

# Periprocedural Anticoagulation

**M**anagement of patients taking anticoagulants around the time of a procedure is a common and complex clinical scenario.

Providing evidence-based care requires estimation of risk for thrombosis and bleeding, knowledge of commonly used medications, multidisciplinary communication and collaboration, and patient engagement and education. This review provides a standardized, evidence-based approach to periprocedural management of anticoagulation, based on current evidence and expert clinical guidelines.

CME/MOC activity available at [Annals.org](https://annals.org).

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doi:10.7326/AITC202304180

This article was published at [Annals.org](https://annals.org) on 11 April 2023.

**CME Objective:** To review current evidence for pharmacology, clinical evaluation, periprocedural management, consultation, follow-up, and practice improvement of periprocedural anticoagulation.

**Funding Source:** American College of Physicians.

**Disclosures:** All relevant financial relationships have been mitigated. Disclosures can also be viewed at [www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M22-2614](https://www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M22-2614).

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Pharmacology

Clinical Evaluation

Periprocedural Management

Consultation and Follow-up

Practice Improvement

An estimated 6 million people in the United States take anticoagulants, and clinicians are likely to encounter situations where they need to weigh the risks and benefits to patients of temporarily stopping use of anticoagulants for invasive procedures. The periprocedural period is complex for clinicians and patients alike. The landscape of anticoagulant management continues to evolve, most notably with the widespread adoption of direct oral anticoagulants (DOACs). In addition, bridging anticoagulation—the use of shorter-acting parenteral anticoagulants when oral anticoagulants are held—has been falling out of favor due to newer evidence suggesting limited benefit (1, 2). Navigating the safest periprocedural anticoagulation plan thus requires understanding an individual patient's risks for bleeding and thrombosis, pharmacokinetics of individual anticoagulants, and details of the procedure as well as appropriate counseling of patients. A standardized and evidence-based approach to management is essential to prevent adverse events. In this article, we review periprocedural management of anticoagulants; we will not review management of other antithrombotic agents, such as

antiplatelets, which have separate indications and recommendations. Our recommendations incorporate the 2022 American College of Chest Physicians (CHEST) updated guidelines for perioperative management of antithrombotic therapy along with other international society guidelines (3).

### What is the prevalence of antithrombotic use in patients undergoing procedures?

More than 6 million Americans take anticoagulants to treat or prevent thrombosis associated with conditions such as atrial fibrillation (AF), venous thromboembolism (VTE), or mechanical heart valves (4). DOACs, which include a direct thrombin inhibitor (dabigatran) and factor Xa inhibitors (rivaroxaban, apixaban, edoxaban), are becoming the most frequently prescribed new anticoagulants, but vitamin K antagonists (VKAs), most commonly warfarin, remain the most prevalent anticoagulant in the United States (2, 5). Each year, at least 250 000 people taking anticoagulants need to temporarily interrupt use of their medication for an invasive procedure (4).

## Pharmacology

### What anticoagulants are commonly encountered in the periprocedural setting, and what is their duration of action?

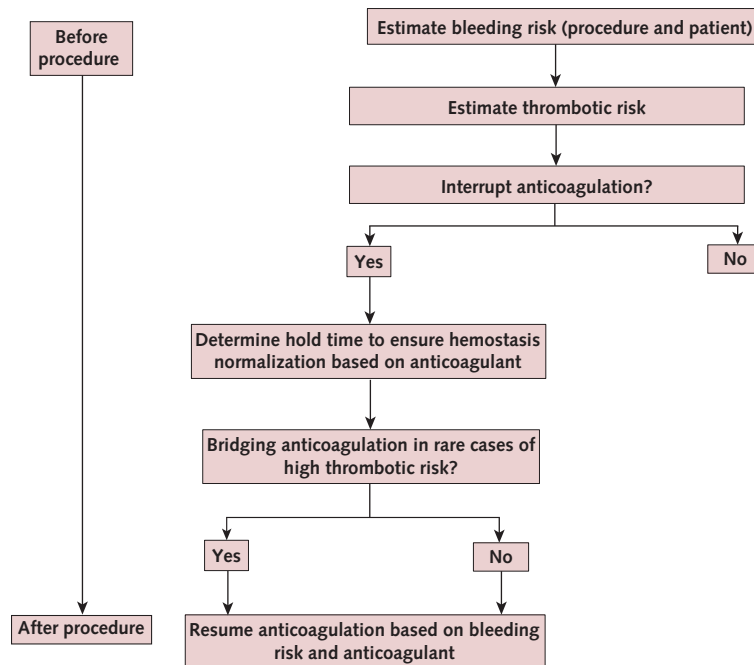
Understanding the mechanism and duration of action of anticoagulants will help clinicians know when to interrupt or resume therapy. Three major categories of anticoagulants are summarized in **Appendix Table 1** (available at [Annals.org](https://annals.org)): VKAs, DOACs, and heparins (low-molecular-weight heparin [LMWH], unfractionated heparin [UFH], and fondaparinux). **Appendix Table 1** summarizes how individual medications differ by mechanism and onset of action, half-life, route of elimination, and reversal strategies and the implications of these differences for periprocedural management.

### How should clinicians approach periprocedural management of anticoagulation?

The key steps in the periprocedural evaluation of anticoagulation are as follows (**Figure**). First, clinicians should evaluate bleeding risk for the procedure and the patient. Next, the patient's risk for thrombosis should be assessed. If interruption of anticoagulation is warranted, a periprocedural plan to ensure normalization of hemostasis should be created, based on whether the patient is taking a VKA or a DOAC. Bridging should be used sparingly and only in select circumstances. Finally, a postoperative plan for resumption of therapeutic anticoagulation should be developed.

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Figure. Key steps in the evaluation of periprocedural anticoagulation.



