Management of anticoagulants in patients undergoing endoscopic procedures

AUTHOR: Patrick S Kamath, MD
SECTION EDITOR: John R Saltzman, MD, FACP, FACG, FASGE, AGAF
DEPUTY EDITOR: Kristen M Robson, MD, MBA, FACG

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INTRODUCTION

Management of anticoagulation in patients undergoing endoscopic procedures is challenging because interrupting anticoagulation for a procedure transiently increases the risk of thromboembolism. At the same time, some endoscopic interventions have associated bleeding risks that are increased by the anticoagulant administered for thromboembolism prevention. In addition, limited data are available to guide the management of anticoagulated patients in these settings.

This topic will review periprocedural management of patients taking anticoagulants. The management of patients taking antiplatelet agents, as well as patients with von Willebrand disease, hemophilia, and other disorders of hemostasis are discussed separately. (See "Management of antiplatelet agents in patients undergoing endoscopic procedures" and "Gastrointestinal endoscopy in patients with disorders of hemostasis".)

Additional details regarding the use of specific anticoagulants are presented separately:

- Vitamin K antagonists (see "Warfarin and other VKAs: Dosing and adverse effects").
- Heparins (see "Heparin and LMW heparin: Dosing and adverse effects").
- Direct oral anticoagulants (direct thrombin inhibitors [dabigatran] and direct factor Xa inhibitors [rivaroxaban, apixaban, edoxaban]) (see "Direct oral anticoagulants (DOACs) and

parenteral direct-acting anticoagulants: Dosing and adverse effects").

Recommendations for patients with prosthetic heart valves are discussed separately. (See "Anticoagulation for prosthetic heart valves: Management of bleeding and invasive procedures".)

The American Society for Gastrointestinal Endoscopy (ASGE) has issued guidelines regarding the management of patients taking anticoagulants based upon the available evidence and consensus opinion [1]. The recommendations in this topic are consistent with ASGE guidelines. This topic is also addressed in an international consensus statement and in guidelines from the American College of Gastroenterology, the American College of Chest Physicians, the American College of Cardiology, and the British Society of Gastroenterology/European Society of Gastrointestinal Endoscopy, which make similar (though not identical) recommendations [2-6].

GENERAL PRINCIPLES

Factors that guide decision-making — The management of anticoagulated patients undergoing endoscopy takes into account the patient's risk of thrombosis, the procedure-related bleeding risk, and the specific features of the anticoagulant that the patient is taking [7,8]. (See "Perioperative management of patients receiving anticoagulants", section on 'Overview of our approach'.)

Much of our approach is based on expert opinion; thrombotic and bleeding risks may vary depending on individual circumstances, and data from randomized trials or well-designed observational studies are not available to guide practice in all settings. In addition, the best surrogate for complete resolution of anticoagulant effect is not always known or available for the direct oral anticoagulants. Thus, this approach should be used as clinical guidance and should not substitute for clinician judgment in decisions about periprocedural anticoagulation management [7-9].

Assess risk — Interruption of anticoagulation temporarily increases thromboembolic risk, while continuing anticoagulation increases the risk of bleeding associated with invasive procedures; both of these outcomes adversely affect mortality [9]:

Estimate thromboembolic risk — The probability of a thromboembolic complication following reversal or discontinuation of anticoagulation depends upon the pre-existing condition for which the medication was prescribed. A higher thromboembolic risk increases the importance of minimizing the time interval without anticoagulation. For example, common conditions that increase thromboembolic risk include atrial fibrillation and venous

thromboembolism (table 1). Further details on estimating the risk of thromboembolism are discussed separately. (See "Perioperative management of patients receiving anticoagulants", section on 'Estimating thromboembolic risk'.)

Recommendations for patients with prosthetic heart valves are discussed separately. (See "Anticoagulation for prosthetic heart valves: Management of bleeding and invasive procedures".)

In UpToDate topics, the categories for thrombotic risk are listed as "moderate, high and very high", although other publications and guidelines list similar categories as "low, moderate (or medium), and high" [1,3]. Therefore, in this topic, patients in the "low or moderate risk" category are similar to patients in the "low risk" category in other publications.

Similarly, the "high risk" category in this topic includes any of the following groups: patients in the "high risk" category (by any classification system), patients in the "very high" category in UpToDate, and patients in the "moderate risk" category in other publications [1,3]. (See 'Patients with low to moderate thrombotic risk' below and 'Patients with high thrombotic risk' below.)

Estimate bleeding risk — The risk of bleeding depends on the endoscopic procedure and the need for (and type of) therapeutic intervention. (See "Gastrointestinal endoscopy in patients with disorders of hemostasis", section on 'Estimating procedure-related bleeding risk'.)

Common low-risk procedures (bleeding risk <1 percent) include (table 2):

- Upper gastrointestinal endoscopy (esophagogastroduodenoscopy [EGD]) including mucosal biopsy
- Colonoscopy including mucosal biopsy
- Endoscopic retrograde cholangiopancreatography (ERCP) without sphincterotomy
- ERCP with biliary stent placement

Common high-risk procedures (bleeding risk ≥1 percent) include:

- EGD with esophageal variceal ligation
- EGD with esophageal dilation
- Percutaneous endoscopic gastrostomy tube placement
- Colonoscopy with polypectomy of large polyp (≥1 cm)

- ERCP with biliary or pancreatic sphincterotomy

The approach to managing anticoagulation depends on whether the procedure is low or high risk for bleeding. (See 'Elective procedures' below.)

For some procedures (eg, screening colonoscopy), the preprocedure estimate of bleeding risk is uncertain because it is unknown whether a high-risk intervention (eg, polypectomy of large polyp [≥1 cm]) will be necessary. For patients undergoing a procedure with uncertain risk, management options depend on the patient's risk of thrombosis, the specific anticoagulant, and patient preference. Our approach (and alternatives) in this setting are discussed separately for patients with low to moderate thrombotic risk (see 'High or uncertain risk procedures' below) and for patients with high thrombotic risk (see 'Procedures with uncertain risk' below).

Specialty consultation — We consult with the clinician and/or clinical service who are managing the patient's long-term anticoagulation (eg, cardiologist, neurologist, anticoagulation clinic) prior to electively interrupting anticoagulation therapy.

