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Editorial

Perioperative Management of Patients on Direct Oral Anticoagulants (DOACs): Challenges and Strategies

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Introduction

In recent years, the use of direct oral anticoagulants (DOACs) has increased substantially owing to their efficacy in preventing and treating thromboembolic disorders such as atrial fibrillation (AF) and venous thromboembolism (VTE). These agents-including apixaban, rivaroxaban, dabigatran, and edoxaban-have become the preferred alternatives to traditional anticoagulants like warfarin because of their convenience, fixed dosing regimens, and minimal need for routine monitoring (1). Nevertheless, the widespread adoption of DOACs presents significant challenges during the perioperative period, particularly in elective surgical procedures. Surgeons, anaesthesiologists, and other healthcare professionals must possess a thorough understanding of the pharmacological properties of these medications and their implications for perioperative care. Effective preoperative management is critical to reducing the risks of both bleeding complications and thromboembolic events. Given the rising number of patients receiving these agents, it is imperative that surgical teams are adequately prepared with the necessary knowledge and strategies to ensure safe perioperative management.

Direct Oral Anticoagulants (DOACs) constitute a class of agents that directly inhibit specific factors within the coagulation cascade to prevent thrombus formation. In contrast to traditional vitamin K antagonists such as warfarin, DOACs do not necessitate routine monitoring of coagulation parameters (e.g., the INR) and exhibit fewer food and drug interactions. These characteristics make them an appealing choice for patients requiring long-term anticoagulation.

The pharmacology of DOACs centres on their direct inhibition of key proteins involved in coagulation, notably Factor Xa or thrombin (Factor IIa). Their mechanism of action is therefore distinct and more predictable than that of conventional anticoagulants (2).

Apixaban is a direct inhibitor of Factor Xa. Through this inhibition, it prevents the conversion of prothrombin to thrombin, thereby reducing thrombus formation. The drug demonstrates high oral bioavailability (approximately 50%) and achieves peak plasma concentration within 3–4 hours of administration. It is primarily metabolised in the liver via the CYP3A4 enzyme, with minor contributions from CYP1A2 and P-glycoprotein. Apixaban has a relatively short elimination half-life of about 12 hours, necessitating twice-daily dosing. Approximately 27% of the compound is excreted renally, with the remainder eliminated through the faeces (3).

Rivaroxaban, like apixaban, is a direct inhibitor of Factor Xa, exerting its anticoagulant effect by preventing Factor Xa from activating thrombin and thereby propagating the coagulation process. When taken with food, rivaroxaban exhibits high oral bioavailability (approximately 80%) and attains peak plasma concentration within 2–4 hours of ingestion. It is primarily metabolised in the liver via the CYP3A4 enzyme, with partial involvement of CYP2J2.

The drug's elimination half-life ranges from 5 to 9 hours, depending on the administered dose, and it is generally taken once daily. Approximately 66% of

rivaroxaban is excreted renally, with the remainder eliminated through the faeces (4).

Dabigatran is a direct inhibitor of thrombin (Factor IIa). By blocking thrombin activity, it prevents the conversion of fibrinogen to fibrin and the activation of platelets—both essential processes in thrombus formation. Dabigatran exhibits poor absorption within the gastrointestinal tract, with only 3–7% of an oral dose reaching systemic circulation. It undergoes minimal metabolism via the CYP3A4 enzyme and is predominantly excreted unchanged in the urine. The drug possesses a relatively long elimination half-life of approximately 12–17 hours, necessitating twice-daily administration. The majority of dabigatran (around 80%) is excreted renally in unchanged form (5).

Edoxaban, like apixaban and rivaroxaban, is a direct inhibitor of Factor Xa. By blocking Factor Xa activity, it prevents the conversion of prothrombin to thrombin and thereby inhibits blood clot formation. Edoxaban demonstrates an oral bioavailability of approximately 62% and is minimally metabolised in the liver via the CYP3A4 enzyme, while also serving as a substrate for P-glycoprotein. The drug has an elimination half-life of around 10–14 hours, permitting once-daily dosing. Approximately 50% of edoxaban is excreted renally in unchanged form, with the remainder eliminated through the faeces (6).