### What is the risk for bleeding with periprocedural anticoagulation?

The first step in periprocedural management is evaluation of the procedure's bleeding risk. This will inform whether antithrombotic therapy needs to be stopped and, if so, for how long. However, estimates of periprocedural bleeding risk are derived from observational studies or expert opinion and are imprecise (7). In general, periprocedural bleeding risk is driven by procedural factors, such as site or length of the procedure, although patient characteristics, choice of anesthetic (for example, neuraxial anesthesia), and other aspects may play a role. To guide clinicians, a 3-tier classification system dividing procedures into minimal, low to moderate, and high bleeding risk at 30 days has been proposed (Table 1) (7). About 20% of patients assessed for perioperative management of anticoagulation in the United States and Canada are scheduled to undergo procedures that are considered to carry minimal risk, where data suggest that bleeding rates are very low, even when the procedure

is done while the patient is receiving anticoagulation (4, 9, 10). Minimal-risk procedures, including most dental, dermatologic, cardiac device, and endoscopic procedures as well as arthrocentesis and electroconvulsive therapy, can safely be performed without stopping anticoagulation. The decision to proceed while the patient is receiving anticoagulation should be made with the proceduralist, and additional options can be considered if there is concern about bleeding. These include allowing the international normalized ratio (INR) to become subtherapeutic without complete reversal of a VKA or skipping 1 or 2 doses of a DOAC before the procedure.

Procedures with greater than minimal risk but less than a 2% risk for postprocedural major bleeding, such as intra-abdominal surgery or coronary angiography, are low- to moderate-risk procedures. High-risk procedures (such as vascular surgery or neurosurgery) are associated with bleeding rates greater than 2% (11, 12). Anticoagulation should be interrupted for procedures that have more than minimal bleeding risk.

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**Table 1. Stratification of Bleeding Risk Associated With Procedures\***

<i>Risk Category</i>	<i>30-Day Risk for Major Bleeding</i>	<i>Type of Surgery or Procedure</i>	<i>Recommendation</i>
High	>2%	Cardiac surgery (heart valve replacement, CABG) Vascular surgery (AAA repair, peripheral artery bypass) Neurosurgery (intracranial or spinal) Urologic surgery (renal, prostate, or bladder) Major cancer surgery Reconstructive plastic surgery Colonoscopy with polypectomy† Major orthopedic surgery (e.g., total hip or knee replacement)	Stop anticoagulation
Low/moderate	0%-2%	Major intra-abdominal surgery (e.g., colectomy, hysterectomy) Major intrathoracic surgery (e.g., lobectomy, esophagectomy) Transfemoral or transradial coronary angiography Most common cutaneous procedures Laparoscopic cholecystectomy or ventral/inguinal hernia repair	Stop anticoagulation
Minimal	~0%	Endoscopy or colonoscopy without polypectomy Pacemaker and AICD placement Minor dental procedures Minor dermatologic procedures (excision of basal and squamous cell carcinomas, actinic keratosis, malignant or premalignant nevi) Cataract removal Electroconvulsive therapy Arthrocentesis	May not require interruption of anticoagulation

AAA = abdominal aortic aneurysm; AICD = automatic implantable cardioverter-defibrillator; CABG = coronary artery bypass grafting.

\* Data are from references 7 and 8.

† Anticoagulation can be continued if no polypectomy is anticipated.

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Because anticoagulation must be held for most invasive procedures, assessment of bleeding risk should be followed by estimation of the risk for thrombosis without anticoagulation. This guides whether bridging therapy should be considered and informs the necessary discussion with patients. Consensus guidelines for thromboembolic risk stratification are available for patients with a mechanical heart valve, chronic AF, or VTE (4, 8, 13, 14).

### **What is the risk for thrombosis in patients with mechanical heart valves?**

For mechanical heart valves, the risk for arterial thromboembolism (ATE) in the form of ischemic stroke hinges on 3 factors: valve type, valve position, and time since valve placement (Table 2). Older caged-ball and tilting-disk valve models have higher thrombosis rates than newer bileaflet models (2.5%,

0.7%, and 0.5% per year, respectively). Mechanical valves in the mitral position are associated with higher risk for thrombosis (22% per year without anticoagulation) than those in the aortic position (12% per year without anticoagulation). Valves placed within the previous 3 months carry the highest risk for thrombosis; valves placed within 1 year also carry higher risk for ATE (17). Other factors that increase ATE risk include the presence of additional cardiac comorbidities (AF, left ventricular dysfunction), prior ATE, hypercoagulable disorder, pregnancy, and older age; a valve placed within 1 year or the presence of any of these additional prothrombotic conditions should prompt consultation with a cardiologist. The 2022 CHEST guidance update similarly recommends against bridging except in patients at high risk for thromboembolism (those with older-generation valves,

**Table 2. Stratification of ATE Risk Associated With Mechanical Heart Valves\***

<i>Risk Factor</i>	<i>Risk for ATE Without Anticoagulation</i>
<b>Type of valve</b>	
Caged-ball	2.5% per year
Tilting-disk	0.7% per year
Bileaflet	0.5% per year
<b>Position of valve</b>	
Mitral	22% per year
Aortic	12% per year
<b>Time since placement</b>	
<3 mo	Highest risk
<1 y	High risk
>1 y	Usual risk
<b>Other factors</b>	
Atrial fibrillation	—
Older age	—
Prior ATE	—
Left ventricular dysfunction	—
Left atrial enlargement	—
Hypercoagulable disorder	—
Pregnancy	—

ATE = arterial thromboembolism.

\* Data are from references 15 and 16.

mitral valves and  $\geq 1$  risk factor, a recent thromboembolic event, or prior perioperative thromboembolism) (3).

### What is the risk for thrombosis in patients with AF?

AF increases risk for thromboembolic stroke, but risk varies on the basis of patient-level factors. The CHA<sub>2</sub>DS<sub>2</sub>-VASc score is used to estimate the risk for stroke (Appendix Table 2, available at [Annals.org](https://annals.org)) (18). Guidelines recommend that patients with CHA<sub>2</sub>DS<sub>2</sub>-VASc scores of 2 or higher receive long-term anticoagulation, based on randomized controlled trials showing benefits of warfarin and DOACs in preventing stroke (19, 20). Stroke within the previous month and rheumatic heart disease also increase risk for ATE. A central tenet of periprocedural management of anticoagulation in patients with AF is that although the annual risk for ATE may be significant, the day-to-day risk is low when

anticoagulation is interrupted. The 2017 American College of Cardiology guidelines suggest that patients with an estimated annual ATE risk greater than 10% (CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $\geq 7$ ) should be considered to be at high risk for thrombosis with periprocedural interruption of anticoagulation. In these patients, bridging should be considered (8). Patients with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 5 to 6 and a history of thromboembolism are often included in the high-risk group (8). Patients with annual ATE risk between 5% and 10% (CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 4 to 6) are considered to be at moderate risk, and in these patients, bridging can be considered on an individual basis (8). Patients with annual ATE risk less than 5% (CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $\leq 3$ ) are considered to be at low risk and should not receive bridging therapy (8). Subsequent guidance from the American College of Chest Physicians in 2018 and 2022 and from the American Heart Association, the American College of Cardiology, and the Heart Rhythm Society in 2019 is concordant with these recommendations (3, 19, 20).

