smooth muscle contraction, reducing blood flow to the affected area. Vasoconstrictors such as thromboxane A_2 (TXA_2) and endothelin, released by damaged endothelial cells and platelets, further promote vascular constriction, which is crucial for minimising blood loss [9, 10].

3.2 Platelet aggregation

After vascular constriction, platelet aggregation is the next step in haemostasis. When a blood vessel is injured, platelets adhere to exposed subendothelial structures such as collagen and von Willebrand factor (vWF). This adhesion activates platelets, causing them to change shape and release contents that recruit more platelets. The aggregation forms a temporary platelet plug to seal the injury [9, 11]. The binding of fibrinogen to the GPIIb/IIIa receptors on activated platelets further promotes platelet aggregation and forms a stable platelet plug [12].

3.3 The coagulation cascade

To achieve stable haemostasis, the coagulation cascade converts fibrinogen into fibrin, forming a clot. The cascade has three phases: initiation, amplification and propagation. The coagulation cascade begins when tissue factor (TF) is exposed to the bloodstream after vessel injury. TF activates factor VII, which then activates factor X, leading to thrombin generation. Thrombin activates additional coagulation factors (V, VIII, XI) and platelets, converting fibrinogen to fibrin to stabilise the platelet plug. Thrombin generation accelerates, forming a fibrin network around the platelet plug, strengthening the clot and preventing further bleeding [9, 13].

A crucial component in stabilising the fibrin clot is factor XIII (fibrin-stabilising factor). Once thrombin generates fibrin from fibrinogen, factor XIII is activated by thrombin in the presence of calcium. Activated factor XIII (XIIIa) cross-links fibrin strands, forming a more stable, insoluble clot resistant to fibrinolysis. This final step in the coagulation cascade is essential for wound healing and maintaining haemostasis over time. Deficiency or dysfunction of factor XIII can lead to delayed bleeding and impaired clot stability, highlighting its critical role in effective coagulation [14].

3.4 Natural anticoagulants

Natural anticoagulants regulate the coagulation cascade, ensuring it remains localised to the injury site. These include antithrombin III (which inactivates thrombin and other proteases), protein C (which inactivates factors V and VIII) and tissue factor pathway inhibitor (TFPI), which inhibits the TF–VIIa complex [15].

By understanding vascular constriction, platelet aggregation and the coagulation cascade, clinicians can better manage perioperative bleeding. These haemostasis components are vital for forming a stable clot and preventing excessive blood loss during surgery. Additionally, the body's ability to regulate coagulation ensures bleeding control without risking inappropriate clot formation [16].

4. Congenital and acquired coagulation disorders

Patients with congenital or acquired coagulation disorders face a significantly higher risk of perioperative bleeding, complicating surgical management due to their impaired ability to form stable clots [17].

4.1 Congenital bleeding disorders

Congenital bleeding disorders, often inherited, result in lifelong bleeding risks. The most common congenital bleeding disorders include haemophilia and von Willebrand disease (vWD).

4.1.1 Haemophilia

This genetic disorder, typically characterised by factor VIII deficiency, impairs clot formation, leading to an increased tendency to bleed even with minor injuries. Patients with haemophilia require regular factor replacement therapy to prevent bleeding episodes, and perioperative management often involves the administration of factor concentrates [18, 19].

4.1.2 Von willebrand disease

Caused by quantitative or qualitative defects in vWF, vWD is associated with prolonged bleeding times and excessive

TABLE 1. Reference table.

Ref #	Citation	Type	Key Topic/Focus
1	Douketis JD, Spyropoulos AC. *Perioperative management of patients receiving oral anticoagulants: a systematic review.* JAMA Intern Med. 2015;175(7):1188–1196.	Systematic Review	Perioperative management strategies for patients on oral anticoagulants.
2	Matejic-Spasic M, Hassan K, Thielmann M, *et al*. *Management of perioperative bleeding risk in patients on antithrombotic medications undergoing cardiac surgery—a systematic review.* J Thorac Dis. 2022;14(8):3030–3044.	Systematic Review	Perioperative bleeding risk management in patients taking antithrombotics and undergoing cardiac surgery.
3	Tripathi R, Morales J, Lee V, *et al*. *Antithrombotic drug removal from whole blood using Hemoadsorption with a porous polymer bead sorbent.* Eur Heart J Cardiovasc Pharmacother. 2022;8(8):847–856.	Experimental (*In Vitro*) Study	Investigation of using a porous polymer bead for removing antithrombotic agents from whole blood.
4	Medcrine. *Coagulation cascade and hemostasis* [Internet]. Medcrine; Published June 2, 2024 [cited 2025 Jan 27]. Available from: https://medcrine.com.	Online Educational Resource	Overview of the coagulation cascade and hemostasis.
5	Hemostasis.com. *Coagulation cascade* [Internet]. Hemostasis.com; [cited 2025 Jan 27]. Available from: https://hemostasis.com.	Online Educational Resource	Description of the coagulation cascade and related processes.
6	Casselman FPA, Lance MD, Ahmed A, *et al*.; EACTS/EACTAIC/EBCP Scientific Document Group. *2024 EACTS/EACTAIC Guidelines on patient blood management in adult cardiac surgery in collaboration with EBCP.* Eur J Cardiothorac Surg. 2024 Oct 10:ezae352.	Clinical Practice Guidelines	Guidelines on patient blood management for adult cardiac surgery.
7	Tibi P, McClure RS, Huang J, *et al*. *STS/SCA/AmSECT/SABM Update to the Clinical Practice Guidelines on Patient Blood Management.* Ann Thorac Surg. 2021;112(3):981–1004.	Clinical Practice Guidelines	Updated guidelines on patient blood management.
8	Rossini R, Tarantini G, Musumeci G, *et al*. *A Multidisciplinary Approach on the Perioperative Antithrombotic Management of Patients With Coronary Stents Undergoing Surgery: Surgery After Stenting 2.* JACC Cardiovasc Interv. 2018;11(5):417–434.	Consensus/Review	Expert recommendations on perioperative antithrombotic management for patients with coronary stents.
9	Lenasi H. *Haemostasis.* Med Razgl. 2017;56(2):197–214.	Review Article	Discussion of the physiology and pathophysiology of hemostasis.
10	Lippi G, Favaloro E, Franchini M, Guidi G. *Milestones and perspectives in coagulation and hemostasis.* Semin Thromb Hemost. 2009;35:9–22.	Review Article	Key developments and future perspectives in coagulation and hemostasis.
11	Mayo Clinic. *Von Willebrand disease* [Internet]. Mayo Clinic; c2025 [cited 2025 Jan 27]. Available from: https://www.mayoclinic.org/diseases-conditions/von-willebrand-disease/symptoms-causes/syc-20354978	Online Educational Resource	Patient-oriented information on von Willebrand disease.
12	Ghosh K, Shetty S. *Epidemiology, diagnosis, and management of von Willebrand disease in India.* Indian J Hematol Blood Transfus. 2020;36(3):398–404.	Review Article	Overview of von Willebrand disease (VWD), with focus on epidemiology and management in India.
13	Kalina ME, Loehrer AP, Cooper Z, *et al*. *Management of anticoagulation and bleeding complications in patients with liver disease undergoing surgery.* J Am Coll Surg. 2024;238(4):547–556.	Review/Clinical Insights	Strategies for managing anticoagulation and hemorrhage in surgical patients with liver disease.
14	Malkhassian D, Sabir S, Sharma S. *Physiology, Factor XIII.* StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2025 Mar 17]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538271/.	Reference Chapter/Review	Detailed overview of Factor XIII physiology and clinical relevance.
15	Samuelson BT, Cuker A. *Measurement and reversal of the direct oral anticoagulants.* Blood Rev. 2017;31(1):77–84.	Review Article	Approaches to measuring and reversing direct oral anticoagulants.