ELECTIVE PROCEDURES

Patients with low to moderate thrombotic risk — Examples of conditions that confer a low or moderate thrombotic risk include (table 1) [1]:

- Atrial fibrillation and a CHA_2DS_2-VASc score of 2 to 3 or $CHADS_2$ score of zero to 2 (assuming no prior stroke or transient ischemic attack) (table 3)
- Venous thromboembolism >12 months previous and no other risk factors

Low risk procedures — Patients at low or moderate risk for thrombosis require no change in anticoagulation prior to low-risk procedures (table 2) (eg, upper gastrointestinal endoscopy [esophagogastroduodenoscopy [EGD] or colonoscopy, including mucosal biopsy) (algorithm 1). However, for most patients scheduled for screening colonoscopy, the bleeding risk is uncertain because it is unknown whether or not polypectomy of a large polyp (≥1 cm) will be needed. Our approach to management in this setting is described below. (See 'High or uncertain risk procedures' below.)

If the international normalized ratio (INR) is >2.5, we postpone elective procedures for patients taking vitamin K antagonists (eg, warfarin) until the INR is ≤2.5. The threshold INR value is based on indirect data in patients undergoing endoscopic procedures for active bleeding and the endoscopist's personal preference, while other experts may use different thresholds. (See 'Patients on warfarin' below.)

High or uncertain risk procedures — For most patients who are at low or moderate risk for thrombosis, anticoagulation can be safely discontinued prior to endoscopic procedure with either high bleeding risk or uncertain bleeding risk (eg, screening colonoscopy) (table 2). (See 'Estimate bleeding risk' above.)

The approach to interruption and resumption of anticoagulation depends on the agent used, as discussed below.

Patients on warfarin — For low to moderate risk patients on vitamin K antagonists (eg, warfarin), we use the following approach [7]:

- Discontinue warfarin five days prior to the procedure.
- Confirm that INR is ≤1.5 on the day before or the day of the procedure.
- Restart warfarin on the evening of the day of the procedure if hemostasis is achieved, as determined by the endoscopist. Special consideration is warranted for patients who have endoscopic retrograde cholangiopancreatography (ERCP) with sphincterotomy. (See 'Patients who undergo sphincterotomy' below.)

Bridging therapy with a heparin product is generally not needed for low-risk patients because they are at low risk for a thromboembolic event with temporary interruption of anticoagulation. The decision to use bridging therapy involves balancing the risk of a thromboembolic event with the risk of procedure-related bleeding, and this is discussed separately. (See "Perioperative management of patients receiving anticoagulants", section on 'Bridging anticoagulation'.)

Patients on direct oral anticoagulants — For low to moderate risk patients taking an oral direct thrombin or factor Xa inhibitor (eg, dabigatran, rivaroxaban, apixaban, or edoxaban) with normal renal function, our approach is the following (see "Perioperative management of patients receiving anticoagulants"):

- Discontinue the drug 48 hours prior to the procedure.
- After the procedure, wait 48 hours before the restarting the drug if hemostasis is achieved, as determined by the endoscopist. Special consideration is warranted for patients who have ERCP with sphincterotomy. (See 'Patients who undergo sphincterotomy' below.)

Preprocedure medication adjustments for patients with renal insufficiency are discussed below. (See 'Patients with renal insufficiency on direct oral anticoagulants (DOACs)' below.)

These drugs have rapid onsets of action (one to three hours) and short half-lives (5 to 17 hours, depending on agent, in patients with normal renal function) [10]. The full anticoagulant effect of direct oral anticoagulants (DOACs) occurs within hours of administration, and for this reason we wait 48 hours prior to restarting a DOAC because of the risk of immediate post-procedure bleeding.

Patients who undergo sphincterotomy — Because of the increased risk of bleeding, we delay restarting anticoagulation after ERCP with sphincterotomy:

- **Patients on** warfarin – Restart warfarin in three days
- **Patients on DOACs** – Restart DOACs in five days

The risk of bleeding following biliary or pancreatic sphincterotomy persists for three to five days after the procedure. For patients at low or moderate risk for thrombosis, it is reasonable to delay attaining therapeutic levels (for those receiving warfarin) or the full effect of anticoagulation (for those receiving DOACs) until five days following the procedure [11].

Patients with high thrombotic risk — Patients at high risk for thromboembolic events include patients with any of the following:

- Atrial fibrillation with CHA_2DS_2-VASc score ≥4 ($CHADS_2$ score of ≥3) (table 3)
- Atrial fibrillation with stroke or transient ischemic attack within three months
- Rheumatic valvular heart disease
- Venous thromboembolism within 12 months
- Thrombophilia (eg, antiphospholipid antibodies, heterozygous factor V Leiden, prothrombin gene mutation)
- Recurrent venous thromboembolism
- Active cancer (treated within six months or palliative)

Patients with certain prosthetic heart valves are also at high thrombotic risk; preprocedural anticoagulation management for these patients is discussed in detail separately. (See "Anticoagulation for prosthetic heart valves: Management of bleeding and invasive procedures".)

Low-risk procedures — Patients at high risk for thromboembolic events require no change in anticoagulation prior to low-risk procedures (table 2), (eg, upper gastrointestinal endoscopy

EGD or colonoscopy, with or without mucosal biopsy). (See "Management and prevention of bleeding after colonoscopy with polypectomy", section on 'Immediate bleeding'.)

For patients taking vitamin K antagonists (eg, warfarin), we prefer an INR ≤2.5 prior to low-risk, elective procedures. The threshold INR value is based on indirect data in patients undergoing endoscopic procedures for active bleeding and personal preference, and other experts may use different thresholds. (See 'Patients on warfarin' below.)

High-risk procedures

Patients on warfarin — High-risk procedures generally warrant interruption of anticoagulation. For patients who are at high risk for thromboembolism and who are undergoing high- risk procedures (table 2), we ask the clinician who is managing the patient's anticoagulation if it is safe to hold warfarin for five days prior to the procedure and if bridging therapy is needed. Warfarin should be discontinued such that the INR is ≤ 1.5 by the day of the procedure.

The need for bridging anticoagulation (ie, use of a short-acting anticoagulant during the interruption of warfarin) is generally determined by the magnitude of the patient's thrombotic risk. For example, a condition that confers a very high risk of thromboembolism and generally necessitates bridge therapy is atrial fibrillation with CHA_2DS_2-VASc score of ≥5. If bridging therapy is warranted, it may be indicated preoperatively, postoperatively, or both. Heparin products (low molecular weight heparin or unfractionated heparin) are used for bridging anticoagulation. The approach to selecting patients for bridge therapy and the administration and dosing of bridge therapy are discussed in detail elsewhere. (See "Perioperative management of patients receiving anticoagulants", section on 'Bridging anticoagulation'.)