### What is the risk for recurrent thrombosis in patients with VTE?

When considering interruption of anticoagulation for a procedure in a patient who is receiving anticoagulation for treatment or secondary prevention of deep venous thrombosis (DVT) or pulmonary embolism, clinicians should consider the risk for VTE after discontinuation of therapy. This depends on the recency of the VTE event, triggers for the initial event, and the presence or absence of prothrombotic conditions (Table 3). An important paradigm when evaluating perioperative management of anticoagulation is that the risk for recurrent VTE decreases over time, from 40% one month after the event to 10% in months 2 and 3 and between 3% and 10% annually thereafter (21). Recurrence of VTE is also driven by risk factors that were present at the time of the initial event. In a systematic review of 15 studies of 5159 patients, risk for recurrence at 24 months was 7.4% for

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**Table 3. Stratification of Risk for Recurrent VTE\***

High Risk	Moderate Risk	Low Risk
<ul style="list-style-type: none"> <li>• VTE within past 3 mo</li> <li>• Deficiency of protein C, protein S, or antithrombin</li> <li>• Antiphospholipid antibody syndrome</li> <li>• Multiple thrombophilic abnormalities</li> </ul>	<ul style="list-style-type: none"> <li>• VTE within past 3–12 mo</li> <li>• Heterozygous factor V Leiden</li> <li>• Prothrombin 20210 mutation</li> <li>• Recurrent VTE</li> <li>• Active cancer</li> </ul>	<ul style="list-style-type: none"> <li>• VTE &gt;12 mo previously</li> <li>• No other risk factors</li> </ul>

VTE = venous thromboembolism.

\* Reproduced from Blood Advances, vol. 2, Witt DM, Nieuwlaat R, Clark NP, et al, American Society of Hematology 2018 guidelines for management of venous thromboembolism: optimal management of anticoagulation therapy, pp. 3257–91, copyright 2018, with permission from Elsevier.

VTE that occurred in the absence of any identifiable risk factor (“unprovoked VTE”), 4.2% for VTE provoked by a non-surgical transient risk factor (for example, hospitalization or trauma), and 0.7% for VTE provoked by surgery (22). The presence of an inherited or acquired thrombophilia that could be associated with a higher risk for recurrence of VTE, such as antiphospholipid syndrome or

protein C, protein S, or antithrombin deficiency, may inform periprocedural management of anticoagulation (23, 24). Active cancer and recurrent VTE also confer a higher risk for recurrence (25, 26). Overall, the American Society of Hematology and CHEST guideline panelists suggested that bridging be considered only among patients who are at high risk for recurrent VTE (Table 3) (3, 14).

**Pharmacology...** Temporary interruption of anticoagulation for a procedure is not uncommon. The 3 major categories of antithrombotic medications are VKAs, DOACs, and heparins, which have differing pharmacokinetics and reversal strategies. Procedural bleeding risk is categorized as minimal (<1%), low to moderate (>1% but <2%), or high (>2%). Risk for thrombosis with mechanical heart valves depends on the type, position, and timing of placement of the valve. For AF, stroke risk can be estimated using the CHA<sub>2</sub>DS<sub>2</sub>-VASc score. Risk for recurrent VTE is mediated by time since the index event, triggers, and prothrombotic risk factors.

## CLINICAL BOTTOM LINE

## Clinical Evaluation

### What should the initial evaluation include, and what is the goal of it?

The goal of the initial evaluation should be to assess the risks and benefits of thrombosis and bleeding in the periprocedural period, engage in shared decision making and patient education, and coordinate periprocedural management of anticoagulation. Patients and clinicians should be aware that recommendations may be based on limited data and the “best” approach may be uncertain.

After estimating risk for bleeding and thrombosis as outlined earlier, clinicians

should decide whether interruption of anticoagulation is warranted. For patients in whom anticoagulation is interrupted, when and how to interrupt therapy and whether to use bridging therapy should be determined by whether the patient is taking a VKA or a DOAC. A plan for restarting anticoagulation after the procedure should also be created.

Clear communication of the plan with proceduralists, anesthesiologists, and the patient is essential. If anticoagulation will not be interrupted, the proceduralist should confirm that they are comfortable with this plan. A calendar

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with specific recommendations for dosing, laboratory testing, and bridging (if applicable) should be given to the patient or their caregiver and the proceduralist before the procedure; an example is available in the CHEST 2022 guidelines (3). The absence of such a standardized framework can result in a cascade of downstream consequences, including conflicting recommendations across providers, inappropriate administration of reversal agents, changes to the anesthetic plan, or postponement of the surgery.

### What are the essential elements of the clinical history?

Before the procedure, the first step is to determine the bleeding risk of the planned procedure via review of the chart and discussion with the patient and proceduralist. Patient-related bleeding risk factors, such as thrombocytopenia, concomitant use of nonsteroidal anti-inflammatory drugs, hepatic or renal dysfunction, and past bleeding, should also be assessed and discussed with the patient and, if possible, modified before the procedure (8). Next, risk for thromboembolism should be estimated through review of the patient's clinical history and documentation. This can include ascertaining the patient's underlying diagnosis, the timing of any thromboses, the type of anticoagulant and adherence, any prior use of bridging, and any previous periprocedural

bleeding or thrombotic complications. In some cases, such as very recent stroke or VTE, delaying surgery if possible is the safest option.