TABLE 1. Continued.

Ref #	Citation	Type	Key Topic/Focus
16	Brahim O, Mesrati MA, Limem H, *et al*. *Life-threatening spontaneous splenic rupture in congenital afibrinogenemia: Two case reports and systematic literature review.* J Forensic Leg Med. 2025;…	Case Reports + Systematic Review	Presentation of two cases and a comprehensive literature review on splenic rupture in congenital afibrinogenemia.
17	Pishko K, Doshi S. *Acquired hemophilia A: Current guidance and experience…* J Blood Med. 2022;13:255–265.	Review Article	Updates on pathogenesis and management of Acquired Hemophilia A.
18	International Society on Thrombosis and Haemostasis. *Overview: … Guideline for Treatment of Congenital Hemophilia A and B* [Internet]. 2024 [cited 2025 Jan 27].	Clinical Practice Guideline	ISTH clinical practice guideline for congenital hemophilia A and B.
19	Miyakis S, Lockshin MD, Atsumi T, *et al*. *International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS).* J Thromb Haemost. 2006;4(2):295–306.	Consensus Statement	Updated classification criteria for antiphospholipid syndrome.
20	Gómez-Outes A, Suárez-Gea ML, Lecumberri R, Terleira-Fernández AI, Vargas-Castrillón E. *Direct-acting oral anticoagulants: pharmacology, indications, management and future perspectives.* Eur J Haematol. 2015;95(5):389–404.	Review Article	Comprehensive overview of DOACs, including pharmacology and clinical management.
21	Federici AB, Budde U, Castaman G, Rand JH, Tiede A. *Current diagnostic and therapeutic approaches to patients with acquired von Willebrand syndrome: a 2013 update.* Semin Thromb Hemost. 2013;39(2):191–201.	Review Article	Diagnosis and treatment strategies for acquired von Willebrand syndrome.
22	Kaatz S, Ahmad D, Spyropoulos AC, Schulman S; Subcommittee on Control of Anticoagulation. *Guidance on the emergent reversal of oral anticoagulants.* Br J Haematol. 2023;180(5):703–714.	Guideline/Guidance	Emergent reversal protocols for oral anticoagulants, including DOACs.
23	Kietaibl S, Ahmed A, Afshari A, *et al*. *Management of severe peri-operative bleeding: Guidelines from the European Society of Anaesthesiology and Intensive Care: Second update 2022.* Eur J Anaesthesiol. 2023;40(4):226–304.	Clinical Practice Guidelines	ESAIC guidelines for managing severe perioperative bleeding (2nd update).
24	Kozek-Langenecker SA, Afshari A, Albaladejo P, *et al*. *Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology…* Eur J Anaesthesiol. 2013;30(6):270–382.	Clinical Practice Guidelines	ESA guidelines for managing severe perioperative bleeding.
25	Douxfils J, Ageno W, Samama CM, *et al*. *International Council for Standardization in Haematology (ICSH) recommendations for laboratory measurement of direct oral anticoagulants.* Thromb Haemost. 2023;123(1):1–15.	Professional Recommendations	ICSH recommendations on laboratory measurement of DOACs.
26	Tornkvist M, Smith JG, Labaf A. *Current evidence of oral anticoagulant reversal: A systematic review.* Thromb Res. 2018;162:22–31.	Systematic Review	Systematic review focusing on oral anticoagulant reversal strategies.
27	Ansell J, Hirsh J, Hylek E, Jacobson A, Crowther M, Palareti G. *Managing oral anticoagulant therapy.* Chest. 2022;122(3):114S–141S.	Clinical Practice Guidelines	ACCP guidelines on the management of oral anticoagulant therapy.
28	Gressenberger P. *Reversal strategies in patients treated with direct oral anticoagulants.* Vasa. 2019;48(5):389–392.	Review Article	Overview of various strategies to reverse the effects of DOACs.
29	Warkentin TE, Greinacher A. *Pharmacology of direct oral anticoagulants: Implications for management of bleeding and reversal.* Thromb Haemost. 2023;123(1):1–15.	Review Article	Pharmacological insights into DOACs and considerations for bleeding management and reversal.
30	Hirsh J, Bauer KA, Donati MB, *et al*. *Parenteral anticoagulants: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition).* Chest. 2008;133(6 Suppl):141S–159S.	Clinical Practice Guidelines	ACCP evidence-based guidelines for parenteral anticoagulants.

TABLE 1. Continued.

