More than 6 million persons in the United States are taking anticoagulants for a number of conditions, including venous thromboembolism and atrial fibrillation. These patients have an increased risk of bleeding, which is associated with a greater risk of morbidity and mortality. This Expert Consensus Decision Pathway from the American College of Cardiology (ACC) aims to provide physicians with decision-making assistance for managing bleeding events in patients taking anticoagulants.

**Major Bleeding Events**

Bleeding is considered to be a major event if it occurs at a critical site, there is accompanying hemodynamic instability, or there is bleeding with a decrease in hemoglobin of at least 2 g per dL (20 g per L) or requiring at least 2 units of red blood cells. Critical site bleeding includes airway, extremity, intra-abdominal, and intracranial and other central nervous system bleeding; pericardial tamponade; hemothorax; and retroperitoneal hematoma. Symptoms of airway bleeding include hemoptysis, shortness of breath, epistaxis, and hypoxia. Symptoms of extremity bleeding include pain, swelling, pallor, paresthesia, weakness, weak pulse, and decreased range of motion, and can result in compartment syndrome, paralysis, joint damage, and limb loss. Symptoms of intra-abdominal bleeding include pain, distension, hypotension, and tachycardia. Symptoms of intracranial bleeding include intense headache, emesis, and neurologic signs such as reduced level of consciousness, ataxia, aphasia, vertigo, and seizures. Other central nervous system bleeding sites include the eyes (e.g., pain, vision changes or blindness) and spine (e.g., pain, weakness, bowel or bladder dysfunction). Symptoms of pericardial tamponade include shortness of breath, tachypnea, hypotension, jugular venous distention, tachycardia, and muffled heart sounds. Symptoms of hemothorax include tachypnea, tachycardia, and hypotension. Symptoms of retroperitoneal hematoma include pain, tachycardia, and hypotension, and a hematoma can result in femoral neuropathy.

**Laboratory Measurements**

When a patient presents with bleeding or requires an emergency procedure, laboratory measurement of anticoagulant activity can aid in the assessment. A prothrombin time and activated partial thromboplastin time should be ordered. If specialized assays are available, these tests can
include dilute thrombin time, ecarin clotting time, and ecarin chromogenic assay for patients on dabigatran (Pradaxa); and a chromogenic anti-factor Xa test for patients on apixaban (Eliquis), edoxaban (Savaysa), or rivaroxaban (Xarelto).

When specialized assays are not available, thrombin time and activated partial thromboplastin time can generally assess drug levels in patients taking dabigatran. For patients on apixaban, edoxaban, or rivaroxaban, prothrombin time is used to assess therapy.

**Withholding Anticoagulants**

Major and nonmajor bleeding requiring hospitalization, surgery, or transfusion should be controlled and oral anticoagulants discontinued. In patients with nonmajor bleeding, temporary discontinuation of anticoagulants may be necessary. Factors affecting this decision include whether the anticoagulation is therapeutic or supratherapeutic, upcoming invasive procedures, the patient’s underlying bleeding risk, concern for slow bleed or need for further evaluation of clinical impact of bleed, presence of anemia requiring transfusion, and medical comorbidities. Collaborative evaluation of future bleeding risk vs. benefit of anticoagulation therapy in patients with ongoing thrombotic risk is needed before resuming therapy. A delay in resuming therapy is recommended if the bleeding occurred at a critical site, the patient is at increased risk of death or disability from rebleeding, an invasive procedure is needed, or the patient prefers not to resume therapy.

**Using Reversal Agents**

In patients with a major bleeding event, even if it is not at a critical site or life threatening, local therapy, manual compression, and supportive care should be provided. Any antiplatelet agents should be discontinued, and those receiving vitamin K agonists should also be given intravenous vitamin K. Any comorbidities that could contribute to bleeding should be managed, and surgical management of bleeding should be considered. Those with major life-threatening bleeding or bleeding at a critical site, including patients with an uncontrollable major bleeding event, should also receive a reversal agent. Available agents include 4-factor prothrombin complex concentrate for warfarin (Coumadin), dabigatran (second line), apixaban, edoxaban, and rivaroxaban; activated prothrombin complex concentrate as a second-line option for dabigatran, apixaban, edoxaban, and rivaroxaban; idarucizumab (Praxbind) for dabigatran; and plasma for warfarin if 4-factor prothrombin complex concentrate is not available.

Patients with nonmajor bleeding that requires hospitalization, surgery, or transfusion and who are on vitamin K agonists should receive oral or intravenous vitamin K. Those not on vitamin K agonists should not receive a reversal agent. Local therapy, manual compression, and supportive care should be provided; antiplatelets discontinued (if appropriate); contributing comorbidities managed; and surgery considered. For all other nonmajor bleeding, anticoagulants may be continued if clinically indicated; however, these patients should also receive local therapy and manual compression. Antiplatelet treatment should be reassessed to determine if it should be discontinued, comorbidities should be managed, and anticoagulant dosing reevaluated.

**Guideline source:** American College of Cardiology

**Evidence rating system used?** No

**Systematic literature search described?** No

**Guideline developed by participants without relevant financial ties to industry?** No

**Recommendations based on patient-oriented outcomes?** Yes

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