### What is the role of laboratory testing in the context of periprocedural anticoagulation?

For patients using a VKA, clinicians should consider checking the INR 7 to 10 days before the procedure to establish a baseline while the patient is receiving therapy. If a procedure has high bleeding risk, normalization of the INR should be confirmed the day before or the day of surgery. In situations where the INR remains elevated, a small dose of vitamin K (1.25 to 2.5 mg) can be given to reduce the INR further before surgery (27). Routine periprocedural testing of DOAC levels is not recommended, although this may be warranted if DOAC clearance is affected by renal or hepatic dysfunction. Standard coagulation tests, such as the INR, do not reliably measure DOAC effect. For urgent procedures or situations when antecedent DOAC exposure is suspected, DOAC-specific laboratory tests may be performed to determine whether there is a residual anticoagulant effect. A normal thrombin time excludes the presence of dabigatran, and normal results on agent-specific chromogenic anti-factor Xa assays rule out factor Xa inhibition.

**Clinical Evaluation...** Clinical evaluation of periprocedural anticoagulation includes assessment and mitigation of patient and procedural bleeding risk, estimation of thrombosis risk (especially if anticoagulation is held), and creation of a clear plan for interruption of anticoagulation. Periprocedural bridging is necessary only in select situations, and in all cases, a plan for resumption of anticoagulation and monitoring after the procedure is necessary.

## CLINICAL BOTTOM LINE

### Which patients should receive periprocedural ("bridging") anticoagulation, and how should this be implemented?

Bridging is defined as use of shorter-acting parenteral anticoagulants, such as

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UFH or LMWH, during periods of subtherapeutic oral anticoagulation with VKAs. Bridging may be administered before and/or after the procedure.

*The BRIDGE (Bridging Anticoagulation in Patients who Require Temporary*

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**Table 4. Stratification of Risk and Bridging Recommendations for Periprocedural Arterial and Venous Thrombosis\***

Risk Category	Mechanical Valve	AF	VTE	Bridging Recommendation
High (>10% risk for ATE [per year] or VTE [per month])	Mitral Caged-ball Tilting-disk Stroke/TIA <6 mo previously	CHA <sub>2</sub> DS <sub>2</sub> -VASc score ≥7 CHA <sub>2</sub> DS <sub>2</sub> -VASc score of 5–6 with prior ATE Stroke/TIA <6 mo previously Valvular AF (in setting of rheumatic heart disease)	VTE within past 3 mo Deficiency of protein C, protein S, or antithrombin Antiphospholipid antibody syndrome Multiple prothrombotic abnormalities	Bridging suggested
Moderate (5%–10% risk for ATE [per year] or VTE [per month])	Bileaflet aortic valve with risk factors (AF, prior stroke/TIA, hypertension, diabetes, heart failure, age >75 y)	CHA <sub>2</sub> DS <sub>2</sub> -VASc score of 4–6	VTE within past 3–12 mo Heterozygous factor V Leiden Recurrent VTE Active cancer	Individual assessment
Low (<5% risk for ATE [per year] or VTE [per month])	Bileaflet aortic valve without risk factors	CHA <sub>2</sub> DS <sub>2</sub> -VASc score ≤3	VTE >12 mo previously No other risk factors	Suggest against bridging

AF = atrial fibrillation; ATE = arterial thromboembolism; TIA = transient ischemic attack; VTE = venous thromboembolism.

\* Data are from references 3, 8, 13, and 14.

*Interruption of Warfarin Therapy for an Elective Invasive Procedure or Surgery) trial compared periprocedural bridging with LMWH versus no bridging in 1884 patients with AF undergoing invasive procedures. The trial found no difference in ATE rates between the groups (risk difference, 0.1% [95% CI, −0.6% to 0.8%]) (1). However, bridging led to a 2-fold increase in bleeding. Of note, few patients with the highest stroke risk (CHA<sub>2</sub>DS<sub>2</sub>-VASc score ≥7) were included, so the results applied largely to patients with low or moderate risk for thrombosis.*

*A second randomized trial, the PERIOP2 (Postoperative low molecular weight heparin bridging treatment for patients at high risk of arterial thromboembolism) study, randomly assigned more than 1400 patients with high-risk AF or mechanical valves to LMWH versus placebo. The study found that postoperative LMWH bridging did not prevent ATE (rates of 1.2% for placebo and 1.0% for LMWH) or increase bleeding risk (rates of 2.0% for placebo and 1.3% for LMWH). The PERIOP2 findings demonstrated the lack of benefit of postprocedural bridging, even in the highest-risk patients (28).*

The quality of the evidence is lower for bridging in VTE, but available evidence suggests that bridging is associated with increased bleeding risk without a substantial reduction in VTE, except in patients who are at high risk for VTE (Table 4) (29).

The available evidence therefore indicates that only patients at the highest risk for thrombosis should receive periprocedural bridging therapy (Table 4). For mechanical valves, this includes patients with mitral, caged-ball, or tilting-disk valves and those with recent stroke or transient ischemic attack (3, 13). For AF, this includes patients with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 7 or higher, a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 5 to 6 and prior ATE, recent stroke or transient ischemic attack, and valvular disease (3, 19). For VTE, this includes VTE in the active treatment phase, strong thrombophilias (protein C, protein S, or antithrombin deficiencies, or antiphospholipid syndrome), or multiple thrombophilias (3, 14). Although these general recommendations apply in many circumstances, individual decisions must take into account the values, context, and preferences of specific patients. Shared decision making about the tradeoffs of different choices is paramount.

If bridging is done, LMWH is the preferred agent because it has more predictable pharmacokinetics than UFH and can be administered outside hospital settings. Typical regimens include enoxaparin, 1 mg/kg of body weight subcutaneously twice daily, or dalteparin, 100 U/kg subcutaneously twice daily. Clearance is substantially affected by renal function, and dose adjustments are required in this circumstance.