The intent of bridging is to minimize the time the patient is not anticoagulated, thereby minimizing the risk for perioperative thromboembolism. However, this needs to be balanced with the importance of mitigating the risk of postoperative bleeding. A slight delay in resumption of postoperative anticoagulation is preferable to premature initiation of postoperative bridging and/or long-term anticoagulation that results in bleeding, which ultimately will lengthen the period without an anticoagulant and thus increase thromboembolic risk.

In general, anticoagulation may be resumed after hemostasis is achieved after a high risk intervention that has a low risk of rebleeding (as determined by the endoscopist).

The time interval prior to resuming anticoagulation also depends on the specific lesion, specific intervention, accessibility of the endoscopic site, and degree of difficulty required to achieve

hemostasis. Examples of anticoagulation management following common high-risk procedures include:

- **Polypectomy of colon polyp ≥1 cm –** Warfarin is resumed in the evening of the day of the procedure since it takes several days to achieve a therapeutic effect. For those receiving bridge therapy, low molecular weight heparin at therapeutic doses can generally be resumed 48 hours after colonoscopic polypectomy. Endoscopic methods that may help lower the risk of postpolypectomy bleeding, including placement of hemoclips, are discussed separately. (See "Endoscopic removal of large colon polyps", section on 'Preventing bleeding'.)

- **Sphincterotomy –** For patients who undergo biliary or pancreatic sphincterotomy, warfarin is not restarted until 72 hours after endoscopic retrograde cholangiopancreatography (ERCP) because of the risk of postsphincterotomy bleeding. For those who are receiving bridge therapy, unfractionated heparin may be started 24 to 48 hours after ERCP with sphincterotomy. We prefer unfractionated heparin because of its short half-life. (See "Post-endoscopic retrograde cholangiopancreatography (ERCP) bleeding".)

Patients on direct oral anticoagulants — We confirm with the clinician managing anticoagulation that it is acceptable to temporarily discontinue the DOAC, and periprocedural management of these high-risk patients is similar to the approach for low- to moderate-risk patients, as described above. (See 'Patients on direct oral anticoagulants' above and 'Specialty consultation' above.)

Bridging therapy for patients on DOACs is not required given their short half-lives.

Procedures with uncertain risk — For some procedures (eg, screening colonoscopy), the preprocedure estimate of bleeding risk is uncertain because it is unknown whether a high-risk intervention (eg, polypectomy of large polyp [≥1 cm]) will be necessary. For most high-risk patients undergoing screening colonoscopy, we perform an initial colonoscopy without interrupting long-term anticoagulation, similar to our approach for a low-risk procedure. (See 'Low-risk procedures' above.)

If a large polyp requiring polypectomy is found, a second colonoscopy can be performed at a later date, with anticoagulant management similar to that for a high-risk procedure. (See 'High-risk procedures' above.)

The decision of whether to proceed in this manner or to discontinue anticoagulation and provide bridging therapy when the need for high-risk intervention is uncertain requires shared

decision-making between the patient and physician. An alternative approach is to manage the patient as if the colonoscopy will include a high-risk intervention. The advantage of this approach is that if a large polyp is found, it can be removed at the index colonoscopy. The disadvantage is that some high-risk patients will have to discontinue anticoagulation when interruption was not necessary.

Patients with transient thrombotic risk — If thromboembolic risk is transiently increased (eg, deep venous thrombosis), we prefer to delay an elective endoscopic procedure until the risk returns to baseline.

URGENT PROCEDURES

Patients with bleeding — For patients with active gastrointestinal bleeding, the risk of reversing anticoagulation should be weighed against the risk of continued bleeding without reversal [1]. In addition, the course of action depends on the antithrombotic agent. (See "Approach to acute upper gastrointestinal bleeding in adults" and "Approach to acute lower gastrointestinal bleeding in adults".)

Patients on warfarin — Patients on warfarin with serious or life-threatening bleeding require rapid, full reversal of any warfarin effect, whereas those with minor bleeding may be best served by holding warfarin without administration of a reversal agent.

For patients with life-threatening hemorrhage, fresh frozen plasma (FFP), and unactivated prothrombin complex concentrate (PCC) can be used to reverse anticoagulation from warfarin (table 4A). FFP is used for most patients. However, PCC is preferred in patients with variceal bleeding or those at risk for cardiac failure, because the volume of FFP may increase portal pressure and precipitate cardiac failure. Vitamin K is less useful than FFP or PCC in the acute setting because of its delayed onset of action (12 to 24 hours). The approach to managing a patient with warfarin-associated bleeding is discussed in detail separately. (See "Management of warfarin-associated bleeding or supratherapeutic INR", section on 'Treatment of bleeding'.)

Once reversal of anticoagulation has been initiated, the target international normalized ratio (INR) prior to an endoscopic intervention is based on endoscopist's preference. Limited data suggest that an endoscopic intervention will be successful within a range of target INRs. Some UpToDate contributors prefer an INR of ≤1.5 prior to a high-risk procedure, while other contributors proceed with the intervention when the INR is ≤2.5 and then continue to reverse anticoagulation or let the INR naturally decline to ≤1.5 for at least 72 hours after endoscopic therapy. The American Society for Gastrointestinal Endoscopy suggests that endoscopic therapy

not be delayed in patients with an INR <2.5 and serious gastrointestinal bleeding [1]. Of note, endoscopic therapy for any actively bleeding lesion is regarded as a high-risk procedure (table 2).

Data from observational studies suggest that the success rates of endoscopic therapy for gastrointestinal bleeding in patients who are mildly to moderately anticoagulated (INRs of 1.3 to 2.7) are comparable to the success rates in patients who are not anticoagulated [12-14]. In one report, successful hemostasis was achieved with endoscopic therapy in 91 percent of 52 patients with acute upper gastrointestinal (GI) bleeding after correcting the INR to 1.5 to 2.5, a success rate comparable to a control population of patients who were not anticoagulated [12]. The distribution of patients' INR values within the goal range was not provided. Outcome data are lacking for patients with INRs above the therapeutic range (≥4.0) who undergo urgent endoscopic intervention.

