CHAPTER 72

Procedures in the Setting of Anticoagulation

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INTRODUCTION

Performing an invasive procedure on an anticoagulated emergency department (ED) patient can be challenging for the emergency provider (EP). Regardless of the procedure, some anticoagulated patients are at potential significant risk of hemorrhage from the procedure. However, emergency reversal of anticoagulation in order to perform the procedure may also place the patient at risk for serious thrombotic complications. When deciding to perform a procedure on an anticoagulated ED patient, the EP must weigh the risks of bleeding with the risk of disrupting anticoagulation, emergency reversal of anticoagulation, and delaying a potentially critical intervention. If the procedure is not needed for life-saving therapy, postponing the procedure or providing empiric treatment may be a reasonable choice. In contrast, emergency procedures to reverse an imminent life-threatening condition should never be withheld and emergency reversal of anticoagulation may be required. This chapter reviews current literature and recommendations for select ED procedures such as lumbar puncture, central venous catheterization, arthrocentesis, paracentesis, thoracentesis, and tube thoracostomy in the anticoagulated patient.

ASSESSING RISK OF BLEEDING AND THROMBOSIS

All anticoagulants inhibit stable clot formation and increase the risk of bleeding. Routine coagulation testing, that is prothrombin time (PT), partial thromboplastin time (PTT), international normalized ratio (INR), and platelet count, in anticoagulated patients, is recommended prior to performing an invasive procedure. Although laboratory tests to determine drug presence, drug concentration, and level of anticoagulant effect can be useful in the assessment of bleeding risk, standard coagulation assays accurately monitor the degree of anticoagulation for only a few agents. PT and INR conveniently assay the extrinsic pathway to monitor the quantitative effect of warfarin therapy. PTT or activated partial thromboplastin time (aPTT) accurately monitors the anticoagulant effect of heparin. Newer nonvitamin K antagonist oral anticoagulants (NOACs) were developed to have predictable pharmacokinetics with minimal interactions to avoid the need for routine laboratory testing. Coagulation assays to quantify the effect or presence of a NOAC would be useful in many clinical circumstances such as in active bleeding, suspected overdose, and the perioperative period, but do not exist for many. The direct measurement of drug concentration is not suitable in clinical practice because of the time required to perform the laboratory analysis. Standard coagulation assays can be useful in extreme scenarios, but are generally insufficient in determining drug concentration or degree of anticoagulant effect of NOACs (Table 72.1).

Normal thrombin time is suitable for excluding significant dabigatran levels but too sensitive for determining the degree of anticoagulant effect.[1,2] Dilute thrombin time, ecarin chromogenic assay, and ecarin clotting time may be useful to determine the degree of anticoagulant effect, but is not standardized across laboratories. Although using standard coagulation assays to quantify dabigatran effect is not recommended, an elevated PT/INR suggests a supratherapeutic dabigatran effect, and a normal PTT excludes it.[2] Unfortunately, none of these tests are accurate predictors of bleeding risk with dabigatran and patients may have bleeding when these tests are within the normal range.[3]

Anti-factor Xa activity is valuable to determine the effect of factor Xa inhibitors such as rivaroxaban and apixaban, but this test is not widely available. Although it is not recommended to use standard coagulation assays to quantify drug effect, a normal PT and INR level virtually excludes supratherapeutic rivaroxaban effect.[2]

For patients on warfarin, understanding how INR correlates to the risk of bleeding is important. Spontaneous bleeding events are uncommon when the INR is normal or within a therapeutic range (i.e., 2 to 3).[4] The relative risk for bleeding with an INR between 3 and 5 is 2.7 (95% confidence interval [CI] 1.8–3.9). However, when the INR is above 5, the relative risk of a spontaneous hemorrhagic event increases dramatically to 21.8 (95% CI 12.1–39.4). These findings are similar to a previous retrospective review in 1995 that also showed adverse events occurred in 75 per 100 patient-years for an INR greater than or equal to 6.5.[5] Patients with severe coagulopathy (INR greater than 9) have a poor prognosis, with 67% experiencing spontaneous hemorrhagic events and a 74% mortality rate.[6]

Patients without a history of bleeding or anticoagulant use do not require routine coagulation studies prior to performing a procedure unless history or physical examination suggest a bleeding disorder or use of anticoagulation.[7] A 2005 systematic review failed to demonstrate the utility of routine coagulation studies on nonanticoagulated patients prior to the performance of a procedure.[8] Abnormal laboratory findings such as thrombocytopenia, an elevated INR, or other coagulation abnormalities are not necessarily absolute contraindications to performing an invasive procedure. Numerous studies have demonstrated that select procedures can safely be performed even in the setting of anticoagulation with a vitamin K antagonist (VKA).[9–12] Determining a patient's risk for bleeding requires examination of both the procedure to be performed, the anticoagulant medication, and the level of anticoagulation. Unfortunately, there are no validated systems available to quantify risk of bleeding.

The risk of thrombosis after anticoagulant reversal is significant for a subset of ED patients. These patients include those with a recent diagnosis of pulmonary embolism, significant clot burden, or those with mechanical hardware such as a prosthetic cardiac valve. When clinically feasible, it is best to allow the anticoagulant effect of a medication to wane rather than emergently reversing the medication in these patients. This approach is rarely possible in the ED, so timing of the procedure should be coordinated with the inpatient provider if the patient requires admission.