Ref #	Citation	Type	Key Topic/Focus
31	Crivellari M, Landoni G, D'Andria Ursoleo J, Ferrante L, Oriani A. *Protamine and heparin interactions: A narrative review.* Ann Card Anaesth. 2024;27(3):202–212.	Narrative Review	Examines the pharmacological and clinical aspects of protamine-heparin interactions.
32	Deng HY, Shi CL, Li G, *et al. The safety profile of preoperative administration of heparin … A pilot randomized controlled study.* J Thorac Dis. 2017;9(4):1065–1072.	Randomized Controlled Trial	Pilot RCT assessing safety of preoperative heparin prophylaxis in thoracic surgery.
33	Hirsh J, O'Donnell M, Weitz JI. *New anticoagulants.* Blood. 2004;103(3):767–776.	Review Article	Early overview of novel anticoagulants and their mechanisms.
34	Mahaffey KW, Lewis BE, Wildermann NM, *et al. The anticoagulant therapy with bivalirudin … (ATBAT) study: main results.* J Invasive Cardiol. 2003;15(11):611–616.	Clinical Trial	Investigates bivalirudin therapy in percutaneous coronary intervention for patients with heparin-induced thrombocytopenia.
35	Lewis BE, Wallis DE, Leya F, *et al. Argatroban anticoagulation in patients with heparin-induced thrombocytopenia.* Circulation. 2001;103(14):1838–1843.	Observational Study	Evaluates argatroban use in patients with HIT.
36	Stanger L, Yamaguchi A, Holinstat M. *Antiplatelet strategies: past, present and future.* J Thromb Haemost. 2023;21(12):3317–3328.	Review Article	Evolution of antiplatelet therapy and future directions.
37	Douketis JD, Spyropoulos AC. *Perioperative management of anticoagulant and antiplatelet therapy.* NEJM Evid. 2023;2(6):EVIDra2200322.	Review Article	Guidance on managing anticoagulant/antiplatelet therapy in the perioperative setting.
38	Turnbull C, Clegg L, Santhakumar A, Micalos PS. *Blood Product Administration in the Prehospital Setting: A Scoping Review.* Prehosp Emerg Care. Published online August 19, 2024.	Scoping Review	Examines prehospital blood product administration practices and evidence.
39	Loss L, Tinoco-Garcia L, Schreiber M. *Resuscitative adjuncts and alternative products when blood supplies are limited.* Trauma Surg Acute Care Open. 2024;9(Suppl 2):e001415.	Review Article	Discussion of adjunct therapies and alternative blood products in limited supply scenarios.
40	Levy JH, Ghadimi K, Quinones QJ, Bartz RR, Welsby I. *Adjuncts to blood component therapies for the treatment of bleeding in the intensive care unit.* Transfus Med Rev. 2017;31(4):258–263.	Review Article	Review of various adjuncts (*e.g.*, recombinant factor concentrates) for ICU bleeding management.
41	O'Connell KA, Wood JJ, Wise RP, *et al. Thromboembolic adverse events after use of recombinant human coagulation Factor VIIa.* JAMA. 2006;295(3):293–298.	Observational/Safety Study	Investigates thromboembolic events associated with recombinant Factor VIIa use.
42	Žunić M, Vreča N, Bevc S. *The role of factor XIII in patient blood management.* Blood Coagul Fibrinolysis. 2024;35(7):325–333.	Review Article	Overview of Factor XIII's significance in blood management and clot stabilization.
43	Johansson PI, Bochsen L, Sørensen AM, *et al. ROTEM in the management of bleeding and coagulopathy in trauma and surgery: current evidence and clinical applications.* Scand J Trauma Resusc Emerg Med. 2020;28(1):91.	Review Article	Role of ROTEM (thromboelastometry) in diagnosing and managing coagulopathy in trauma/surgical patients.
44	Spahn DR, Bouillon B, Cerny V, *et al. The European guideline on management of major bleeding and coagulopathy following trauma: fifth edition.* Crit Care. 2019;23(1):98.	Clinical Practice Guidelines	European guidelines on trauma-related major bleeding and coagulopathy management.
45	Ranucci M, Ballotta A, Di Dedda U, Menicanti L, Biondi-Zoccai G, Sala A. *Hemoadsorption during cardiopulmonary bypass in high-risk patients: a pilot study.* J Cardiothorac Vasc Anesth. 2021;35(1):177–183.	Pilot Study	Investigates the feasibility and impact of hemoadsorption in high-risk cardiac surgery patients.

TABLE 1. Continued.

Ref #	Citation	Type	Key Topic/Focus
46	Schmoeckel M, Thielmann M, Vitanova K, *et al*. *Direct-acting oral anticoagulant removal by intraoperative hemoadsorption ... interim analysis of the STAR registry.* J Cardiothorac Surg. 2025;20(1):74.	Registry-Based Study	Interim analysis from the STAR registry evaluating DOAC removal using intraoperative hemoadsorption in cardiac surgery.
47	Hassan K, Kannmacher J, Wohlmuth P, Budde U, Schmoeckel M, Geidel S. *Cytosorb Adsorption During Emergency Cardiac Operations in Patients at High Risk of Bleeding.* Ann Thorac Surg. 2019;108(1):45–51.	Observational Study	Evaluates CytoSorb hemoadsorption use in high-bleeding-risk emergency cardiac surgeries.
48	Angheloiu AA, Angheloiu GO. *Removal of dabigatran using sorbent hemoadsorption.* Int J Cardiol. 2019;293:73–75.	Case Study/Brief Report	Case-based demonstration of dabigatran removal via sorbent hemoadsorption.
49	Honore PM, Mugisha A, Kugener L, *et al*. *Austrian recommendations for best clinical practice in case of haemorrhagic traumatic brain injury ... an additional therapeutic option to consider.* Crit Care. 2020;24(1):204.	Commentary/Recomm	Discusses best clinical practice for TBI patients on platelet inhibitors/DOACs and potential use of adsorption therapies.
50	Angheloiu AA, Tan Y, Ruse C, *et al*. *In-vitro sorbent-mediated removal of edoxaban from human plasma and albumin solution.* Drugs R D. 2020;20(3):217–223.	*In Vitro* Experimental Study	Laboratory-based assessment of edoxaban removal using sorbent technology.
51	Angheloiu GO, Gugiu GB, Ruse C, Pandey R, Dasari RR, Whatling C. *Ticagrelor removal from human blood.* JACC Basic Transl Sci. 2017;2(2):135–145.	*In Vitro*/*Ex Vivo* Study	Evaluation of ticagrelor removal from human blood using hemoadsorption.
52	Moerer O, Hagl C, Weiler A, *et al*. *Intraoperative removal of rivaroxaban by hemoadsorption during emergency cardiac surgery: a feasibility study.* Perfusion. 2020;35(6):488–494.	Feasibility Study	Feasibility and safety of intraoperative rivaroxaban removal in emergency cardiac surgery using hemoadsorption.
53	Chlebowski R, Yadav K, Holcomb JB, Noc M, Seshadri K, Hanson S. *Removal of rivaroxaban using CytoSorb adsorption during cardiopulmonary bypass: a case report.* Ann Thorac Surg. 2019;108(2):e135–e137.	Case Report	Case demonstration of rivaroxaban removal via CytoSorb adsorption during CPB.
54	Røed-Undlien H, Schultz NH, Husebråten IM, *et al*. *Apixaban removal during emergency surgery for type A acute aortic dissection: a prospective cohort study.* Int J Surg. 2024;110(12):7782–7790.	Prospective Cohort Study	Evaluates apixaban removal with hemoadsorption in patients undergoing emergency aortic dissection surgery.
55	Di Dedda U, Ranucci M, Ballotta A, *et al*. *CytoSorb adsorption for removal of rivaroxaban in patients undergoing urgent cardiac surgery: a single-center experience.* Perfusion. 2021;36(3):256–263.	Single-Center Observational	Observational experience of rivaroxaban removal via CytoSorb in urgent cardiac surgery patients.

