Perioperative Management of the Direct Oral Anticoagulants: A Case-Based Review

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KEYWORDS

• Direct oral anticoagulants • Perioperative management • Algorithm • Thrombosis

KEY POINTS

- Not all procedures require anticoagulants to be held (eg, minor dental and skin procedures, cataract extraction, selected cardiac device implantation).
- Bridging anticoagulation does not seem to mitigate the risk for perioperative thromboembolism, but is associated with an increase in major bleeding; consequently, bridging anticoagulation is not routinely recommended for DOAC-treated patients during treatment interruption for an elective surgery/procedure.
- DOACs should be held for 1 to 4 days preprocedure, with the interruption interval depending on the DOAC, patient renal function, and surgery/procedure bleeding risk.
- Postoperative resumption of DOACs should take into account their rapid onset of action (1–3 hours postingestion), and can be restarted approximately 24 hours after low-bleed-risk and 48 to 72 hours after high-bleed-risk procedures.
- With urgent surgery, there is no evidence for more bleeding among DOAC-treated compared with warfarin-treated patients.

INTRODUCTION

There are an estimated 33.5 million people worldwide with atrial fibrillation (AF), and an additional 5 million cases are diagnosed annually.[1] Because AF is more common among the elderly, the North American incidence is expected to rise as the population ages.[2] Most patients with AF should receive an oral anticoagulant to prevent stroke, and practice guidelines recommend the direct oral anticoagulants (DOACs) in preference to warfarin.[3,4]

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Approximately 10% of patients on anticoagulants require treatment interruption annually for a surgery or invasive procedure.[5] It is important that such treatment interruptions balance the procedure-related bleeding risk against the patient's thrombotic risk. Thus, excess bleeding may occur if an anticoagulant is not interrupted soon enough or restarted too quickly postprocedure[6]; conversely, extended interruption of anticoagulants may expose patients to an increased risk for thrombotic complications.[7] Of concern, observational studies have shown that periprocedural management of anticoagulants is variable and often not in keeping with guideline recommendations.[8]

Clinical guidelines are available for the periprocedural management of warfarin (and other vitamin K antagonists) but are lacking for patients who are receiving DOACs, which comprise dabigatran, rivaroxaban, apixaban, and edoxaban.[9] There are key differences between the DOACs and warfarin related to elimination half-life (10–14 hours for DOACs vs 38–42 hours for warfarin), dependence on renal elimination (25%–75% renal clearance for DOACs vs nonrenal clearance for warfarin), and peak action after oral intake (1–3 hours for DOACs vs 4–6 days for warfarin), which necessitate different periprocedural management approaches.

Using a case-based approach, this article provides practical clinical guidance for the periprocedural management of patients who are receiving a DOAC and require an elective or urgent surgery/procedure. Current practice recommendations are based on low-quality evidence derived mainly from DOAC pharmacokinetic data (**Table 1**), retrospective studies, and patient registries.[10] However, there are emerging prospective studies assessing the safety of standardized periprocedural DOAC management protocols, including the one recommended in this text.[11] In addition, the PAUSE trial (NCT02228798) will assess standardized, DOAC-specific management protocols in approximately 3000 patients who are receiving a DOAC.

CASE 1: MINIMAL-BLEED-RISK PROCEDURE

A 78-year-old woman with AF, hypertension, mildly impaired left ventricular function, and a transient ischemic attack 7 months ago is scheduled to have multiple teeth extracted. Her estimated creatinine clearance is 56 mL/min. She takes rivaroxaban, 20 mg daily with breakfast, for stroke prevention. Her dentist asks you if the rivaroxaban can be continued through the procedure.

When considering withholding anticoagulants, one should balance the risk of bleeding associated with a procedure and the patient's risk for thromboembolic complications while off anticoagulants. Patients' risk for procedure-related bleeding is stratified as minimal, low, and high bleed risk based on observed bleeding rates postoperatively for patients not on anticoagulants (**Table 2**).[5] Neuraxial blocks or anesthesia are somewhat unique procedures because they are associated with a low

Table 1
Pharmacologic characteristics of the DOACs

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Target	Factor IIa (Thrombin)	Factor Xa	Factor Xa	Factor Xa
Dosing (atrial fibrillation)	150 mg bid[a]	20 mg daily[b]	5 mg bid[c]	60 mg daily[d]
Cmax	1–2 h	2–4 h	3–4 h	1–2 h

[a] 110 mg bid if older than age 80 or if additional risk factors for bleeding.
[b] 15 mg od if creatinine clearance 30 to 50.
[c] 2.5 mg bid if two of the following: age greater than 80, serum creatinine greater than 133, weight less than 60 kg.
[d] 30 mg daily if creatinine clearance 30 to 50 or weight less than 60 kg.