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**Table 5. Recommendations for Implementation of Bridging Therapy in Patients Receiving VKA Therapy, Based on Renal Function**

Renal Function	Before Procedure	After Procedure
CrCl $\geq$ 50 mL/min	Hold VKA starting 5 d before procedure If INR is 2–3, start LMWH 36 h after stopping VKA Continue LMWH twice per day Last dose of LMWH 24 h before surgery	High bleeding risk: Prophylactic dose of LMWH after 24–48 h Therapeutic dose of LMWH after 48–72 h Low/moderate bleeding risk: Prophylactic dose of LMWH after 12 h Therapeutic dose of LMWH after 24–48 h Minimal bleeding risk: Interruption of VKA therapy not required
CrCl of 30–50 mL/min*	Hold VKA starting 5 d before procedure If INR is 2–3, start LMWH 36 h after stopping VKA Continue LMWH twice per day Last dose of LMWH 36 h before surgery	High bleeding risk: Prophylactic dose of LMWH after 24–48 h Therapeutic dose of LMWH after 48–72 h Low/moderate bleeding risk: Prophylactic dose of LMWH after 12 h Therapeutic dose of LMWH after 24–48 h Minimal bleeding risk: Interruption of VKA therapy not required
CrCl <30 mL/min*	Hold VKA starting 5 d before procedure Admit patient the day before procedure for IV UFH (70-U/kg bolus, 15-U/kg/h infusion) Stop IV UFH 6 h before procedure	High bleeding risk: Prophylactic dose of LMWH after 24–48 h Therapeutic dose of LMWH after 48–72 h Low/moderate bleeding risk: Prophylactic dose of LMWH after 12 h Therapeutic dose of LMWH after 24–48 h Minimal bleeding risk: Interruption of VKA therapy not required

CrCl = creatinine clearance; INR = international normalized ratio; IV = intravenous; LMWH = low-molecular-weight heparin; UFH = unfractionated heparin; VKA = vitamin K antagonist.

\* For patients or procedures with very high bleeding risk, omission of bolus and reduced UFH infusion rates (e.g., 8 U/kg/h) may be considered.

Routine monitoring of anticoagulant effect (anti-factor Xa level) is not recommended (30).

For patients with severe renal impairment, subcutaneous UFH can be used. UFH may also be preferred in patients at the highest risk for periprocedural bleeding because of its short half-life and the ease and rapidity of reversal compared with LMWH. In addition, some clinicians recommend UFH in pregnant women with mechanical heart valves, as there are case reports of valve thrombosis with perioperative bridging with LMWH (31, 32). However, UFH is also associated with a 3-fold increased risk for heparin-induced thrombocytopenia (HIT), an antibody-mediated disorder associated with thromboembolism and death (4).

A typical patient with an INR between 2 and 3 during therapy should be directed to start LMWH 36 hours after discontinuing a VKA (Table 5). The last dose of LMWH should be administered 24 hours before the surgery to avoid

intraoperative presence of residual LMWH (33). Resumption of bridging anticoagulation with LMWH is informed by procedural bleeding risk. For high-risk procedures, prophylactic doses of LMWH or UFH can be started along with VKAs 24 to 48 hours after the procedure, with a gradual increase to therapeutic dosing 48 to 72 hours after the procedure. For procedures with low or moderate bleeding risk, a prophylactic dose can be started along with VKAs the evening of the day of the procedure (about 12 hours after the procedure). Therapeutic dosing may be considered 24 to 48 hours after the procedure depending on the patient's estimated risk for thrombosis. If bridging anticoagulation is used, it should be continued until a VKA is in the therapeutic range and the INR is 2.

### Which patients should not receive periprocedural bridging?

Bridging anticoagulation is not indicated for procedures with minimal bleeding risk performed in patients

**Table 6. Recommended Periprocedural Management of VKAs**

<i>Time</i>	<i>Recommendations</i>
Before procedure	Check INR 7–10 d before surgery Hold VKAs for 5 d if INR is 2–3 If bleeding risk is high, check INR day of surgery and administer vitamin K if INR is >1.5 Implement bridging therapy if warranted
After procedure	High bleeding risk: restart VKA after 24–36 h Low/moderate bleeding risk: restart VKA after 12 h Minimal bleeding risk: interruption of VKA therapy not required Continue bridging therapy if warranted until INR is 2

INR = international normalized ratio; VKA = vitamin K antagonist.

using oral anticoagulants or in most patients taking DOACs. The appropriateness of LMWH as a bridging agent should be carefully considered in people with severe kidney impairment (creatinine clearance [CrCl] <30 mL/min) or those receiving dialysis, who have a particularly high risk for bleeding due to drug accumulation. Finally, barriers to safe use of LMWH, such as the ability to administer injections outside the hospital or cost, should be carefully considered when determining the suitability of bridging.

### **How may clinicians implement periprocedural management of anticoagulation?**

Because of their pharmacokinetic differences, distinct strategies are needed for periprocedural management of VKAs and DOACs. Recommendations for VKA management before and after a procedure are summarized in **Table 6**. Procedures with minimal bleeding risk do not require interruption of anticoagulation. For patients taking VKAs who do need to stop therapy, clinicians should consider checking the INR 7 to 10 days before surgery (34). If the INR is in the therapeutic range of 2 to 3, holding VKAs for 5 days generally results in a normal INR; however, an INR above 3 may require a longer hold time. For high-risk procedures, INR measurement should be repeated the day before surgery, and if the INR remains above 1.5, low-dose vitamin K can be given orally (or subcutaneously or intravenously if oral intake is prohibited) to accelerate normalization (27).

After the procedure, the timing of VKA resumption should be guided by bleeding risk (**Table 6**) (3). For procedures with high bleeding risk, guidelines suggest restarting use of VKAs 24 to 36 hours after the procedure, as it usually takes several days for them to become therapeutic again. For low- to moderate-risk procedures, VKAs can be restarted 12 hours after the procedure. Clinicians should still evaluate whether standard VTE prophylaxis is appropriate.