Many procedures report contraindications with severe coagulopathy (INR greater than 9) and disseminated intravascular coagulation (DIC). Proper coagulation is significantly

TABLE 72.1 Summary of Anticoagulant Testing and Management

ANTICOAGULANT	LABORATORY TESTING TO CONSIDER	PHARMACOLOGY	AGENTS TO REVERSAL OF REMOVAL
Vitamin K Antagonists			
Low-molecular-weight heparin (LMWH)	Anti-Factor Xa	3–6 hours	Consider protamine sulfate or rVIIa in life-threatening bleeding
Unfractionated heparin	PTT, aPTT	60–90 minutes	Protamine sulfate
Warfarin	PT/INR	20–60 hours (duration of action 2–5 days)	Vitamin K, fresh frozen plasma (FFP), prothrombin complex concentrate (PCC), recombinant Factor VIIa
Direct Thrombin Inhibitors			
Argatroban	Activated clotting time (ACT), aPTT	39–51 minutes	Consider hemodialysis, rFVIIa or FFP but generally not indicated due to short half-life
Dabigatran	Thrombin time (TT), dilute TT, ecarin chromogenic assay (ECA), and ecarin clotting time (ECT), PT/INR, PTT	12–17 hours	Idaruczimab, PCC, hemodialysis
Factor Xa Inhibitors			
Apixaban Rivaroxaban	Anti-Factor Xa, PT/INR	12 hours 5–9 hours	PCC
Anti-Platelet Agents			
Aspirin Clopidogrel Prasugrel Ticgrelor	Platelet function testing	Duration of action 7–10 days, irreversibly inhibits platelet 7–10 hours	Platelet transfusion

aPTT, Activated partial thromboplastin time; *INR*, international normalized ratio; *PT*, prothrombin time; *PTT*, partial thromboplastin time.

disrupted in these clinical settings and invasive procedures may lead to severe bleeding. However, life-saving measures such as thoracostomy, central venous catheterization, and endotracheal intubation are sometimes required even in these severe settings. Additional life-saving procedures that may carry a high risk of bleeding in the setting of anticoagulation, but should not be withheld, include defibrillation and pericardiocentesis. The gravity of the clinical scenario is important to keep in mind when weighing the risk of performing a procedure in the setting of anticoagulation.

Limited data are available on the safety of performing procedures on patients taking newer NOACs. These NOACs may confer the same, less, or increased risk of bleeding as traditional VKA agents. The lack of an effective reversal agent for many of the NOACs is another factor that complicates the decision to perform a procedure in the setting of anticoagulation. Fortunately, many of the NOACs have a duration of action that is less than the traditional VKAs.

MANAGEMENT OF ANTICOAGULANT ASSOCIATED BLEEDING

Although periprocedural bleeding is typically not life threatening and can often be controlled with direct pressure, predicting which anticoagulated patients will bleed from a procedure is difficult. Furthermore, the simple act of controlling periprocedural bleeding may not entirely end the risk of serious harm. For instance, periprocedural bleeding with percutaneous coronary intervention is associated with an increased short- and long-term morbidity and mortality, including major adverse cardiovascular events and readmission rates well after the bleeding is controlled.[13,14]

When managing spontaneous, periprocedural, or postprocedural bleeding associated with anticoagulation, there are a few principles to consider. Most importantly, never withhold emergency life-saving procedures such as endotracheal intubation, tube thoracostomy, cardiac defibrillation, pericardiocentesis, or vascular access when necessary.

Stabilization with supportive treatments such as oxygenation, intravascular volume resuscitation, and repletion of blood products via transfusion are the initial steps of assessment and management of bleeding in the anticoagulated patient. Patients with prolonged or severe bleeding may have presenting symptoms in various stages of circulatory shock. Poor blood supply and intravascular volume leads to poor tissue perfusion. Cellular hypoxia, damage, and resulting inflammatory response from hypoperfusion can exacerbate the patient's clinical status. Adequate resuscitation and stabilization is key to the initial phase of management.

Hemostatic measures such as direct compression of a bleeding or oozing vessel, wound, or region should be performed concurrently with stabilization to prevent further blood loss. Additional measures may be needed to control bleeding when compression fails or when the bleeding originates from a noncompressible site. These measures include the use of topical hemostatic agents, systemic hemostatic agents (i.e., tranexamic acid), procedural intervention, operative management, or intraarterial embolization.

The clinician can assess the severity of coagulopathy with laboratory analysis. Patients may experience bleeding at subtherapeutic, therapeutic, or supratherapeutic levels of anticoagulation. Determining qualitative level of anticoagulation may help guide therapy. However, many anticoagulants do not have an associated diagnostic test that is accurate, timely, and clinically relevant to determine severity of coagulopathy like warfarin or heparin. Obtain routine coagulation assays (i.e., PT, PTT, and INR) when no relevant study exists. Routine coagulation assays may sometimes be helpful in determining the lack of a supratherapeutic anticoagulant effect but are often difficult to interpret.

When bleeding is severe, life-threatening, refractory to hemostatic efforts, or the coagulopathy is determined to be severe, restoring the ability to generate an effective clot by administration of an antidote, coagulation factor, blood product, or removal of the offending anticoagulant (i.e., hemodialysis) may be necessary. Consideration for the anticoagulant's duration of action is also important when deciding whether to reverse anticoagulation.