Direct Oral Anticoagulants (DOACs) are highly effective in reducing the risk of stroke in patients with atrial fibrillation (AF), as well as in preventing venous thromboembolism (VTE) and treating deep vein thrombosis (DVT) and pulmonary embolism (PE). Their direct action on specific coagulation factors results in a rapid onset and offset of anticoagulation. Overall, the safety profile of DOACs is favourable compared with traditional agents such as warfarin, particularly with respect to their markedly lower incidence of intracranial haemorrhage. Nevertheless, DOACs still carry a risk of major bleeding, especially among patients with renal impairment, advanced age, or concurrent use of other drugs that influence coagulation. A notable limitation remains the limited availability of reversal agents. However, progress has been made: idarucizumab is approved for reversing dabigatran, while andexanet alfa has been developed to reverse rivaroxaban and apixaban, although it is not yet universally accessible. Ongoing research is exploring the development of universal reversal agents, such as ciraparantag. As many DOACs are renally excreted—particularly dabigatran and edoxaban—impaired renal function can substantially alter drug concentrations and heighten bleeding risk. In such cases, dose adjustment or the consideration of alternative anticoagulation strategies may be necessary (7).

One of the principal challenges in managing surgical procedures for patients receiving DOACs or NOACs lies in determining the optimal timing for discontinuing the medication. Premature cessation can elevate the risk of thromboembolism, whereas delayed discontinuation may lead to excessive or uncontrolled bleeding. For surgeries associated with a low risk of bleeding, it is generally recommended that DOACs or NOACs be withheld 24 hours before the procedure. However, for agents such as dabigatran—owing to its longer half-life—discontinuation should occur approximately 48 hours in advance. In operations with a high bleeding risk, the interruption interval may need to be further extended. Moreover, patients with renal impairment require individualised adjustment of discontinuation timing, as these drugs are predominantly cleared through the kidneys and may therefore accumulate, heightening the risk of perioperative bleeding (8).

Managing bleeding in patients taking DOACs or NOACs presents a considerable clinical challenge. These agents may increase the risk of uncontrolled haemorrhage during surgery, thereby necessitating specific intraoperative measures to achieve haemostasis.

In major or complex procedures, severe bleeding can occur, requiring the use of targeted techniques such as haemostatic agents or the application of direct pressure to control blood loss. In cases of life-threatening bleeding, reversal agents such as andexanet alfa or idarucizumab may be administered to counteract the anticoagulant effects of DOACs or NOACs. Following surgery, patients should be closely monitored to detect and manage any ongoing haemorrhage. If bleeding persists despite conventional measures, adjunctive therapies such as platelet-rich

plasma or procoagulant factor concentrates may be warranted (9).

Another important challenge involves determining the appropriate timing and method for reinitiating anticoagulation therapy following surgery. Premature resumption may increase the risk of postoperative haemorrhage, whereas excessive delay can heighten the likelihood of thromboembolic events. Anticoagulant therapy should therefore be resumed only once adequate haemostasis has been achieved and the patient's condition is stabilised. In most cases, anticoagulation may be reinitiated within 6 to 12 hours after surgery; however, in patients at high risk of significant bleeding, resumption should be postponed until the bleeding risk has subsided.