*The results of the PAUSE (Perioperative Anticoagulant Use for Surgery Evaluation) study inform recommended perioperative management of DOACs (12). In this single-group study, 3000 patients with AF who required interruption of a DOAC for an elective procedure participated in a standardized perioperative management plan. The timing of DOAC interruption and resumption was based on estimated bleeding risk for the procedure, DOAC type, and renal function. Patients using apixaban, rivaroxaban, or dabigatran (the latter in those with a CrCl ≥50 mL/min) held the drug for 1 day for low-risk procedures or 2 days for high-risk procedures. In patients with impaired kidney function (CrCl <50 mL/min), dabigatran was held for 2 days for low-risk procedures and 4 days for high-risk procedures. DOACs were restarted after 1 day for procedures with low bleeding risk and after 2 to 3 days for those with high bleeding risk. With this protocol, the 30-day rates of bleeding were 0.90% to 1.85%, and the rates of thromboembolism were 0.16% to 0.60%. In*

**Table 7. Recommended Pre- and Postprocedural Management of DOACs\***

<i>Risk Category</i>	<i>Before Procedure</i>	<i>After Procedure</i>
<b>Minimal</b>	Does not require DOAC interruption	Does not require DOAC interruption
<b>Low/moderate</b>		
Apixaban, rivaroxaban, dabigatran (CrCl $\geq 50$ mL/min)	Stop 1 d before procedure	Restart no sooner than 1 d after procedure
Dabigatran (CrCl $< 50$ mL/min)	Stop 2 d before procedure	Restart no sooner than 1 d after procedure
<b>High</b>		
Apixaban, rivaroxaban, dabigatran (CrCl $\geq 50$ mL/min)	Stop 2 d before procedure	Restart no sooner than 2-3 d after procedure
Dabigatran (CrCl $< 50$ mL/min)†	Stop 4 d before procedure	Restart no sooner than 2-3 d after procedure

CrCl = creatinine clearance; DOAC = direct oral anticoagulant.

\* Data are from reference 12.

† Because of dabigatran's reliance on renal elimination, longer preoperative hold times are recommended, based on the results of the PAUSE (Perioperative Anticoagulant Use for Surgery Evaluation) study.

addition, more than 90% of patients using DOACs had little to no measurable DOAC when following this protocol.

Overall, these findings suggest that a standardized approach to periprocedural management of DOACs can result in good outcomes for patients with AF (Table 7). A similar approach may be extrapolated to patients with VTE. However, caution should be taken in applying the results of PAUSE to patients undergoing procedures with the potential for devastating bleeding complications (such as neurosurgical or neuraxial procedures) because they were not included in the PAUSE trial. Lengthening DOAC hold times may be reasonable in patients with a CrCl less than 30 mL/min or when the need to ensure complete reversal of the anticoagulant effect is important. Resumption of DOACs after the procedure should be considered on a case-by-case basis and depends on intraoperative factors and the consequences of potential rebleeding.

### **Are there unique conditions or medications that warrant a different periprocedural approach?**

Recommendations for urgent or emergent situations differ from those discussed earlier. In situations where there

is insufficient time for normalization of hemostasis, administering agents to actively reverse anticoagulation may be necessary (6, 14, 35). Vitamin K and prothrombin complex concentrates are used for urgent VKA reversal. Fresh frozen plasma may be given for VKA reversal if no other reversal agents are available or if the patient is receiving massive transfusions for severe ongoing bleeding. Fresh frozen plasma is not recommended as first-line therapy because vitamin K and prothrombin complex concentrates are associated with a higher probability of achieving near-normalized INR and fresh frozen plasma requires time to thaw and can lead to volume overload and transfusion reactions (14, 36). For DOACs, idarucizumab is the specific reversal agent for dabigatran, and andexanet alfa can be given to reverse factor Xa inhibitors. Prothrombin complex concentrates may be alternatives to DOAC-specific reversal agents. It is important to note that several of these agents increase risk for thrombosis and should be used with caution. Another issue is the potential for anticoagulation rebound, in which recurrent anticoagulant activity is detected after neutralization and can contribute to bleeding. A study found that, with andexanet alfa, more than 75% of patients had detectable levels of rivaroxaban 4 hours after completing the infusion (37).

Careful consideration should be given to patients with advanced kidney disease (CrCl <30 mL/min) or those receiving hemodialysis who have higher baseline bleeding risk even in the absence of anticoagulation (38). Clinicians should carefully assess the benefits and risks of bridging in this setting. LMWH should be avoided, and inpatient admission for intravenous UFH may be necessary (38).

If periprocedural bridging is indicated, clinicians should screen for a history of HIT. Extensive clinical guidance exists for management of HIT (39). Neither LMWH nor heparin (including low doses present in flushes or as prophylaxis) should be administered to patients with a history of HIT because they can trigger recurrence. Instead, alternative agents may be considered, such as DOACs, direct thrombin inhibitors (for example, bivalirudin or argatroban), or fondaparinux (which binds antithrombin to inhibit factor Xa). During acute HIT, up to half of patients develop ATE or VTE without anticoagulation; thus, in patients with HIT receiving therapeutic anticoagulation, avoiding interruption of anticoagulation should be prioritized.

Unlike anticoagulation, inferior vena cava (IVC) filters do not treat VTE but

instead mechanically block the IVC to prevent embolization of thrombosis to the lungs. They are associated with complications, including insertion complications, filter migration, vessel perforation, filter thrombosis, and distal DVT (40). The only widely accepted indication for IVC filter placement is acute pulmonary embolism or proximal DVT and a contraindication to anticoagulation (for example, urgent surgery, active bleeding, or a high estimated risk for anticoagulant-associated bleeding) (36, 41). For patients with acute VTE who are scheduled to undergo a procedure requiring interruption of anticoagulation, every effort should be made to delay the procedure until after 3 months of uninterrupted anticoagulation. If the duration of the hold is anticipated to be less than 48 hours, some experts advocate for aggressive prophylactic anticoagulation with timely advancement to therapeutic anticoagulation instead of IVC filter placement. Placement of a retrievable IVC filter can be considered for VTE that occurred within 30 days for urgent procedures requiring a longer hold of anticoagulation (42). A plan to remove the filter should be made before or in conjunction with placement.