Withholding further doses of anticoagulation may be necessary after stabilization and disposition. When the clinical decision to withhold anticoagulant is not clear, consultation with the prescribing physician (e.g., cardiologist prescribing aspirin and clopidogrel for cardiac stent) or hematologist may be warranted.

Reversal of Anticoagulation

The decision to discontinue or reverse anticoagulation prior to a procedure is difficult. Although there are no validated data that can accurately stratify risk for peri- or postoperative thromboembolism, the American College of Chest Physicians (ACCP) has published guidelines that stratify patients into low-, moderate-, and high-risk groups.[15] These guidelines are listed in Table 72.2.

Risk factors that increase the likelihood of a thromboembolic event with anticoagulant disruption include a prosthetic heart valve, atrial fibrillation, recent cerebrovascular accident (CVA) or transient ischemic attack, recent venous thromboembolism (VTE), the presence of a VTE risk factor (i.e., protein C/S deficiency, antiphospholipid antibody), and a high $CHAD_2$ score (congestive heart failure, hypertension, age, diabetes mellitus, CVA).[15,16] Patients with mechanical valves are at higher risk for thromboembolic events when anticoagulation is disrupted than patients with bioprosthetic valves. Mitral valves present a higher risk of thromboembolic events than aortic prosthetic valves. The postoperative period just after (less than 3 months) mechanical valve placement is also a high-risk time for thromboembolic events.[16]

Procedures on patients with prosthetic valves typically require a delayed approach to operative management, except when there is an emergency. In general, discontinuing anticoagulation in a patient with a prosthetic valve is safer than reversal of anticoagulation to perform a procedure. Reversal of anticoagulation puts patients at higher risk for thromboembolic events than does simply discontinuing the anticoagulant. When possible, discontinue anticoagulation and delay invasive procedures on patients with prosthetic valves until coagulation status returns to near normal. For patients with low risk bioprosthetic valves that require discontinuation of anticoagulation, warfarin should be discontinued 48 to 72 hours prior to the procedure or until the

TABLE 72.2 Suggested Patient Risk Stratification for Perioperative Arterial or Venous Thromboembolism

	Indication for VKA Therapy		
RISK STRATUM	**MECHANICAL HEART VALVE**	**ATRIAL FIBRILLATION**	**VTE**
High	Any mitral valve prosthesis Older (caged-ball or tilting disc) aortic valve prosthesis Recent (within 6 mo) stroke or transient ischemic attack	CHADS2 score of 5 or 6 Recent (within 3 mo) stroke or transient ischemic attack, Rheumatic valvular heart disease	Recent (within 3 mo) VTE Severe thrombophilia (e.g., deficiency of protein C, protein S or antithrombin, antiphospholipid antibodies, or multiple abnormalities)
Moderate	Bileaflet aortic valve prosthesis and one of the following: atrial fibrillation, prior stroke or transient ischemic attack, hypertension, diabetes, congestive heart failure, age > 75 yr	CHADS2 score of 3 or 4	VTE within the past 3 to 12 mo; Nonsevere thrombophilic conditions (e.g., heterozygous factor V Leiden mutation, heterozygous factor II mutation); Recurrent VTE; Active cancer (treated within 6 mo or palliative)
Low	Bileaflet aortic valve prosthesis without atrial fibrillation and no other risk factors for stroke	CHADS2 score of 0 to 2 (and no prior stroke or transient ischemic attack)	Single VTE occurred 12 mo ago and no other risk factors

CHADS2, Congestive heart failure-hypertension-age-diabetes-stroke; *VTE*, venous thromboembolism.
From Douketis JD, Berger PB, Dunn AS, et al: The perioperative management of antithrombotic therapy: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition), *Chest* 133:299S, 2008.

INR drops below 1.5.[16] Anticoagulation may then be restarted 24 hours following the procedure. High-risk patients with prosthetic valves (e.g., mitral valve) require bridging therapy to reduce the time off anticoagulation.[16]

For patients taking VKAs that require reversal of anticoagulation for an urgent procedure, administration of oral vitamin K is recommended.[15] If more immediate reversal is required for a procedure, administration of fresh-frozen plasma or prothrombin complex concentrate in addition to oral vitamin K is recommended.[15] For patients taking antiplatelet agents such as aspirin or clopidogrel, platelet transfusion is recommended for reversal of the effect (Fig. 72.1).[15]