In patients at high risk of thromboembolism receiving DOACs or NOACs, bridging therapy with low molecular weight heparin (LMWH) or unfractionated heparin may be indicated. These agents help mitigate the risk of thromboembolic complications in the perioperative period, both before and after surgery. Bridging therapy is generally unnecessary for procedures with a low bleeding risk, where temporary discontinuation of DOACs for approximately 24 hours is typically sufficient. However, in surgeries associated with a high risk of bleeding, the use of LMWH or unfractionated heparin as bridging therapy may be warranted to prevent thromboembolic events (10). Prior to surgery, it is crucial for clinicians to evaluate each patient's individual risk of bleeding and thromboembolism through validated risk assessment models. Such evaluation informs key perioperative decisions, including the optimal timing for discontinuation of anticoagulant therapy, the potential need for bridging, and the appropriate point at which to resume anticoagulation postoperatively. In the event of bleeding, reversal agents such as idarucizumab (for dabigatran) and andexanet alfa (for rivaroxaban and apixaban) may be employed. These specific agents rapidly counteract the anticoagulant effects of DOACs and NOACs, thereby reducing the likelihood of severe perioperative haemorrhage.

Renal function should be carefully assessed prior to surgery to ensure that the appropriate dose of DOACs or NOACs is administered. In patients with impaired renal function, dose adjustment or alternative management strategies may be required to minimise the risks of both bleeding and thromboembolism (11).

Close collaboration between the surgeon, anaesthesiologist, and pharmacological specialists is vital in determining the optimal approach for discontinuing anticoagulant therapy and subsequently reinitiating it. Such multidisciplinary coordination is also crucial to maintain adequate haemostatic control throughout the intraoperative and postoperative periods.

Before discontinuing any DOAC or NOAC, clinicians should review the original indication for anticoagulation. If the underlying condition continues to present a significant thromboembolic risk-such as in atrial fibrillation or a history of venous thromboembolism-careful deliberation is warranted prior to interrupting therapy. Where necessary, consultation with appropriate specialists, including cardiologists or haematologists, should be undertaken to evaluate the relative risks and benefits of continuing versus pausing anticoagulation. Coordinated, specialist-guided decision-making ensures the safe and effective management of anticoagulation during the perioperative phase.

References

1. Amaraneni A, Chippa V, Goldin J, Rettew AC. Anticoagulation Safety. StatPearls. Treasure Island (FL) 2025.

2. Julia S, James U. Direct Oral Anticoagulants: A Quick Guide. Eur Cardiol. 2017; 12(1): 40-5.

3. Agrawal A, Manna B. Apixaban. StatPearls. Treasure Island (FL) 2025.

4. Singh R, Emmady PD. Rivaroxaban. StatPearls. Treasure Island (FL) 2025.

5. Ganetsky M, Babu KM, Salhanick SD, Brown RS, Boyer EW. Dabigatran: review of pharmacology and management of bleeding complications of this novel oral anticoagulant. J Med Toxicol. 2011; 7(4): 281-7.

6. Stacy ZA, Call WB, Hartmann AP, Peters GL, Richter SK. Edoxaban: A Comprehensive Review of the Pharmacology and Clinical Data for the Management of Atrial Fibrillation and Venous Thromboembolism. Cardiol Ther. 2016; 5(1):

1-18.
7. Tran HA, Merriman E, Baker R, Curnow J, Young L, Tan CW, et al. 2025 Guidelines for direct oral anticoagulants: a practical guidance on the prescription, laboratory testing, peri-operative and bleeding management. Intern Med J. 2025; 55(7): 1174-83.
8. Polania Gutierrez JJ, Rocuts KR. Perioperative Anticoagulation Management. StatPearls. Treasure Island (FL) 2025.
9. Ruff CT, Giugliano RP, Antman EM. Management of Bleeding With Non-Vitamin K Antagonist Oral Anticoagulants in the Era of Specific Reversal Agents. Circulation. 2016; 134(3): 248-61.
10. 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. J Thromb Haemost. 2016; 14(5): 875-85.
11. Dubois V, Dincq AS, Douxfils J, Ickx B, Samama CM, Dogne JM, et al. Perioperative management of patients on direct oral anticoagulants. Thromb J. 2017; 15: 14.