Patients on direct oral anticoagulants — The approach to patients on direct oral anticoagulants (DOAC) therapy with acute gastrointestinal bleeding depends on the severity of the bleeding:

- **Severe, life-threatening bleeding -** For patients with severe, life-threatening gastrointestinal bleeding, strategies for reversing the effects of DOACs include (table 4B):

  - Use a specific reversal agent, if available. Specific reversal agents are approved for use for dabigatran (idarucizumab) and for the oral direct factor Xa inhibitors (andexanet alfa) [15,16]. However, andexanet alfa (reversal agent for rivaroxaban or apixaban) is not yet widely available [16]. The onset of action of the reversal agents is approximately two to four hours.

  - Use a nonspecific reversal agent (eg, prothrombin complex concentrates, which are prothrombotic).

  The approach to selecting a strategy for reversing the effects of DOACs in patients with major bleeding is presented separately. (See "Management of bleeding in patients receiving direct oral anticoagulants", section on 'Major bleeding'.) Patients are monitored clinically since routine coagulation testing cannot be used as evidence that the DOAC effect has been reversed. The specific reversal agents for DOACs typically take effect within minutes of administration. (See "Management of bleeding in patients receiving direct oral anticoagulants", section on 'Assessment of anticoagulation status'.)

We proceed with urgent endoscopy with possible therapeutic intervention following administration of the nonspecific and/or specific reversal agents, if available.

- **Nonsevere bleeding** – For most patients with nonsevere but active gastrointestinal bleeding, the DOAC is held while the patient receives general supportive measures, fluid resuscitation, and transfusion of blood products if needed. Because of the relatively short half-lives for these drugs (5 to 17 hours, depending on agent), the anticoagulation effect is relatively short-lived in patients with normal renal function. (See "Approach to acute lower gastrointestinal bleeding in adults", section on 'Initial management' and "Approach to acute upper gastrointestinal bleeding in adults", section on 'General management'.)

  For patients who are hemodynamically stable following resuscitation, endoscopic evaluation can typically be performed within 12 to 24 hours because the DOAC effect has diminished [4]. In addition, bleeding may stop without endoscopic intervention for some patients, although most patients undergo endoscopy to evaluate the source of bleeding [10].

Resuming anticoagulants after hemostasis

Patients with low rebleeding risk — We generally restart anticoagulation after hemostasis has been achieved for hemodynamically stable patients who have lesions with low-risk of rebleeding (eg, duodenal ulcer with a clean base) (table 5). (See "Overview of the treatment of bleeding peptic ulcers", section on 'Stigmata of recent hemorrhage'.)

The approach to and timing for restarting anticoagulation following hemostasis depends on the specific anticoagulant and if bridging is required:

- **Patients on** warfarin **-** We restart warfarin in the evening of the procedure day, if no further bleeding occurs. Patients who resume warfarin will require several days to achieve therapeutic levels of anticoagulation.

  For those patients who had high enough thrombotic risk to warrant bridge therapy, we restart intravenous unfractionated heparin 48 hours after hemostasis is achieved for patients who require bridge therapy. Initial postprocedure anticoagulation with intravenous unfractionated heparin is preferable to low molecular weight heparin (which is typically used in patients who have undergone surgery) due to its relatively short half-life of 1.5 hours [1]. This allows for quick reversal following discontinuation of unfractionated heparin if bleeding recurs. (See 'Patients with high thrombotic risk' above.)

- **Patients on DOACs** – We restart DOACs 48 to 72 hours after hemostasis has been achieved, if no further bleeding occurs. Administration of DOACs (dabigatran, rivaroxaban, apixaban, or edoxaban) results in therapeutic levels of anticoagulation within one to three hours of administration [10].

A detailed approach to resuming DOACs, warfarin and/or using bridging therapy is discussed in detail elsewhere. (See "Perioperative management of patients receiving anticoagulants", section on 'Bridging anticoagulation' and "Perioperative management of patients receiving anticoagulants", section on 'Timing of anticoagulant interruption'.)

Studies suggest that patients who resume anticoagulation have better outcomes compared with those who remain without long-term anticoagulation [17-20]. In a meta-analysis of three studies including over 1800 patients on warfarin with gastrointestinal bleeding, patients who resumed warfarin following interruption were less likely to have thromboembolic events (HR 0.68, 95% CI 0.52-0.88) or to die (HR 0.76, 95% CI 0.66-0.88) [19]. There was a trend toward an increase in the risk of rebleeding (HR 1.20, 95% CI 0.97-1.48).

Subsequent observational studies have demonstrated similar findings [18,20]. In a cohort study of 4602 anticoagulated patients with atrial fibrillation and GI bleeding, patients who resumed an oral anticoagulant had lower rate of all-cause mortality and thromboembolism compared with patients who did not resume treatment (HR 0.39, 95% CI 0.34-0.46 and HR 0.41, 95% CI 0.31-0.54, respectively) [20].

Data are limited with regard to the specific timing for resuming anticoagulation for patients who are recovering from an episode of GI bleeding. In one study, the median time to resumption of warfarin was four days (range two to nine days) [17].

Patients with high rebleeding risk — For patients with lesions at high risk of rebleeding, we delay restarting anticoagulation (if possible, depending on the patient's thrombotic risk) until the rebleeding risk is lower. (See 'Patients with low rebleeding risk' above.)

The duration of the delay is based on several factors, including the source and location of bleeding, the endoscopic method used to achieve hemostasis, the hemodynamic status of the patient, and the potential consequences of rebleeding (eg, need for surgical intervention). Risk factors associated with rebleeding and the natural history of specific gastrointestinal lesions are discussed in various UpToDate topics on gastrointestinal bleeding:

- (See "Overview of the treatment of bleeding peptic ulcers", section on 'Risk factors for persistent or recurrent bleeding'.)

- (See "Approach to acute upper gastrointestinal bleeding in adults", section on 'Risk stratification'.)
- (See "Methods to achieve hemostasis in patients with acute variceal hemorrhage", section on 'Natural history and prognosis with treatment'.)
- (See "Colonic diverticular bleeding", section on 'Risk of rebleeding and complications'.)

Patients without bleeding — When urgent endoscopic procedures are required in anticoagulated patients who are not actively bleeding (eg, patients with acute cholangitis from biliary obstruction), management options include a temporary, low risk endoscopic intervention (ie, biliary stent without sphincterotomy) in order to delay the need for a procedure that carries a high risk of bleeding (table 2). (See "Post-endoscopic retrograde cholangiopancreatography (ERCP) bleeding", section on 'Preventive strategies'.)