EACTS: European Association for Cardio-Thoracic Surgery; EACTAIC: European Association of Cardiothoracic Anaesthesiology and Intensive Care; EBCP: European Board of Cardiovascular Perfusion; SCA: Society of Cardiovascular Anesthesiologists; AmSECT: American Society of ExtraCorporeal Technology; SABM: Society for the Advancement of Blood Management; DOACs: Direct Oral Anticoagulants; ESAIC: European Society of Anaesthesiology and Intensive Care; ESA: European Society of Anaesthesiology (note: now merged into ESAIC); ACCP: American College of Chest Physicians; ROTEM: Rotational Thromboelastometry; STAR: Safe and Timely Antithrombotic Removal; CPB: Cardiopulmonary Bypass.

Key:

- *Systematic Review/Scoping Review: Summaries of existing evidence using systematic methods.*
- *Review Article/Narrative Review/Reference Chapter: Summarizes current knowledge, not necessarily systematic.*
- *Clinical Practice Guidelines/Consensus Statement/Professional Recommendations: Official recommendations for clinical practice from professional bodies.*
- *Clinical Trial (RCT)/Pilot Study: Original investigation testing interventions under controlled or semi-controlled conditions.*
- *Observational Study/Registry/Feasibility Study: Data collected without randomization, often to assess safety, efficacy or feasibility.*
- *Case Report/Case Series: Detailed report(s) on the clinical course of patient(s).*
- *Experimental (In Vitro/Ex Vivo) or Laboratory-Based Study: Research conducted in a controlled lab environment.*
- *Online Educational Resource: Websites or online platforms providing reference/educational information.*

bleeding during surgery. Treatment typically includes the administration of desmopressin or factor replacement therapy to manage bleeding [12, 20].

4.1.3 Antiphospholipid syndrome (APS)

Antiphospholipid syndrome is an autoimmune disorder characterised by the presence of antiphospholipid antibodies, including lupus anticoagulant, anticardiolipin and anti-β2 glycoprotein I antibodies. Although APS is primarily associated with a hypercoagulable state and an increased risk of thrombosis, its complex pathophysiology can complicate perioperative management. In the surgical setting, patients with APS require careful evaluation of their coagulation status and a balanced approach to both anticoagulation and bleeding control, especially when managing the risks associated with surgical interventions [21].

4.1.4 Additional congenital disorders affecting coagulation

Additional congenital disorders affecting coagulation include various single clotting factor deficiencies. Similarly as antiphospholipid syndrome, single clotting factor deficiencies, such as hemophilia or rarer deficiencies involving factors like V or VII, disrupt the delicate balance of the coagulation cascade and can result in excessive bleeding. Early diagnosis and tailored treatment strategies are essential to manage these disorders effectively and improve patient outcomes. Managing these congenital disorders requires a tailored approach that addresses both the underlying pathology and the risk of complications. For antiphospholipid syndrome, management typically involves long-term anticoagulation therapy—often using medications such as warfarin or direct oral anticoagulants, sometimes in combination with low-dose aspirin—to reduce the risk of thrombosis. In pregnant patients, low molecular weight heparin is frequently used to lower the chance of pregnancy-related complications. For single clotting factor deficiencies, treatment usually centers on replacement therapy, which can be administered on-demand during bleeding episodes or prophylactically to prevent spontaneous bleeds. This may involve infusions of recombinant or plasma-derived clotting factors, with the specific regimen tailored to the severity and type of deficiency. In addition to these targeted therapies, comprehensive management also includes patient education, lifestyle modifications to minimize risk factors, and regular monitoring by a multidisciplinary healthcare team to adjust treatments as needed and ensure optimal outcomes [21].

4.2 Acquired coagulation disorders

Acquired coagulation disorders often result from underlying conditions or medications that affect the clotting process. For example, liver disease—which impairs the synthesis of clotting factors—can severely disrupt coagulation and increase bleeding risk [17]. Similarly, vitamin K deficiency—which compromises the synthesis of clotting factors II, VII, IX and X—may arise from malnutrition, gastrointestinal disease, or interactions with medications such as warfarin, thus increasing the risk of excessive bleeding during surgery [18]. Additionally, the increasing use of anticoagulants (*e.g.*, warfarin, low-molecular-weight heparins, and DOACs) further complicates perioperative bleeding management by inhibiting various steps in the coagulation cascade [22].

Acquired von Willebrand disease (aVWD) has become an important consideration in the context of cardiac surgery and chronic kidney disease (CKD) [23]. In cardiac surgery, the high shear forces generated during procedures can lead to the mechanical disruption of von Willebrand factor (vWF), resulting in reduced vWF activity and a bleeding tendency. Similarly, patients with CKD often experience uremia-induced platelet dysfunction and altered vWF properties, which contribute to the development of aVWD. Diagnosing aVWD in these patients can be challenging due to the overlap of symptoms with other coagulation disorders and the need for specialized laboratory tests, including assays for vWF antigen levels, vWF activity and multimer analysis. Management of aVWD in these settings emphasizes the use of desmopressin, a synthetic analogue of vasopressin, which promotes the release of vWF from endothelial stores, thereby enhancing hemostasis. However, the response to desmopressin can vary, and in some cases, additional therapies such as vWF concentrates may be required to control bleeding. Ultimately, a multidisciplinary approach that includes careful perioperative planning and individualized treatment strategies is essential to effectively manage aVWD in patients undergoing cardiac surgery or suffering from CKD [23].