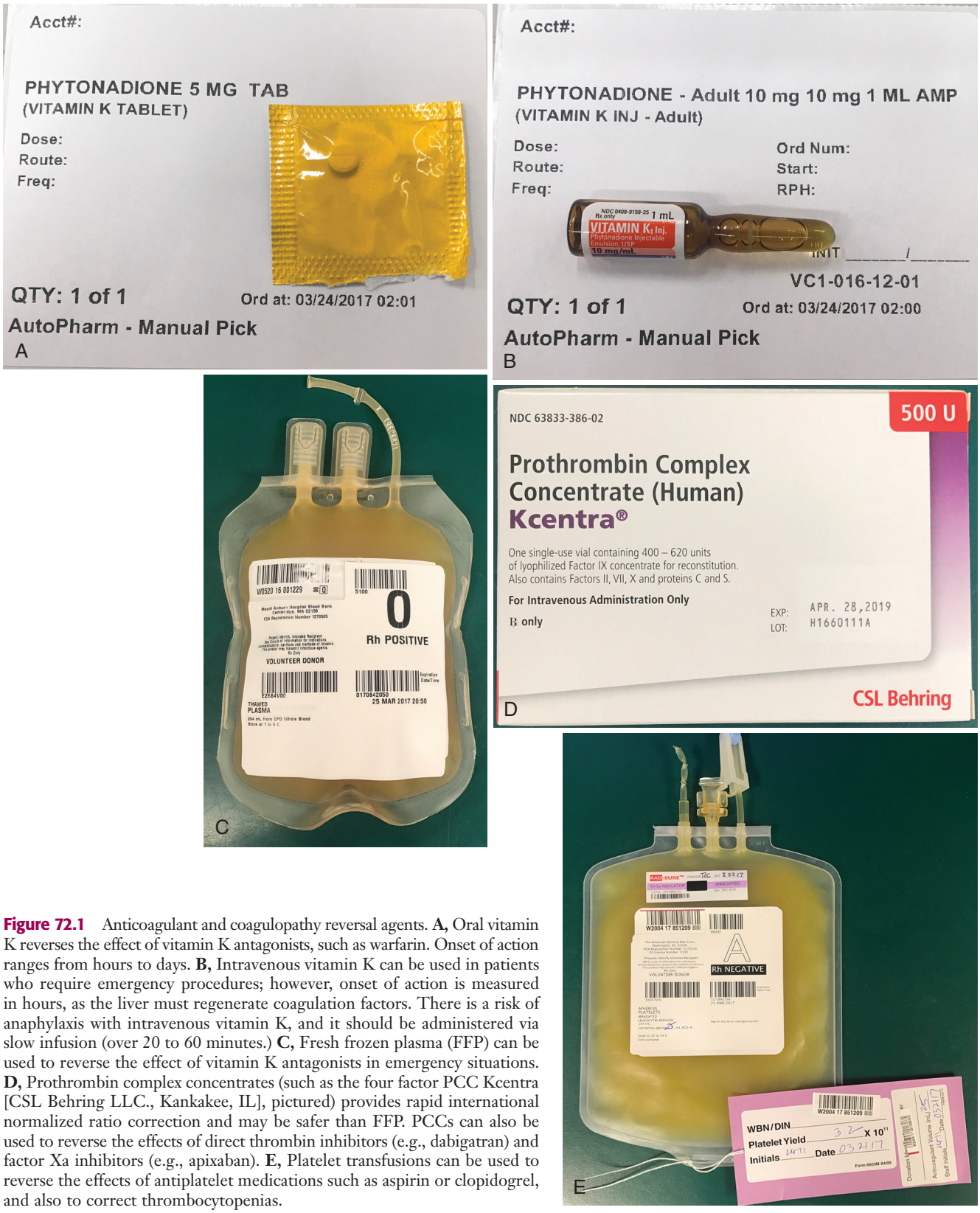

Figure 72.1 Anticoagulant and coagulopathy reversal agents. **A,** Oral vitamin K reverses the effect of vitamin K antagonists, such as warfarin. Onset of action ranges from hours to days. **B,** Intravenous vitamin K can be used in patients who require emergency procedures; however, onset of action is measured in hours, as the liver must regenerate coagulation factors. There is a risk of anaphylaxis with intravenous vitamin K, and it should be administered via slow infusion (over 20 to 60 minutes.) **C,** Fresh frozen plasma (FFP) can be used to reverse the effect of vitamin K antagonists in emergency situations. **D,** Prothrombin complex concentrates (such as the four factor PCC Kcentra [CSL Behring LLC., Kankakee, IL], pictured) provides rapid international normalized ratio correction and may be safer than FFP. PCCs can also be used to reverse the effects of direct thrombin inhibitors (e.g., dabigatran) and factor Xa inhibitors (e.g., apixaban). **E,** Platelet transfusions can be used to reverse the effects of antiplatelet medications such as aspirin or clopidogrel, and also to correct thrombocytopenias.

Procedures

Lumbar Puncture

The decision to perform a lumbar puncture (LP) should be individualized and based on an assessment of the risks and benefits of the procedure. When the risks of an LP are high, empiric antibiotic therapy may be appropriate for conditions such as meningitis. When the condition is difficult to diagnose or treat, LP may be necessary. In these cases, consultation with interventional radiology or anesthesiology may be warranted to reduce the risk of hemorrhage.

When an LP is performed in an anticoagulated ED patient, it is critical to monitor for complications. The most important complication associated with LP in the setting of anticoagulation is a spinal epidural hematoma (SEH). This rare, but catastrophic, complication is more likely to occur with a difficult or traumatic LP in anticoagulated patients or those with a platelet disorder.[17] An emergency magnetic resonance image should be performed if there is suspicion for an SEH. If an SEH is diagnosed, immediate decompression with a laminectomy should be performed to avoid irreversible spinal cord ischemia.[18]