**Periprocedural Management...** Bridging anticoagulation is now recommended only in a small subset of patients at the highest risk for thrombosis. When bridging is indicated, LMWH is the preferred agent for most patients. Patients undergoing procedures with minimal bleeding risk do not need to interrupt anticoagulation. For procedures with higher bleeding risk, management strategies depend on the type of anticoagulant. VKAs require longer preprocedural holding time and take longer after resuming to become therapeutic, for which bridging anticoagulation is sometimes indicated. In contrast, DOACs can be stopped closer to the procedure and do not require bridging, and resumption is often delayed longer than with VKAs.

## CLINICAL BOTTOM LINE



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### **When should consultation be obtained for periprocedural management of anticoagulation?**

Every patient receiving anticoagulation who is undergoing a procedure needs careful, interdisciplinary planning and discussion that includes the anticoagulation provider, the person performing the procedure, pharmacists, and other members of the care team. Although the standardized approach presented in this article can be applied to many patients, some clinical scenarios merit additional consultation. These consultations should occur well before the procedure so that any required plans (laboratory testing, medication prescription, cost assistance) can be made. For situations at the extremes of thrombosis risk (such as highly thrombotic conditions like antiphospholipid syndrome or a recent stroke) or patients with high bleeding risk (such as those having neurosurgery or those with recent bleeding), involvement of a hematologist or a thrombosis expert should be sought. For patients with a history of volatile INRs, coordination with an anticoagulation clinic is warranted if one is available. The same is true for patients with chronic renal failure, particularly those taking DOACs or those who might be prescribed bridging therapy with heparin. Input from an anesthesiologist can be particularly

## **Consultation and Follow-up**

helpful if there are any anticipated issues with coordination of surgery with preoperative blood tests, the type of anesthesia (such as neuraxial anesthesia), or patients who have cardiopulmonary compromise as a result of their underlying condition (43).

### **How should patients whose anticoagulation is changed be followed?**

Close communication after the procedure is needed to ensure safe resumption of anticoagulation. Procedural complications and postprocedural medication instructions should be communicated to patients and their outpatient clinicians. If bridging was used, a clear schedule for when and how to transition back to a VKA should be developed. The periprocedural period can be an opportunity to ensure that patients are receiving optimal anticoagulation management and to provide patient education. For example, inappropriate coadministration of aspirin can be identified and rectified, recommended renal dosing can be implemented for DOACs, and patients can receive additional education about the symptoms of recurrent VTE. For patients with mounting bleeding risk factors or increasingly limited life expectancy, the periprocedural period can also be an opportunity to reassess the net benefit of ongoing anticoagulation.

**Consultation and Follow-up...** Effective communication before and after the procedure with the patient, the anticoagulation provider, and the proceduralist is essential. Patients for whom additional consultation should be considered are those at the extremes of thrombosis or bleeding risk and those with volatile INR measurements, chronic renal impairment, or excess anesthetic risks.

### **CLINICAL BOTTOM LINE**

## Practice Improvement

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### **What measures do stakeholders use to measure the quality of care?**

The perioperative period has been identified as a target for several quality improvement initiatives. To encourage adoption of a standardized approach, the Centers for Medicare & Medicaid Services provides incentive payments for documentation of both a plan and a discussion with the patient for periprocedural management plans that cover necessary laboratory monitoring, when to stop use of the drug, how to manage antiplatelet therapy, a plan for bridging, and a timeline for restarting use of the drug (44). The Joint Commission recently established a National Patient Safety Goal to include a new measure of performance for periprocedural anticoagulants that assesses the use of approved

and evidence-based protocols (45). In addition, there has been growth in anticoagulation stewardship programs across health systems to implement evidence-based periprocedural management (46).

### **What do professional organizations recommend with regard to periprocedural anticoagulation?**

Because this topic spans several disciplines, multiple professional societies issue distinct guidelines addressing periprocedural anticoagulation, including the American College of Cardiology and American Heart Association, the International Society on Thrombosis and Haemostasis, the American College of Chest Physicians, and the American Society of Hematology (3, 4, 7, 8, 13, 14). The recommendations in this article reflect this guidance.

# In the Clinic Tool Kit

## Periprocedural Anticoagulation

### *Patient Information*

<https://medlineplus.gov/bloodthinners.html>

<https://medlineplus.gov/languages/bloodthinners.html>

Information and handouts on blood thinners in English and other languages from the National Institutes of Health's MedlinePlus.

[www.stoptheclot.org/new-patient-resource-guide-2](http://www.stoptheclot.org/new-patient-resource-guide-2)

Resources from the National Blood Clot Alliance.

<https://sites.uw.edu/anticoag/education/patient-education>

Educational materials on anticoagulation from the University of Washington Anticoagulation Services.

### *Information for Health Professionals*

[https://journal.chestnet.org/article/S0012-3692\(22\)01364-2/fulltext](https://journal.chestnet.org/article/S0012-3692(22)01364-2/fulltext)

2022 clinical practice guideline on perioperative management of antithrombotic therapy from the American College of Chest Physicians.

[www.jacc.org/doi/10.1016/j.jacc.2016.11.024](http://www.jacc.org/doi/10.1016/j.jacc.2016.11.024)

2017 expert consensus decision pathway for periprocedural management of anticoagulation in patients with nonvalvular atrial fibrillation from the American College of Cardiology.

<https://ashpublications.org/bloodadvances/article/2/22/3257/16107/American-Society-of-Hematology-2018-guidelines-for>

2018 guidelines for management of venous thromboembolism and optimal management of anticoagulation from the American Society of Hematology.

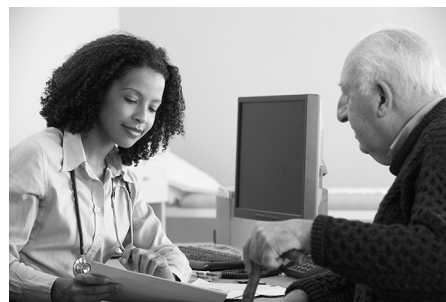
In the Clinic

# WHAT YOU SHOULD KNOW ABOUT PERIPROCEDURAL ANTICOAGULATION

In the Clinic  
Annals of Internal Medicine

## What Is Periprocedural Anticoagulation?

Periprocedural anticoagulation is the use of blood-thinning medications, such as warfarin or direct oral anticoagulants, around the time of surgical or invasive procedures. An evidence-based approach is needed to support decision making for patients who use blood-thinning drugs or for those who may need blood thinners around the time of surgical procedures.