If a high-risk endoscopic intervention cannot be delayed, agents that quickly reverse anticoagulation can be administered if the risk of bleeding outweighs the risk of thrombotic events. The management of anticoagulated patients who need an urgent, high-risk endoscopic intervention for conditions other than gastrointestinal bleeding (eg, acute cholangitis) is similar to the management of patients who need urgent endoscopic treatment for bleeding. (See 'Patients with bleeding' above.)

SPECIAL POPULATIONS

Patients with prosthetic heart valves — Anticoagulation management for patients with prosthetic heart valves is discussed separately. (See "Anticoagulation for prosthetic heart valves: Management of bleeding and invasive procedures".)

Patients with renal insufficiency on direct oral anticoagulants (DOACs) — Patients with renal insufficiency who take DOACs require a longer discontinuation period prior to high-risk endoscopic procedures.

Because of the predominantly renal excretion (>80 percent) of dabigatran, the hold time varies depending on the patient's creatinine clearance (CrCl):

- CrCl 30 to 49 mL/min: Hold dabigatran for at least three days prior to the procedure
- CrCl <30 mL/min (ie, drug half-life is >24 hours): Hold dabigatran for at least five to seven days prior to the procedure

Because other DOACs (ie, edoxaban, rivaroxaban and apixaban) have ≤50 percent renal excretion, special dose adjustment is needed only for patients with severe renal impairment

(CrCl<30 mL/min). These DOACs are held for two to three days prior to high-risk procedures in such patients [1].

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Endoscopy preparation, sedation, and special considerations".)

SUMMARY AND RECOMMENDATIONS

- **General principles –** The probability of a thromboembolic complication following reversal or discontinuation of anticoagulation depends upon the preexisting condition for which the medication was prescribed (table 1). (See 'Estimate thromboembolic risk' above and "Perioperative management of patients receiving anticoagulants", section on 'Estimating thromboembolic risk'.)

  The risk of bleeding from endoscopic procedures can be classified as low or high. In general, diagnostic procedures are low risk, whereas therapeutic procedures are high risk (table 2). (See 'Estimate bleeding risk' above and "Gastrointestinal endoscopy in patients with disorders of hemostasis", section on 'Estimating procedure-related bleeding risk'.)

  We consult with the clinician and/or clinical service who are managing the patient's long-term anticoagulation (eg, cardiologist, neurologist, anticoagulation clinic) prior to electively interrupting anticoagulation therapy. (See 'Specialty consultation' above.)

- **Elective procedures**

  - **Preprocedure management –** Most patients require no interruption in anticoagulation prior to low-risk procedures (algorithm 1 and table 2). For patients taking vitamin K antagonists (eg, warfarin), we confirm that the international normalized ratio (INR) is ≤2.5 prior to low risk, elective procedures. We suggest delaying the procedure until it is below that threshold (**Grade 2C**). (See 'Low risk procedures' above.)

    In patients undergoing high-risk endoscopic procedures, we discontinue long-term anticoagulation (algorithm 1). Vitamin K antagonists (eg, warfarin) are discontinued five days before a high-risk procedure, and direct oral anticoagulants (eg, dabigatran,

rivaroxaban, apixaban, or edoxaban) are discontinued one to two days before a high-risk procedure in patients with normal renal function. While warfarin is held for high-risk procedures, indications for bridging anticoagulation with a heparin product before and after the procedure depends on the patient's risk of thromboembolism. Bridging anticoagulation is not necessary for patients at low risk for thromboembolism, but may be warranted in certain high-risk patients. (See 'High or uncertain risk procedures' above and "Perioperative management of patients receiving anticoagulants".)

- **Resuming anticoagulation –** The time interval prior to resuming anticoagulation depends on the specific lesion, specific intervention, accessibility of the endoscopic site, and degree of difficulty that was required to achieve hemostasis (algorithm 1). (See 'High-risk procedures' above and 'High or uncertain risk procedures' above.)

- **Urgent procedures –** For patients with gastrointestinal bleeding, the risk of reversing anticoagulation should be weighed against the risk of continued bleeding without reversal. Anticoagulants are held in patients with acute gastrointestinal bleeding, while the use of reversal agents depends on the severity of bleeding, the characteristics of the specific anticoagulant (eg, half-life), and the availability of the reversal agent (table 4A-B). For patients on warfarin, we proceed with nonelective endoscopy when the target INR ranges between 1.5 and 2.5, based on limited data and the endoscopist's preference. (See 'Urgent procedures' above.)

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Topic 2609 Version 38.0

GRAPHICS

Perioperative thrombotic risk

Thrombotic risk	Indication for anticoagulant therapy		
	Mechanical heart valve	Atrial fibrillation	VTE
High thrombotic risk*	Any mitral valve prosthesis Any caged-ball or tilting disc aortic valve prosthesis Recent (within 6 months) stroke or transient ischemic attack	$CHADS_2$ score 5-6 CHA_2DS_2-VASc score 7-9 Recent (within 3 months) stroke or transient ischemic attack Rheumatic valvular heart disease	Recent (within 3 months) VTE Severe thrombophilia (eg, deficiency of protein C, protein S, or antithrombin; antiphospholipid antibodies; multiple abnormalities)
Moderate thrombotic risk	Bileaflet aortic valve prosthesis and 1 or more of the of following risk factors: atrial fibrillation, prior stroke or transient ischemic attack, hypertension, diabetes, congestive heart failure, age >75 years	$CHADS_2$ score 3-4 CHA_2DS_2-VASc score 4-6	VTE within the past 3 to 12 months Nonsevere thrombophilia (eg, heterozygous factor V Leiden or prothrombin gene mutation) Recurrent VTE Active cancer (treated within 6 months or palliative)
Low thrombotic risk	Bileaflet aortic valve prosthesis without atrial fibrillation and no other risk factors for stroke	$CHADS_2$ score 0-2 CHA_2DS_2-VASc score 0-3 (assuming no prior stroke or transient ischemic attack)	VTE >12 months previous and no other risk factors

The risk classification is largely based on indirect evidence and is intended to be used as a starting point to estimate risk. Patient-specific factors and clinical judgment should also be incorporated into the risk estimate. The source guideline used $CHADS_2$ scores for risk estimation; additional information from CHA_2DS_2-VASc scores may also inform risk, but these scores have not been directly

compared in a clinical trial. Refer to UpToDate topics on perioperative anticoagulation management for details.