Many clinicians feel that spinal procedures such as an LP may be safely performed on patients taking aspirin or a nonsteroidal antiinflammatory drug (NSAID) without discontinuing the medication or transfusing platelets.[19–24] It is important to consider the specific medication. Aspirin irreversibly inactivates cyclooxygenase-1 (COX-1) and blocks thromboxane production for the life of a platelet (7–10 days) within an hour of ingestion. Therefore platelet function does not return to normal until the permanently inhibited platelets are replaced by enough newly synthesized active platelets. The ability for platelets to aggregate can be seen after 4 days following aspirin cessation, as it requires only a few uninhibited platelets (newly synthesized or transfused) to recruit aspirin treated platelets to action.[25,26] Horlocker and colleagues studied 391 patients undergoing spinal anesthesia and also on antiplatelet therapy including aspirin, naproxen, piroxicam, ibuprofen, indomethacin, dipyridamole, and sulindac.[21] One hundred and thirteen patients were on multiple antiplatelet agents preoperatively. No SEHs were reported in this study. The authors concluded that preoperative antiplatelet medication was not a contraindication to spinal anesthesia. Importantly, it is not recommended to perform an LP on patients who are using aspirin or an NSAID concurrently with another anticoagulant such as heparin, low-molecular-weight heparin (LMWH), or other antiplatelet agents.[24]

The safety of performing an LP in patients receiving newer antiplatelet agents, including clopidogrel, ticlopidine, abciximab, eptifibatide, or tirofiban is not well studied. The American Society of Regional Anesthesia and Pain Medicine (ASRA) recommends discontinuation of these medications prior to LP.[24] Reversing the effect of these medications and the period of discontinuation prior to the performance of the procedure depends on the medication. Pharmacologically, normal platelet activity is expected 8 hours after discontinuing tirofiban and eptifibatide, 24 to 48 hours after discontinuing abciximab, and 1 to 2 weeks after discontinuing clopidogrel and ticlopidine.[24] The ASRA, ACCP, and the American Heart Association (AHA) recommend discontinuing clopidogrel 7 to 10 days prior to neuraxial anesthesia or surgery. Other organizations recommend a 5-day washout period prior to giving spinal injections in patients receiving these medications.[15,19,24,27]

Heparin increases the risk of SEH. In a study from 1981, 2% (7 of 342) of patients receiving heparin for anticoagulation developed SEH after LP. Risk for SEH increased with a traumatic procedure, starting anticoagulation within an hour of the LP, and concomitant aspirin therapy.[28] Patients with preexisting coagulopathy were excluded from this study. This study suggests that the risk of SEH in patients on heparin prior to the LP is at least 2%. In a study by Tryba and colleagues, the risk of SEH increased tenfold in patients receiving heparin or aspirin who experienced a traumatic LP.[29] As intravenous (IV) heparin has a short duration of action, it should be discontinued for at least 4 hours prior to the LP and the aPTT has normalized.[19] Heparin infusion should not be resumed for at least an hour after an LP is performed.[28] The risk for SEH from LP in patients on twice daily subcutaneous heparin for the prophylaxis of deep venous thrombosis is low.[30] Nonetheless, it is recommended to discontinue for at least 8 hours prior to neuraxial procedures.[19]

LMWH has a half-life that can range between 2 and 6 hours depending on the dose, route of administration, and renal function. The ASRA guidelines recommend discontinuing LMWH 12 hours prior to neuraxial procedures when used at doses intended for deep vein thrombosis prophylaxis and 24 hours when used at doses intended for anticoagulation.[19] Anticoagulation with LMWH should be withheld for 18 to 24 hours after the LP to prevent SEH.[23]

Warfarin is associated with a high risk of SEH following an LP. Warfarin should be stopped for 5 days and the INR normalized prior to performing an LP.[19] The administration of vitamin K with fresh frozen plasma (FFP), or the administration of prothrombin complex concentrates (PCCs) is recommended for complete warfarin reversal.

There is currently no study that has evaluated the safety of LP in the setting of anticoagulation with the new direct thrombin inhibitors or factor Xa inhibitors. Little is known about procedural safety when anticoagulated with these medications, although many clinicians assume that the risk of bleeding is increased similarly to warfarin.[19,20] Duration of action, reversal strategies, and diagnostic testing are complicated and medication specific.

Performance of an LP in patients with hemophilia is safe following 100% factor replacement. In a study by Silverman and colleagues, 30 of 33 patients (91%) with severe factor deficiency had no serious complications with LP after adequate factor replacement.[17] In a review of six articles that evaluated neuraxial procedures in patients with hemophilia, there were no SEHs in 107 procedures on 85 patients, of which 53 of the procedures were diagnostic LPs in the ED. In 105 of the 107 procedures (98%), factor levels were replaced to normal. One case of an SEH with neurologic impairment occurred in a patient with undiagnosed hemophilia.[31]

There is scant literature on the performance of an LP in patients with select platelet disorders, including von Willebrand disease (vWD) and idiopathic thrombocytopenic purpura (ITP). Choi and colleagues evaluated 74 neuraxial procedures (all for obstetrical anesthesia) performed in 72 patients with vWD.[31] Sixty-four patients (86%) required no treatment secondary to normal vWD indices, whereas 10 patients required treatment with desmopressin (DDAVP), vWF/factor VIII concentrate, or factor VIII alone. No complications were noted. In the same study, there were no complications reported in 326 neuraxial procedures in patients with ITP. Pretreatment with corticosteroids, IV immune globulin, or platelet transfusion

was variable among the reports. No pretreatment was provided in 103 procedures that included a patient with a platelet count of 2×10^9/L. Based on the results of their study, the authors concluded that it is safe to perform a lumbar puncture without providing platelet transfusion when the platelet count is greater than 50×10^9/L.