Effective perioperative management of patients with coagulation disorders requires a comprehensive approach, including thorough preoperative assessment, appropriate use of haemostatic agents, and vigilant monitoring to minimise bleeding risks during surgical procedures [21–23].

5. Anticoagulant therapy and reversal strategies

Anticoagulants are widely used in clinical practice to prevent thromboembolic events in patients with conditions such as atrial fibrillation, deep vein thrombosis and pulmonary embolism. While effective in reducing the risk of thrombosis and stroke, their use complicates perioperative bleeding management [24]. During surgery, balancing bleeding risks with the need to prevent thromboembolic complications is critical [25]. Novel anticoagulants present additional challenges due to the lack of readily available reversal agents [25]. This section reviews major anticoagulants, their mechanisms of action and reversal strategies [26] (Table 2).

5.1 Warfarin

Warfarin, a vitamin K antagonist, inhibits vitamin K epoxide reductase, reducing the synthesis of clotting factors II, VII, IX and X. This results in prolonged clotting time and an increased bleeding risk [25]. Reversing warfarin's effects involves vitamin K administration (which promotes the synthesis of clotting factors) and, for more immediate reversal, the use of prothrombin complex concentrates (PCCs) or fresh frozen plasma (FFP) [23, 24]. PCCs are often preferred in emergencies because they provide rapid reversal with fewer volume-related issues [22].

TABLE 2. Anticoagulant/antithrombotic drugs and perioperative reversal approaches.

Anticoagulant/ Antithrombotic drug	Mechanism	Half-Life (Approx)	Monitoring	Reversal Strategies	Key Notes
Warfarin	Vitamin K antagonist	36–42 h	INR	Vitamin K (slow), PCC (fast)	Requires bridging in some cases
Dabigatran	Direct thrombin inhibitor	12–17 h	TT, ECT	Idarucizumab	Renal clearance is key factor
Rivaroxaban/Apixaban/ Edoxaban	Factor Xa inhibitor	8–14 h	Anti-FXa level	Andexanet alfa (specific)	Off-label PCC or aPCC if no antidote
Unfractionated heparin (UFH)	Potentiates antithrombin	1–2 h (IV)	aPTT/ACT	Protamine sulfate	Short half-life, easy to titrate
LMWH (*e.g.*, enoxaparin)	Factor Xa > IIa inhibition	4–7 h	Anti-FXa level	Partial reversal by protamine	Clearance depends on renal function
Bivalirudin	Direct thrombin inhibitor	25 min	aPTT	Dialysis may expedite clearance	Used in HIT, increases bleeding risk
Argatroban	Direct thrombin inhibitor	45 min	aPTT	No specific reversal, supportive care	Used in HIT, hepatic clearance
Fondaparinux	Factor Xa inhibitor	17–21 h	Anti-FXa level	No specific reversal, PCC/aPCC off-label	Prolonged half-life, complicates emergency management
Danaparoid	Inhibits factors Xa and IIa	24 h	Anti-FXa level	No specific reversal, FFP has limited efficacy	Used in HIT, bleeding risk with renal impairment
Aspirin	COX-1 inhibitor	7–10 d (platelet lifespan)	None	Platelet transfusion, DDAVP	Irreversible platelet inhibition
Clopidogrel	P2Y12 receptor inhibitor	3–5 d	None	Platelet transfusion, DDAVP	Irreversible inhibition, genetic variability in response
Prasugrel	P2Y12 receptor inhibitor	7–10 d	None	Platelet transfusion, DDAVP	Higher bleeding risk, irreversible inhibition
Ticagrelor	P2Y12 receptor inhibitor (reversible)	5–7 h	None	Platelet transfusion (partial reversal), DDAVP	Reversible inhibition, short half-life
Cangrelor	IV P2Y12 receptor inhibitor	3–6 min	None	Rapid clearance upon discontinuation	Ultra-short acting, used for bridging
Eptifibatide	GPIIb/IIIa inhibitor	2–4 h	None	Platelet transfusion	Short half-life, rapid onset
Abciximab	GPIIb/IIIa inhibitor	12–24 h	None	Platelet transfusion	Longer half-life, increased bleeding risk
Tirofiban	GPIIb/IIIa inhibitor	2–4 h	None	Platelet transfusion	Short-acting, used in acute coronary syndrome

COX-1: Cyclooxygenase-1; P2Y12: P2Y12 Adenosine Diphosphate Receptor (a platelet receptor targeted by antiplatelet drugs like clopidogrel); INR: International Normalized Ratio; TT: Thrombin Time; ECT: Ecarin Clotting Time; FXa: Factor Xa (activated Factor X in the coagulation cascade); aPTT: Activated Partial Thromboplastin Time; ACT: Activated Clotting Time; aPCC: Activated Prothrombin Complex Concentrate; FFP: Fresh Frozen Plasma; HIT: Heparin-Induced Thrombocytopenia; DDAVP: Desmopressin (1-deamino-8-D-arginine vasopressin).

5.2 Direct oral anticoagulants (DOACs)

DOACs—including direct thrombin inhibitors like dabigatran and factor Xa inhibitors such as rivaroxaban, apixaban and edoxaban—are preferred for their predictable pharmacokinetics and reduced need for routine monitoring [24]. However, they complicate perioperative bleeding management due to the

lack of universally available reversal agents [25].

Dabigatran can be reversed with idarucizumab, a monoclonal antibody that neutralizes its anticoagulant effects [24]. Factor Xa inhibitors can be reversed with andexanet alfa, a recombinant factor Xa decoy protein that binds to the inhibitors and prevents their anticoagulant effects. Andexanet alfa is primarily indicated for reversing the effects of rivaroxaban and apixaban, and also plays a role in managing edoxaban-related bleeding [22]. However, its use depends on DOAC blood levels, and it is contraindicated in patients requiring heparinization, such as those undergoing cardiac surgery with cardiopulmonary bypass (CPB).