VTE: venous thromboembolism; $CHADS_2$: congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, and stroke or transient ischemic attack; CHA_2DS_2-VASc: congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism (2 points), vascular disease (peripheral artery disease, myocardial infarction, or aortic plaque), age 65 to 74 years, sex category female.

* Very high-risk patients may also include those with a prior stroke or transient ischemic attack occurring <3 months before the planned surgery and a $CHADS_2$ score >5 or CHA_2DS_2-VASc score >6 (those with prior thromboembolism during temporary interruption of anticoagulation, or those undergoing certain types of surgery associated with an increased risk for stroke or other thromboembolism [eg, cardiac valve replacement, carotid endarterectomy, major vascular surgery]).

Modified from Douketis JD, Spyropoulos AC, Spencer FA, et al. Perioperative management of antithrombotic therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012; 141(2 Suppl):e326S. Copyright © 2012. Reproduced with permission from the American College of Chest Physicians.

Graphic 86930 Version 7.0

Procedure-related bleeding risk from gastrointestinal procedures

Higher-risk procedures
Polypectomy*
Biliary or pancreatic sphincterotomy
Treatment of varices
PEG placement[¶]
Therapeutic balloon-assisted enteroscopy
EUS with FNA[Δ]
Endoscopic hemostasis
Tumor ablation
Cystgastrostomy
Ampullary resection
EMR
Endoscopic submucosal dissection
Pneumatic or bougie dilation
PEJ
Low-risk procedures
Diagnostic (EGD, colonoscopy, flexible sigmoidoscopy) including mucosal biopsy
ERCP with stent (biliary or pancreatic) placement or papillary balloon dilation without sphincterotomy
Push enteroscopy and diagnostic balloon-assisted enteroscopy
Capsule endoscopy
Enteral stent deployment (controversial)
EUS without FNA
Argon plasma coagulation
Barrett's ablation

EGD: esophagogastroduodenoscopy; ERCP: endoscopic retrograde cholangiopancreatography; PEG: percutaneous endoscopic gastrostomy; EUS: endoscopic ultrasound; FNA: fine-needle aspiration; EMR: endoscopic mucosal resection; PEJ: percutaneous endoscopic jejunostomy.

* Among patients undergoing colonic polypectomy, the size of the polyp influences the risk of bleeding, and it may be more appropriate to categorize polyps less than 1 cm in size as low risk for bleeding.

¶ PEG on aspirin or clopidogrel therapy is low risk. Does not apply to dual antiplatelet therapy.

Δ EUS-FNA of solid masses on aspirin/nonsteroidal anti-inflammatory drugs is low risk.

Reproduced from: ASGE Standards of Practice Committee, Acosta RD, Abraham NS, et al. The management of antithrombotic agents for patients undergoing GI endoscopy. Gastrointest Endosc 2016; 83:3. Table used with the permission of Elsevier Inc. All rights reserved.

Graphic 50700 Version 8.0

Comparison of the $CHADS_2$ and CHA_2DS_2-VASc risk stratification scores for patients with nonvalvular AF

Definition and scores for $CHADS_2$ and CHA_2DS_2-VASc		Stroke risk stratification with the $CHADS_2$ and CHA_2DS_2-VASc scores	
$CHADS_2$ acronym[1]	**Score**	**$CHADS_2$ acronym**	**Unadjusted ischemic stroke rate (% per year)***
Congestive HF	1	0	0.6
Hypertension	1	1	3.0
Age ≥75 years	1	2	4.2
Diabetes mellitus	1	3	7.1
Stroke/TIA/TE	2	4	11.1
Maximum score	6	5	12.5
		6	13.0
CHA_2DS_2-VASc acronym[2]	**Score**	**CHA_2DS_2-VASc acronym**	**Unadjusted ischemic stroke rate (% per year)***
Congestive HF	1	0	0.2
Hypertension	1	1	0.6
Age ≥75 years	2	2	2.2
Diabetes mellitus	1	3	3.2
Stroke/TIA/TE	2	4	4.8
Vascular disease (prior MI, PAD, or aortic plaque)	1	5	7.2
Age 65 to 74 years	1	6	9.7
Sex category (ie, female sex)	1	7	11.2
Maximum score	9	8	10.8
		9	12.2

AF: atrial fibrillation; $CHADS_2$: Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, prior Stroke or TIA or thromboembolism (doubled); CHA_2DS_2-VASc: Congestive heart failure, Hypertension, Age ≥75 years (doubled), Diabetes mellitus, prior Stroke or TIA or thromboembolism (doubled), Vascular disease, Age 65 to 74 years, Sex category; HF: heart failure; TIA: transient ischemic attack; TE: thromboembolism; MI: myocardial infarction; PAD: peripheral artery disease.