Performing an LP in the setting of thrombocytopenia has been well studied in the pediatric oncology population. In 2000, Howard and colleagues reported on the safety of performing LPs in children with platelet counts greater than 10×10^9/L without transfusing platelets. Nine hundred forty-one procedures were performed on patients with platelet counts below 50×10^9/L without the development of an SEH. Twenty-nine procedures were performed on patients with platelet counts less than or equal to 10×10^9/L. No complications were reported, although the study was not powered to determine patient safety. Nonetheless, the authors recommended platelet transfusion for an LP when the platelet count is less than or equal to 10×10^9/L.[32]

A 2010 systematic review by van Veen states that a platelet count greater than or equal to 40×10^9/L is safe to perform an LP provided that the platelet count is stable, the patient does not have an acquired or congenital coagulopathy, the platelet function is normal, and the patient is not receiving an antiplatelet or anticoagulant medication. The authors also stated that it may be safe to perform an LP at platelet counts 20 to 40×10^9/L, however there were insufficient data to recommend safety at this platelet level without transfusion.[32a] The American Association of Blood Banks recommends prophylactic platelet transfusion for patients having an elective diagnostic LP for a platelet count less than 50×10^9/L.[33] However, this is a weak recommendation based on very low-quality evidence.

Vascular Access

Patients frequently require central venous access for resuscitation, medication administration, or hemodynamic monitoring. Critically ill patients are sometimes anticoagulated or develop a coagulopathy secondary to their illness. Providers are oftentimes hesitant to perform central venous cannulation in anticoagulated patients or those with a coagulopathy because of the risk of bleeding.

Bleeding complications during central venous catheterization in patients with abnormal hemostasis is relatively low.[34,35] Arterial puncture is the most common complication associated with central venous catheter insertion, and occurs in 3% of catheters placed in the internal jugular vein and 0.5% of catheters placed in the subclavian vein.[36] Numerous studies have demonstrated that central venous cannulation is safe in patients with a coagulopathy or disorder of hemostasis.[8,33,34,36–38] Emergency reversal of anticoagulation prior to the insertion of a central venous catheter is common practice but does not appear to be evidence-based.[8,34,35,40] In one study, 76 consecutive patients with various disorders of hemostasis (thrombocytopenia, anticoagulation with heparin, anticoagulation with warfarin, and abnormalities in coagulation assays) received central venous access procedures. Of the 104 procedures, only one patient required an intervention beyond 20 minutes of site compression to control bleeding.[34] The authors noted that bleeding problems are uncommon and serious bleeding is rare. Providers should make a case-based clinical decision weighing the risk of hemorrhage versus the risk of thrombosis and fluid overload associated with reversal.

In a 2000 study evaluating the complications of central venous catheter placement in patients with various hemostasis disorders, thrombocytopenia (platelet count less than 50×10^9/L) was the only significant predictor for bleeding complications.[35] However, the authors call into question the utility of platelet transfusion because the complications were easily addressed with compression and suturing. Other studies have also found that a platelet count less than 50×10^9/L is an independent risk factor for bleeding.[34,35,41] Further studies are required to assess the benefit of preprocedural platelet transfusion for central venous catheter insertion.[42] Platelet transfusion to maintain counts greater than 50×10^9/L is recommended in patients with evidence of postprocedural bleeding at catheter insertion site until hemostasis is achieved.[43]

In 1999, Fisher and colleagues demonstrated a low incidence of major vascular complications in patients with cirrhosis and an elevated INR. Of 658 cannulations, there was one major event (hemothorax) caused by accidental subclavian artery puncture. The mean INR was 2.4 (range 1 to 16) and no attempt was made to reverse coagulopathy prior to the procedure.[41] Similar results were found in two additional studies on coagulopathic patients including patients with liver disease receiving central venous access.[34,39]

Patients with DIC should have vigorous correction of coagulation abnormalities in conjunction with hematology consultation prior to central venous catheterization when patient stability allows for it.[43] Targets for correction include PT less than 1.5 times normal and fibrinogen greater than 1.0 g/L.

Factor replacement is recommended for patients with hemophilia prior to central venous cannulation.[44,45] The goal of management is to achieve a circulating factor level of 100% prior to the procedure followed by a continuous factor infusion for 2 to 3 days afterwards to prevent serious bleeding complications.

In nonurgent situations IV heparin infusion should be discontinued for 3 hours prior to central venous cannulation.[43] In patients receiving therapeutic anticoagulation with subcutaneous LMWH, the recommendation is to wait 18 hours after the last injection before performing nonurgent central venous cannulations.[43] Similarly, nonurgent central venous cannulation in patients on warfarin should be withheld until the INR is less than 1.5.[43]

The use of ultrasound for the placement of central venous catheters is well established and has been shown to increase success rates and decrease complication rates.[46–50] The use of ultrasound in patients with disorders of hemostasis is safe and preferred when available.[46,50] There are no data comparing ultrasound-guided versus traditional approach in the setting of anticoagulation.[49]

In emergency situations site selection for central venous cannulation may improve outcomes. The safest technique in an anticoagulated patient appears to be an ultrasound-guided internal jugular approach. The lower risk of malposition, ease of ultrasound-guided technique, and the ability to manually compress a bleeding vessel in the event of a bleeding complication, makes the internal jugular access approach favored over the subclavian approach.[36] Though the subclavian approach is associated with fewer arterial punctures, the provider is unable to manually compress bleeding vessels effectively. The femoral approach is also suitable for emergency central venous access because it is amenable to ultrasound-guided technique, and the provider is able to manually compress a bleeding vessel.