In cases where specific reversal agents are unavailable, non-specific reversal agents such as activated prothrombin complex concentrate (aPCC) are recommended as an alternative for DOAC reversal. Additionally, prothrombin complex concentrate (PCC) can also be used, though its efficacy compared to aPCC remains under evaluation. Fresh frozen plasma (FFP) may also be considered, but it is generally less effective and carries higher risks [27].

Managing perioperative bleeding in patients on anticoagulant therapy requires a clear understanding of each drug's pharmacodynamics and available reversal strategies [28]. While warfarin has well-established reversal methods, newer DOACs present challenges due to limited specific agents [29]. Renal impairment, whether acute or chronic, significantly reduces dabigatran clearance, leading to elevated plasma concentrations and an increased bleeding risk, which necessitates vigilant dose adjustments and regular monitoring of renal function during treatment. However, recent advancements, including the availability of idarucizumab and andexanet alfa, have improved bleeding management [30, 31].

5.3 Indirect parenteral anticoagulants—heparins

Heparins, including unfractionated heparin (UFH) and low-molecular-weight heparin (LMWH), are widely used for prophylactic and therapeutic anticoagulation. UFH works by enhancing antithrombin III activity, which inactivates clotting factors such as thrombin and factor Xa [32]. LMWH, with its more predictable pharmacokinetic profile, primarily inhibits factor Xa. Because of its short half-life, UFH is easier to manage in urgent surgeries, and its effects can be reversed with protamine sulfate. In contrast, LMWH reversal is more challenging; protamine only partially neutralises its effects, so careful timing of the last dose is required—particularly given that LMWH clearance is significantly affected by renal function. Although protamine is the standard reversal agent, additional strategies, such as adsorption techniques, may help mitigate bleeding risks [32–34].

5.4 Non-heparin parenteral anticoagulants

Non-heparin parenteral anticoagulants—such as bivalirudin, argatroban, fondaparinux and danaparoid—are used in situations like heparin-induced thrombocytopenia (HIT) or when rapid anticoagulation is required [32, 35]. These agents increase bleeding risks during urgent surgeries. Bivalirudin and argatroban, which are direct thrombin inhibitors, impair clot formation and prolong activated partial thromboplastin time (aPTT), necessitating careful monitoring. In contrast, fondaparinux (a factor Xa inhibitor) has a prolonged half-life, complicating emergency management. Danaparoid, a glycosaminoglycan mixture that inhibits factors Xa and IIa, may be used in HIT patients, though bleeding risks remain—especially in those with renal impairment or when used in combination with other anticoagulants [32, 35].

Urgent surgical management typically involves cessation of the anticoagulant and supportive care. Bivalirudin and argatroban clear relatively quickly (with half-lives of approximately 25 and 45 minutes, respectively), while fondaparinux (17–22 hours) and danaparoid (approximately 24 hours) have slower clearance. Dialysis can expedite the clearance of bivalirudin but not argatroban. In cases of severe bleeding, off-label use of recombinant Factor VIIa (rFVIIa) or PCC/aPCC may be considered, though these carry thrombotic risks. Antifibrinolytics, such as tranexamic acid, help stabilize clots and reduce bleeding. Supportive care—including FFP, platelet transfusions and local bleeding control measures—is critical, although FFP is less effective for reversing danaparoid-induced coagulopathies. Frequent clinical and laboratory monitoring is essential to guide treatment [32, 36, 37].

5.5 Antiplatelet agents

Antiplatelet agents—including aspirin and P2Y12 inhibitors (P2Y12 Adenosine Diphosphate Receptor, a platelet receptor targeted by antiplatelet drugs like clopidogrel, prasugrel and ticagrelor)—are essential for preventing arterial thrombosis, yet they complicate surgical haemostasis. Aspirin irreversibly inhibits cyclooxygenase-1 (COX-1), reducing TXA_2 production, while P2Y12 inhibitors block ADP (Adenosine Diphosphate)-mediated platelet activation. Aspirin's effects last 7–10 days; clopidogrel and prasugrel also cause irreversible receptor inhibition, whereas ticagrelor, with its reversible mechanism and shorter half-life, is easier to manage in urgent settings [38].

In the perioperative setting, managing patients on antiplatelet therapy requires a delicate balance between minimizing bleeding risks and preventing thrombotic complications. For example, aspirin irreversibly inhibits cyclooxygenase-1, leading to reduced thromboxane A_2 production, and is typically held for 7–10 days before surgery when the bleeding risk is high. Similarly, irreversible P2Y12 inhibitors such as clopidogrel and prasugrel require discontinuation 5–7 days prior to a surgical procedure to allow for adequate recovery of platelet function. In contrast, ticagrelor, with its reversible binding and shorter half-life, may permit a shorter interruption period, which is particularly useful in urgent surgical scenarios. When delaying surgery is not feasible, additional strategies—such as preoperative platelet function testing, platelet transfusions, or the administration of adjuncts like desmopressin—can be considered to help restore hemostatic balance. Ultimately, the approach must be tailored to each patient's clinical situation, weighing the individual risks of bleeding against the potential for thrombotic events to ensure optimal perioperative outcomes [34].

In urgent surgery, delaying the procedure to allow drug clearance is ideal; if not feasible, platelet transfusions (sometimes combined with adjuncts like Desmopressin (1-deamino-8-D-arginine vasopressin) (DDAVP)) can help restore platelet function, although the benefit is limited with irreversible inhibitors [39].

6. Blood products and adjunct therapies

Blood products and adjunct therapies are essential in managing anticoagulant-induced bleeding [40–42] (Table 3):