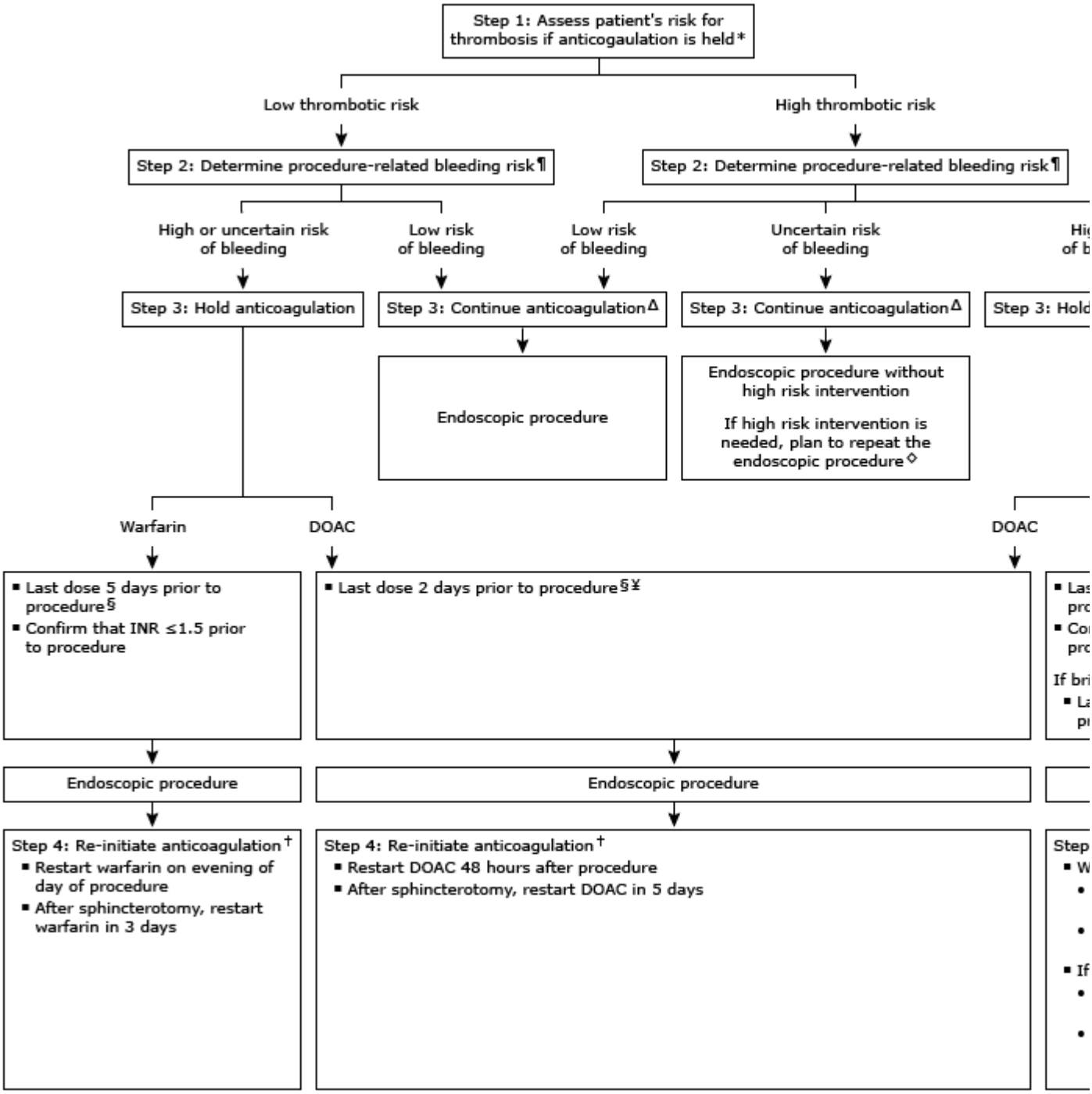
* These unadjusted (not adjusted for possible use of aspirin) stroke rates were published in 2012[3]. Actual rates of stroke in contemporary cohorts might vary from these estimates.

References:

1. *Gage BF, Waterman AD, Shannon W, et al. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. JAMA 2001; 285:2864.*
2. *Lip GYH, Nieuwlaat R, Pisters R, et al. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. Chest 2010; 137:263.*
3. *Friberg L, Rosenqvist M, Lip GY. Evaluation of risk stratification schemes for ischaemic stroke and bleeding in 182 678 patients with atrial fibrillation: the Swedish Atrial Fibrillation cohort study. Eur Heart J 2012; 33:1500.*

Graphic 94752 Version 15.0

Management of anticoagulation for patients scheduled for elective endoscopic



This flowchart does not apply to patients with prosthetic heart valves and does not substitute for the clinical treating specialist. Refer to UpToDate content on managing anticoagulated patients in the periprocedure se

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LMW: low molecular weight; DOAC: direct oral anticoagulant; INR: international normalized ratio; ERCP: end cholangiopancreatography.

* Consult the clinician who is managing the patient's long-term anticoagulation prior to any interruption in t conditions that confer a low or moderate thrombotic risk include atrial fibrillation with CHA2DS2-VASc score thromboembolism greater than 12 months previously. Examples of conditions that confer a high thrombotic

fibrillation with CHA2DS2-VASc score ≥4 or venous thromboembolism within the past 12 months. Refer to U discussion on estimating thrombotic risk.

¶ Examples of low risk procedures include upper gastrointestinal endoscopy or colonoscopy, including muc of high risk procedures include colonoscopy with polypectomy of large polyp (≥1cm) or ERCP with sphincter procedure with uncertain risk is a screening colonoscopy.

Δ For patients on warfarin, confirm that INR is ≤2.5 prior to procedure.

◇ If a lesion is found that requires a high risk intervention, the procedure is repeated while following peripr for high risk patients undergoing a high risk procedure.

§ The day of the procedure is regarded as day 0. The day of the last dose is determined by counting each ho with the procedure day (day 0). For example, warfarin is held for 5 days prior to the procedure. If the proced last dose of warfarin will be taken on day –5 (ie, the Wednesday before the procedure).

¥ For patients with renal impairment, a longer discontinuation period may be required. Please refer to UpTo for patients with renal impairment.

‡ Some patients at high risk for thromboembolism require bridging anticoagulation. Refer to other UpToDat when bridging therapy is warranted and how it is given before the procedure and resumed after the proced

† The decision to restart anticoagulation is contingent upon achieving hemostasis as determined by the end who undergo ERCP with sphincterotomy, a longer delay is needed prior to resuming anticoagulation becaus of bleeding.

Graphic 119161 Version 1.0

Emergency reversal of anticoagulation from warfarin for life-threatening hemorrhage in adults: Suggested approaches based upon available resources

A. If 4-factor prothrombin complex concentrate (4F PCC) is available (preferred approach):
1. Give 4F PCC* 1500 to 2000 units¶ IV over 10 minutes. Check INR 15 minutes after completion of the infusion. If INR is not ≤1.5, give additional 4F PCC (refer to topic or drug reference for details).
2. Give vitamin K 10 mg IV over 10 to 20 minutes.
B. If 3-factor prothrombin complex concentrate (3F PCC) is available but 4F PCC is not available:
1. Give 3F PCC* 1500 to 2000 units¶ IV over 10 minutes. Check INR 15 minutes after completion of the infusion. If INR is not ≤1.5, give additional 3F PCC (refer to topic or drug reference for details).
2. Give Factor VIIa 20 mcg/kg IV **OR** give FFP 2 units IV by rapid infusion. Factor VIIa may be preferred if volume overload is a concern.
3. Give vitamin K 10 mg IV over 10 to 20 minutes.
C. If neither 3F PCC nor 4F PCC is available:
1. Give FFP 2 units IV by rapid infusion. Check INR 15 minutes after completion of infusion. If INR ≥1.5, administer 2 additional units of FFP IV rapid infusion. Repeat process until INR ≤1.5. May wish to administer loop diuretic between FFP infusions if volume overload is a concern.
2. Give vitamin K 10 mg IV over 10 to 20 minutes.