Importantly, femoral venous catheters are less favorable long-term because of an increased risk of infection.

The use of intraosseous access is not contraindicated in anticoagulated patients. The manufacturer of the EZ-IO (Vida-Care, San Antonio, TX) device notes that applying pressure to the site for 1 to 2 minutes controls bleeding after needle removal, but more time may be required for patients on anticoagulant therapy.[51]

Patients requiring temporary placement of a hemodialysis catheter for emergency hemodialysis may have an increased risk of complications with central venous access as a result of comorbid conditions leading to anticoagulation or impaired hemostasis, particularly uremia-induced platelet dysfunction. If a patient requires emergency access for hemodialysis, the preferred approach site is the femoral vein because of the lower complication rate. Whereas complication rates are similar to typical central venous catheter placement, inadvertent dilation of the artery or unrecognized arterial puncture with a hemodialysis catheter can lead to massive bleeding. Although there are no data or guideline specifically targeted for the placement of hemodialysis catheters in the setting of anticoagulation, mechanical errors may be complicated by anticoagulation.

Arthrocentesis

Though numerous providers recommend reversing anticoagulation in patients receiving warfarin who require an arthrocentesis, there are little data to support this practice.[52,53] In the largest study to date, Ahmed and Gertner evaluated the safety of arthrocentesis in patients receiving a VKA medication.[11] Among the 456 procedures performed, there were no statistical differences in overall bleeding complications between patients with an INR greater than 2 and those with an INR less than 2. The authors concluded that arthrocentesis can be performed on patients who are anticoagulated without the need for reversal or discontinuation of anticoagulation prior to the procedure. Of note, 103 of the procedures were on patients with an INR greater than 3 and the highest INR was 7.8. In the latest study by Bashir and colleagues, 2084 knee and shoulder joint injections were performed on patients taking warfarin.[12] The mean INR was 2.77 (range 1.7 to 5.5). Eighty-seven percent of the patients had an INR greater than or equal to 2. Nineteen- or 21-gauge needles were used for the arthrocentesis. There were no procedural complications noted in this study, leading the authors to conclude that joint injections are safe in the setting of therapeutic anticoagulation with warfarin. Additional studies have failed to demonstrate a higher risk of bleeding with arthrocentesis in the setting of anticoagulation.[9–12] There appears to be no difference between the types of joint requiring arthrocentesis. Most studies have included both shoulder and knee joint aspiration.

There is no available literature evaluating the safety of arthrocentesis in patients receiving an antiplatelet agent or a nonvitamin K anticoagulant.

Hemarthrosis is a common presentation for patients with bleeding disorders such as hemophilia. It is typically recommended that patients or parents replace factors to achieve circulating factor activity of 40% to 50% at the first sign of acute bleeding episodes. Arthrocentesis is not always required to make the diagnosis of hemarthrosis in this clinical setting. However, if performing an arthrocentesis in the setting of hemophilia is required, the recommendation is to perform the procedure after appropriate factor replacement.

Spontaneous nontraumatic hemarthrosis is an infrequent complication with supratherapeutic anticoagulation and may even occur within the target therapeutic range.[54] Routine coagulation studies are recommended if hemarthrosis is suspected in an anticoagulated patient. Temporary discontinuation of anticoagulants is typically recommended as part of treatment of hemarthrosis. If arthrocentesis is required, reversal of anticoagulation is not recommended if the INR is less than 4.5.[9] Although arthrocentesis can safely be performed in the setting of supratherapeutic anticoagulation as previously mentioned, there are no safety data for the setting of hemarthrosis.[11] Clinical judgement should be used to determine the necessity of this procedure.

Paracentesis

Paracentesis is a relatively safe procedure. The frequency of complications such as minor bleeding, or major complications such as abdominal hematoma that require a transfusion is low.[55] In one report, abdominal hematomas occurred in only 1% of patients despite cirrhosis being a common comorbidity.[56] There are currently no data to support the routine administration of FFP or platelets prior to paracentesis in patients with mild to moderate coagulopathy (PT or PTT up to twice normal) or thrombocytopenia (platelet count 50 to 99 $\times$ 10^9/L).[55,57,58] However, caution should be exercised in patients with severe coagulopathy or DIC.[55]

In a 2009 prospective study evaluating the complication rate of paracentesis in cirrhotic patients, local bleeding occurred in 2.3% of cases and major bleeding requiring a medical or surgical intervention occurred in 1% of cases. Two of the five patients with major bleeding included a major hematoma, whereas three cases involved bleeding into the peritoneal cavity. A nonsignificant trend towards increased risk of complications was seen in patients with a platelet count less than 50×10^9/L. Therefore, the authors advised caution when performing paracentesis on patients with a platelet count greater than 50 $\times$ 10^9/L.[59]

In a 2011 retrospective study evaluating the safety of paracentesis in patients with cirrhosis, the authors concluded that the procedure was safe.[60] Of 209 paracenteses reviewed for the study, 19% were performed on patients with a coagulopathy. The most common complication was local bleeding (3%). One patient experienced an abdominal hematoma, but no further data were given about this patient. The authors concluded that performing a paracentesis in the setting of coagulopathy is safe and the only absolute contraindications are DIC and fibrinolysis.