- Fresh Frozen Plasma (FFP): Provides a broad spectrum of clotting factors but has a slower onset of action and risks such as fluid overload and transfusion-related complications.
- Prothrombin Complex Concentrates (PCCs): Offer rapid correction of coagulopathy with fewer complications and lower volume requirements compared to Fresh Frozen Plasma (FFP). PCCs contain the vitamin K–dependent coagulation factors II, VII, IX and X, as well as the natural anticoagulants protein C and protein S, making them particularly useful for immediate reversal of elevated INR in patients receiving vitamin K antagonists (*e.g.*, warfarin) who present with severe bleeding or require emergency surgery. PCCs are also useful for replacing multiple coagulation factors when FFP is unavailable or time-consuming to administer, and for off-label reversal of direct oral anticoagulants like apixaban and rivaroxaban in cases of severe bleeding or urgent interventions.
- Platelet Transfusions: Can help restore platelet function in patients on antiplatelet agents, though they are less effective for irreversible inhibitors unless combined with adjuncts like DDAVP.
- Tranexamic Acid (TXA): An antifibrinolytic that stabilises clots and reduces bleeding, though it may increase thrombotic risk in predisposed patients.
- Cryoprecipitate: This is derived from thawed fresh frozen plasma and is a pooled blood product containing fibrinogen, von Willebrand factor, factor VIII, factor XIII and fibronectin—thus offering a broader spectrum of clotting factors. While there can be variability in fibrinogen content, many transfusion medicine laboratories measure and report the exact fibrinogen concentration, allowing clinicians to order Cryoprecipitate by specifying the desired grams of fibrinogen. In modern practice, Cryoprecipitate can be prepared in a volume of approximately 250–300 mL to match the necessary fibrinogen dose without causing significant volume overload. Additionally, its content of factor XIII is crucial for stable clot formation.
- Fibrinogen concentrate: By comparison, it is a purified, lyophilized product that provides a standardized, precisely dosed supply of fibrinogen, facilitating rapid reconstitution and potentially reducing transfusion-related complications. This can be especially advantageous in critically ill patients who require timely, exact correction of hypofibrinogenemia. Both Cryoprecipitate and fibrinogen concentrate play important roles in managing fibrinogen deficiency, with the choice often guided by patient factors, laboratory availability and institutional protocols.

In life-threatening bleeding, off-label agents such as rFVIIa (NovoSeven) or factor XIII (which stabilises fibrin clots) may be used, though they carry thrombotic risks [43, 44]. In addition, cryoprecipitate (rich in fibrinogen, factor VIII, factor

TABLE 3. Blood products and adjunct therapies.

Product/Therapy	Indication	Pros	Cons/Cautions
FFP	Deficiency of multiple factors	Broad factor replacement	Large volume; transfusion risks
Platelets	Thrombocytopenia or platelet dysfunction	Rapid functional improvement	Ineffective if irreversible inhibitors remain
Cryoprecipitate	Low fibrinogen (<1.5 g/L)	Targeted fibrinogen replacement	Volume overload, infection risk
Fibrinogen Concentrate	Hypofibrinogenemia (<2.0 g/L)	Rapid correction, low volume	Cost/availability in some regions
TXA	Excessive fibrinolysis	Good evidence in trauma, cardiac	Thrombotic risk in susceptible pts
DDAVP	Mild hemophilia A, von Willebrand disease	Enhances platelet adhesion via vWF release	Thrombotic risk, tachyphylaxis with repeated use
PCC	Rapid correction of Vit K factors	Less volume *vs.* FFP	Potential prothrombotic risk
aPCC/FEIBA	Hemophilia with inhibitors	Bypasses missing clotting factors	High thrombotic risk, expensive
rFVIIa	Refractory bleeding (off-label)	Highly concentrated factor VII	Thrombotic risk, high cost, limited data
Factor XIII	Congenital Factor XIII deficiency	Stabilizes clot formation	Rare, limited availability, risk of allergic reactions

FFP: fresh frozen plasma; TXA: Tranexamic Acid; aPCC: Activated Prothrombin Complex Concentrate; DDAVP: Desmopressin (1-deamino-8-D-arginine vasopressin); FEIBA: Factor Eight Inhibitor Bypass Activity; vWF: von Willebrand factor.

XIII and vWF) is useful in massive transfusion protocols—which often employ fixed ratios (*e.g.*, 1:1:1 for red blood cells, plasma and platelets)—to preempt coagulopathy, especially in trauma or cardiovascular surgery.

7. Novel diagnostic tests in perioperative bleeding management

The management of perioperative bleeding is evolving rapidly with the development of new therapies and technologies designed to improve bleeding control, particularly in patients receiving anticoagulant therapy. These advances aim to enhance the precision of bleeding management and improve outcomes in high-risk surgeries. Point-of-care testing (POCT) provides clinicians with real-time information about a patient's coagulation status during surgery, enabling more precise and timely treatment decisions. Viscoelastic devices such as thromboelastography (TEG) and rotational thromboelastometry (ROTEM) assess the viscoelastic properties of blood, offering insights into clot formation, stabilization and dissolution. For example, ROTEM provides comprehensive information on the dynamics of clot formation, while TEG reports parameters such as R-time, K-time, α-angle and maximum amplitude (MA) to help target deficiencies in platelets, fibrinogen, or clotting factors for optimal transfusion therapy [44, 45].

Viscoelastic testing, performed by devices such as TEG and ROTEM, provides real-time insights into the dynamics of clot formation and stability. In TEG, R-time represents the time until the initial fibrin formation, serving as an indicator of clotting factor activity—prolonged R-time may suggest a deficiency. The maximum amplitude (MA) in TEG reflects the ultimate strength of the clot, primarily influenced by platelet function and fibrinogen levels; a lower MA can indicate issues such as platelet dysfunction or low fibrinogen. Similarly, in ROTEM, clotting time (CT) is the equivalent parameter to TEG's R-time, marking the period until clot initiation, while maximum clot firmness (MCF) corresponds to the overall clot strength, analogous to TEG's MA. ROTEM also includes specific assays: EXTEM uses tissue factor to activate the extrinsic coagulation pathway, and INTEM employs ellagic acid to stimulate the intrinsic pathway. These distinctions enable clinicians to better understand and manage coagulation abnormalities, tailoring interventions to the patient's specific needs [44, 45].

8. Novel treatment options in perioperative bleeding management

CytoSorb is an innovative hemoadsorption device that removes anticoagulants and other harmful substances from the bloodstream. This technology shows promise—particularly in patients undergoing cardiopulmonary bypass or other high-risk surgeries—by adsorbing drugs such as rivaroxaban and ticagrelor, thereby reducing plasma concentrations and mitigating bleeding risk [46, 47]. Studies have demonstrated that CytoSorb can significantly reduce plasma concentrations of anticoagulants like rivaroxaban and ticagrelor, resulting in fewer transfusions and reduced bleeding complications [48]. Experimental data also suggest that agents such as dabigatran, edoxaban, and ticagrelor can be effectively removed *in vitro*; however, larger randomised trials are needed to optimise protocols and assess cost-effectiveness [49–53]. Additional hemoadsorption technologies are under investigation for their ability to adsorb anticoagulants and antiplatelet medications during the perioperative period. These devices offer an alternative to traditional reversal strategies—such as specific antidotes or blood product transfusions—and may become critical tools for managing perioperative bleeding, particularly when specific reversal agents are unavailable or ineffective [53, 54].