These products and doses are for use in life-threatening bleeding only. Evidence of life-threatening bleeding and over-anticoagulation with a vitamin K antagonist (eg, warfarin) are required. Anaphylaxis and transfusion reactions can occur.

It may be reasonable to thaw 4 units of FFP while awaiting the PT/INR. The transfusion service may substitute other plasma products for FFP (eg, Plasma Frozen Within 24 Hours After Phlebotomy [PF24]); these products are considered clinically interchangeable. PCC will reverse anticoagulation within minutes of administration; FFP administration can take hours due to the volume required; vitamin K effect takes 12 to 24 hours, but administration of vitamin K is needed to counteract the long half-life of warfarin. Subsequent monitoring of the PT/INR is needed to guide further therapy. Refer to topics on warfarin reversal in individual situations for further management.

PCC: unactivated prothrombin complex concentrate; 4F PCC: PCC containing coagulation factors II, VII, IX, X, protein S and protein C; 3F PCC: PCC containing factors II, IX, and X and only trace factor VII; FFP: fresh frozen plasma; PT: prothrombin time; INR: international normalized ratio; FEIBA: factor eight inhibitor bypassing agent.

* Before use, check product label to confirm factor types (3 versus 4 factor) and concentration. Activated complexes and single-factor IX products (ie, FEIBA, AlphaNine, Mononine, Immunine, BeneFix) are NOT used for warfarin reversal.

¶ PCC doses shown are those suggested for initial treatment of emergency conditions. Subsequent treatment is based on INR and patient weight if available. Refer to topic and Lexicomp drug reference included with UpToDate for INR-based dosing.

Graphic 89478 Version 10.0

Direct oral anticoagulant-associated bleeding reversal strategies

Type of bleeding	Agent	Possible interventions
Life-threatening or imminently fatal bleeding (eg, intracranial, retroperitoneal, compartment syndrome, massive gastrointestinal)	Dabigatran (Pradaxa)	▪ Idarucizumab ▪ Activated PCC* (eg, FEIBA) ▪ Antifibrinolytic agent (eg, tranexamic acid, epsilon-aminocaproic acid) ▪ Anticoagulant discontinuation ▪ Oral activated charcoal (if last dose within prior two hours) ▪ Hemodialysis ▪ RBC transfusions if needed for anemia ▪ Platelet transfusions if needed for thrombocytopenia or impaired platelet function (eg, due to aspirin) ▪ Surgical/endoscopic intervention if appropriate
	Rivaroxaban (Xarelto), apixaban (Eliquis), edoxaban (Lixiana)	▪ Andexanet alfa (AndexXa) **or** a 4-factor unactivated PCC (eg, Kcentra) ▪ Antifibrinolytic agent (eg, tranexamic acid, epsilon-aminocaproic acid) ▪ Anticoagulant discontinuation ▪ Oral activated charcoal (if last dose recent enough) ▪ RBC transfusions if needed for anemia ▪ Platelet transfusions if needed for thrombocytopenia or impaired platelet function (eg, due to aspirin) ▪ Surgical/endoscopic intervention if appropriate
Minor bleeding (eg, epistaxis, uncomplicated soft tissue bleeding, minor [slow] gastrointestinal bleeding)	Dabigatran (Pradaxa)	▪ Local hemostatic measures ▪ Possible anticoagulant discontinuation • Half-life (normal renal function¶): 12 to 17 hours ▪ Possible antifibrinolytic agent (eg, tranexamic acid, epsilon-aminocaproic acid)
	Rivaroxaban (Xarelto), apixaban (Eliquis), edoxaban (Lixiana)	▪ Local hemostatic measures ▪ Possible anticoagulant discontinuation • Half-lives (normal renal function¶):

		◦ Rivaroxaban 5 to 9 hours ◦ Apixaban 8 to 15 hours ◦ Edoxaban 6 to 11 hours ▪ Possible antifibrinolytic agent (eg, tranexamic acid, epsilon-aminocaproic acid)

The table describes measures that may be used to manage bleeding associated with DOACs. Clinical judgment is essential in all cases of DOAC-associated bleeding in order to assess the risks of bleeding and weigh these against the risks of thrombosis if anticoagulation is discontinued or reversed. Refer to UpToDate topics on the use of direct thrombin inhibitors and direct factor Xa inhibitors and management of DOAC-associated bleeding for further details and dosing. The onset of all of the agents discussed herein is approximately 2 to 4 hours.

PCC: prothrombin complex concentrate; FEIBA: factor eight inhibitor bypassing activity; RBC: red blood cell; DOAC: direct oral anticoagulant.

* Use activated PCC only if idarucizumab is unavailable and/or if continued bleeding is reasonably likely to be fatal within hours.

¶ The anticoagulant effect of these agents (especially dabigatran) will dissipate more slowly as renal function declines. Severe hepatic failure may also prolong the half-life for apixaban, edoxaban, and rivaroxaban.

Graphic 96230 Version 18.0

Endoscopic predictors of recurrent peptic ulcer hemorrhage[1,2]

Endoscopic stigmata of recent hemorrhage	Prevalence, percent	Risk of rebleeding on medical management, percent
Active arterial bleeding (Forrest Ia)	12% (arterial bleeding + oozing)	55 (arterial bleeding + oozing)
Oozing without visible vessel (Forrest Ib)		
Non-bleeding visible vessel (Forrest IIa)	8	43
Adherent clot (Forrest IIb)	8	22
Flat spot (Forrest IIc)	16	10
Clean ulcer base (Forrest III)	55	5

References:

1. Katschinski B, Logan R, Davies J, et al. Prognostic factors in upper gastrointestinal bleeding. Dig Dis Sci 1994; 39:706.
2. Laine L, Jensen DM. Management of patients with ulcer bleeding. Am J Gastroenterol 2012; 107:345.

Graphic 78607 Version 8.0

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Patrick S Kamath, MD No relevant financial relationship(s) with ineligible companies to disclose. **John R Saltzman, MD, FACP, FACG, FASGE, AGAF** No relevant financial relationship(s) with ineligible companies to disclose. **Kristen M Robson, MD, MBA, FACG** No relevant financial relationship(s) with ineligible companies to disclose.

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