## Who May Need Periprocedural Anticoagulation?

The following patients may need guidance on treatment with blood thinners around the time of surgery:

- Patients currently receiving blood thinners, such as warfarin or direct oral anticoagulants
- Patients with certain kinds of mechanical heart valves
- Patients with a history of blood clotting problems or those who have had recent blood clots
- Those who are deemed to be at high risk for blood clots during the time of surgery
- Those who are deemed to be at high risk for bleeding during the time of surgery

## How Are Recommendations on Periprocedural Anticoagulation Managed and Delivered?

Most people who need management of blood thinners around the time of surgery are identified before the procedure. Medical teams then make plans for how to manage these treatments—including if or when to stop, resume, or start treatment—or how to substitute medications during the procedural period. These decisions are made by medical and surgical specialists involved in the procedure and are communicated to the patient and their primary care providers. Standardized risk scores and tools are used to estimate the risk for bleeding or clotting during surgery.

## What Kinds of Medications May Prompt Periprocedural Anticoagulation?

Medications that thin the blood are the principal drugs that need to be managed during surgery to balance bleeding and clotting risks. These drugs include:

- Warfarin, coumadin, or other vitamin K antagonists
- Direct oral anticoagulants, including apixaban, rivaroxaban, edoxaban, or dabigatran
- Injectable anticoagulants, such as enoxaparin, fondaparinux, or heparin
- Aspirin, clopidogrel, and related antiplatelets

## Questions for My Doctor

- Which of my medications may need to be managed around the time of a procedure?
- Do I need to have other tests to determine my bleeding or clotting risk?
- What are the risks or benefits of stopping and starting treatments?
- If I do stop using medications, when should I resume using them?
- Should I follow up with a specialist?

## For More Information



University of Washington  
<https://sites.uw.edu/anticoag/education/patient-education>



**Appendix Table 1. Anticoagulants That Are Commonly Used or Managed During the Periprocedural Period**

Agent	Mechanism of Action	Formulation	Peak Effect	Half-Life	Renal Elimination	Reversal Agent	Periprocedural Implications
Warfarin	Vitamin K antagonist	Oral	5 d	40 h	None	Vitamin K or PCC	Longer hold time (5 d) before procedure due to long half-life May require periprocedural INR monitoring Bridging may be needed in patients at high risk for thrombosis due to subtherapeutic period Restart sooner (12–36 h) after procedure due to slow onset
Dabigatran	Factor IIa inhibitor	Oral	2–3 h	12–17 h	80%	Idarucizumab*	Shorter hold time (1–4 d) before procedure due to short half-life No periprocedural monitoring No bridging needed Restart later (1–3 d) after procedure due to quick onset
Rivaroxaban	Factor Xa inhibitor	Oral	2–4 h	5–9 h	33%	Andexanet alfa or PCC*	Shorter hold time (1–4 d) before procedure due to short half-life No periprocedural monitoring No bridging needed Restart later (1–3 d) after procedure due to quick onset
Apixaban	Factor Xa inhibitor	Oral	1–3 h	9–14 h	25%	Andexanet alfa or PCC*	Shorter hold time (1–4 d) before procedure due to short half-life No periprocedural monitoring No bridging needed Restart later (1–3 d) after procedure due to quick onset
Edoxaban	Factor Xa inhibitor	Oral	1–2 h	9–11 h	35%–50%	Andexanet alfa or PCC*	Shorter hold time (1–4 d) before procedure due to short half-life No periprocedural monitoring No bridging needed Restart later (1–3 d) after procedure due to quick onset
LMWH	Indirect factor Xa/IIa inhibitor via AT	Subcutaneous	20–30 min	3–5 h	90%	70% reversal with protamine	Can be used for bridging Monitoring not required
UFH	Indirect factor Xa/IIa inhibitor via AT	Subcutaneous, intravenous, or parenteral	Instantaneous	45 min to 1 h	None	100% reversal with protamine	Can be used for bridging Monitoring often required May be preferred over LMWH in cases of severe renal dysfunction or pregnancy with mechanical heart valve Higher risk for HIT than LMWH

*Continued on following page*

Appendix Table 1.—Continued

Agent	Mechanism of Action	Formulation	Peak Effect	Half-Life	Renal Elimination	Reversal Agent	Periprocedural Implications
Fondaparinux	Selective factor Xa inhibitor via AT	Subcutaneous	2–3 h	17–21 h	90%	No approved reversal agent; consider recombinant factor VIIa†	Can be used for bridging if UFH or LMWH is contraindicated (e.g., history of HIT)

AT = antithrombin; HIT = heparin-induced thrombocytopenia; INR = international normalized ratio; LMWH = low-molecular-weight heparin; PCC = prothrombin complex concentrate; UFH = unfractionated heparin.

\* Although direct oral anticoagulant reversal agents are available, randomized controlled trials to inform use are limited, having principally enrolled patients who experienced major bleeding, and their use should be restricted to urgent or emergent situations. Andexanet alfa carries a black box warning for thromboembolism and ischemic events, which were seen in 10% of patients in the single-group ANNEXA-4 (Andexanet Alfa, a Novel Antidote to the Anticoagulation Effects of FXA Inhibitors) study. Nonspecific agents, such as PCCs, are also used, and a recent meta-analysis suggests they may have efficacy and safety similar to those of specific antidotes (6, 47).

† No reversal agent for fondaparinux has been approved by the U.S. Food and Drug Administration. Small studies suggest that recombinant factor VIIa can reverse the effects of fondaparinux on laboratory parameters.

**Appendix Table 2. CHA<sub>2</sub>DS<sub>2</sub>-VASc Annual Risk for Arterial Thromboembolism in Atrial Fibrillation\***

<i>CHA<sub>2</sub>DS<sub>2</sub>-VASc Score</i>	<i>Annual Risk for Stroke, %</i>
0	0.2
1	0.6
2	2.5
3	3.2
4	4.8
5	7.2
6	9.7
7	11.2
8	10.8
9	14.4

\* Data are from reference 48.