The major advantage of these technologies is their ability to rapidly and effectively remove anticoagulants from the circulation, thereby reducing bleeding complications without relying solely on slower processes such as drug metabolism or antidote administration. However, many hemoadsorption devices remain in pilot phases or early clinical trials, and factors such as cost, availability, and the risk of excessive removal (which may promote thrombosis) must be carefully considered.

Recent evidence suggests that hemoadsorption devices, such as CytoSorb, can effectively reduce plasma concentrations of various anticoagulants—most notably rivaroxaban and ticagrelor—by adsorbing these agents from the bloodstream during high-risk surgical procedures like cardiopulmonary bypass. This reduction in drug levels may translate into a decreased risk of perioperative bleeding and a lower need for transfusions. Preliminary studies have also indicated potential for removing other anticoagulants, including dabigatran and edoxaban, though much of this data comes from *in vitro* experiments or small-scale clinical trials. Despite these promising findings, larger randomized controlled studies are required to confirm their clinical efficacy, determine optimal usage protocols, and evaluate cost-effectiveness before hemoadsorption devices can be widely adopted in clinical practice [50–54].

9. Our experiences with novel techniques

The use of hemoadsorption devices has attracted considerable attention in recent years, particularly for managing complex cases requiring CPB. Among these devices, Cytosorb has shown promise in removing excess anticoagulants and antithrombotic agents in situations where precise control of blood coagulation is paramount. Early experience in our center has been encouraging, and we are now organizing a formal study to further investigate the effectiveness and safety of Cytosorb in this context.

The study aims to: assess perioperative bleeding rates, transfusion requirements and short-term outcomes; evaluate any device-related complications or adverse events; and, optimize protocols for integrating the Cytosorb cartridge into standard CPB circuits.

We anticipate that this investigation will help delineate best practices, including patient selection criteria, dosing adjustments for anticoagulants, and standardized timelines for cartridge use. Furthermore, long-term follow-up data will clarify whether the benefits of intraoperative adsorption translate to

faster postoperative recovery and decreased healthcare costs.

10. Challenges and future directions

Managing drug-induced haemostatic disorders remains complex. The limited availability and high costs of specific reversal agents (such as idarucizumab and andexanet alfa) restrict their use. Further research is needed to develop affordable alternatives and to establish standardised protocols for reversal timing and blood product utilisation. Long-term studies should also assess the impact of perioperative bleeding on outcomes such as infection risk and wound healing.

Emerging interest in universal reversal agents that target multiple anticoagulants may simplify management, and the development of shorter-acting anticoagulants with predictable pharmacokinetics could reduce reliance on reversal strategies, thereby improving safety in both elective and emergency surgical settings.

11. Limitations

Our review aimed to comprehensively cover current knowledge and emerging approaches to perioperative bleeding, but it has several limitations. First, our literature search was confined to English-language studies from 2014–2024, possibly overlooking relevant findings published outside these constraints. Second, we did not conduct a formal meta-analysis, relying on narrative synthesis and expert consensus, which may affect the strength of our recommendations. Third, the cited studies were heterogeneous in design, populations and surgical settings, complicating direct comparisons and limiting generalizability. Fourth, because the field of anticoagulation therapy and related technologies evolves rapidly, certain off-label uses may quickly become outdated. Fifth, many novel therapies, such as hemoadsorption devices, have limited real-world data and short follow-up durations. Sixth, the predominance of research from high-income settings restricts applicability to regions with different resources and patient demographics. Finally, although we underscore personalized strategies, we could not address all patient-specific factors, emphasizing the need for multidisciplinary evaluation and further large-scale research to validate and refine these emerging approaches.

12. Conclusions

Perioperative bleeding management is a multifaceted challenge that requires careful consideration of a patient's medical history, coagulation status and current medications. The advent of newer anticoagulants and the rising incidence of bleeding disorders necessitate the development of more targeted, personalised approaches. Modern diagnostic systems—including point-of-care testing—along with innovative hemoadsorption therapies (such as Cytosorb) and other novel technologies, show great potential for improving outcomes by enabling more precise and effective management of bleeding risks.

ABBREVIATIONS

ADP, Adenosine Diphosphate; aPCC, activated Prothrombin Complex Concentrate; aPTT, activated Partial Thromboplastin Time; APS, Antiphospholipid Syndrome; aVWD, acquired von Willebrand disease; CKD, Chronic Kidney Disease; COX-1, cyclooxygenase-1; CPB, Cardiopulmonary Bypass; DDAVP, Desmopressin; DOACs, Direct Oral Anticoagulants; FFP, Fresh Frozen Plasma; FVIIa, activated Factor VII; FX, Factor X; HIT, Heparin-Induced Thrombocytopenia; LMWH, Low-Molecular-Weight Heparin; MA, Maximum Amplitude; MCF, Maximum Clot Firmness; P2Y12, Platelet ADP Receptor; PCCs, Prothrombin Complex Concentrates; POCT, Point-of-Care Testing; RBC, Red Blood Cell; rFVIIa, recombinant Factor VIIa; ROTEM, Rotational Thromboelastometry; STAR, Safe and Timely Antithrombotic Removal; TEG, Thromboelastography; TF, Tissue Factor; TFPI, Tissue Factor Pathway Inhibitor; TXA, Tranexamic Acid; TXA_2, Thromboxane A_2; UFH, Unfractionated Heparin; VKA, Vitamin K Antagonist; vWD, von Willebrand Disease; vWF, von Willebrand Factor; CT, clotting time; ISTH, International Society on Thrombosis and Haemostasis; EACTS, European Association for Cardio-Thoracic Surgery; EACTAIC, European Association of Cardiothoracic Anaesthesiology and Intensive Care; EBCP, European Board of Cardiovascular Perfusion; STS, Society of Thoracic Surgeons; SCA, Society of Cardiovascular Anesthesiologists; AmSECT, American Society of ExtraCorporeal Technology; SABM, Society for the Advancement of Blood Management.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

AUTHOR CONTRIBUTIONS

GTŠ and IP—conceived and designed the review, collected and analyzed the literature, and wrote the manuscript. GTŠ and IP—contributed equally to all aspects of the work and share first authorship. Both authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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CONFLICT OF INTEREST

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