Although ultrasound-guidance technique has been shown to decrease the risk of bleeding with paracentesis in typical conditions, there are no data demonstrating this benefit in anticoagulated patients.[61]

Thoracentesis and Tube Thoracostomy

The major procedural complication associated with thoracentesis is pneumothorax, not bleeding.[62] Numerous studies have failed to demonstrate an increased risk of bleeding with thoracentesis in the setting of anticoagulation.[57,63,64]

Additionally, the correction of abnormal coagulation laboratory values prior to the procedure is unlikely to have benefit. In a 2013 retrospective study of 1009 ultrasound-guided thoracenteses, Hibbert and colleagues evaluated patients treated with and without preprocedural transfusion of FFP or platelets for abnormal coagulation profiles.[64] The authors

found no statistical difference in the bleeding complication rate (overall 0.4%) between those treated with transfusion prior to the procedure and patients not treated with blood products. In this study, the patients who did not receive FFP or platelet transfusions had a mean INR of 1.9 prior to the procedure. Seventy-four patients (14%) who were not treated with a transfusion had a platelet level of less than 50×10^9/L. There were no bleeding complications seen in the group that did not receive FFP or platelets compared with four bleeding complications that occurred in the group that received transfusions.

When performed under ultrasound guidance, the risk of bleeding is low even when coagulation studies or the platelet count are abnormal.[61,63–65] However, there are no data available to demonstrate a lower bleeding complication rate of ultrasound-guided technique compared to the traditional approach in anticoagulated patients.

Recent studies have raised concerns about the risk of bleeding when thoracentesis is performed on patients taking clopidogrel. One prospective study of 25 consecutive patients noted a low rate of clinically significant hemorrhage in patients receiving thoracentesis while on clopidogrel, but further studies are required to determine safety. In that study, one patient developed a significant hemothorax requiring blood transfusion and tube thoracostomy.[66] A 2013 case report also raised similar concerns as a patient on clopidogrel and aspirin developed a hemothorax after chest tube insertion.[67] However, there are no data to support this recommendation. In fact, two studies failed to demonstrate a high risk for bleeding in patients taking clopidogrel especially when using small bore chest tubes.[68,69]

In patients with a tension pneumothorax there are no absolute contraindications to tube thoracostomy. In stable patients undergoing chest tube placement, the need for anticoagulation reversal should be considered. Several clinicians have recommended that coagulopathies and platelet defects be corrected prior to tube thoracostomy.[70,71]

Dental Procedures

Managing postoperative bleeding after a dental procedure can be a challenging task for EPs especially in the setting of anticoagulation. Dental procedures such as extractions are commonly performed without the cessation of anticoagulants. Multiple studies and authors have concluded that the risk of cessation of anticoagulation including antiplatelet therapy is much greater than the risk of significant bleeding with continued anticoagulation for dental procedures.[72–78] Multiple organizations including the AHA, ACCP, American College of Surgeons, American Dental Association, and The American College of Cardiology all agree that single or dual antiplatelet therapy should not be interrupted for dental procedures. To date there are no clinical trials demonstrating the safety of dental procedures in patients taking NOAC medications. Some have concluded that it appears safe to continue NOAC medications such as dabigatran or rivaroxaban for dental procedures based on management recommendations for warfarin and LMWH.[79]

Bleeding and oozing from a dental procedural site is common after extractions such as wisdom tooth extractions even in the setting of normal coagulation. Patients commonly come to the ED after futile attempts to control the bleeding at home. Simple local therapy such as compression, packing, and vasoconstrictor infiltration is typically sufficient to control bleeding, even in the anticoagulated patient (see Chapter 72). Although none are specific for anticoagulated patients, there are multiple commercially available products that can be utilized to achieve hemostasis. Thrombin soaked gelatin sponges, oxidized cellulose material, chitosan coated gauze dressing, and topical tranexamic acid have all been described for this purpose.

Patients with hemophilia and vWD have an increased risk of bleeding during and after dental procedures. In addition to utilizing standard therapies, IV or local tranexamic acid and epsilon-aminocaproic acid in patients with hemophilia may also aid in achieving hemostasis, as has been described in a limited number of trials.[80–82] However, a 2015 Cochrane review was unable to definitively conclude its efficacy.[83]

Although no studies exist looking specifically at the safety of performing simple oral and dental procedures in the ED such as incision and drainage of a dental abscess, they are likely benign, considering the safety data for more invasive dental procedures such as extraction.

Epistaxis

Epistaxis is a common presenting symptom in the ED and may be complicated by anticoagulant use. Whether the bleeding is the result of excessive anticoagulation, achieving hemostasis may be more difficult than normal clinical scenarios. Evaluation of coagulation parameters (PT, INR, PTT, platelet count, or other anticoagulant-specific laboratory assays) should be routinely ordered for anticoagulated patients presenting with epistaxis. A complete blood count is also suggested for patients with prolonged or severe bleeding with epistaxis.

Anticoagulant reversal is rarely necessary unless laboratory findings reveal a markedly abnormal degree of anticoagulation or the patient has severe, symptomatic, or life-threatening bleeding. Specific factor replacement is necessary for patients with hemophilia and severe bleeding.

A variety of topical hemostatic agents are available and can be applied to the nasal cavity for the management of epistaxis in the anticoagulated patient when standard therapy is not adequate. Cellulose, gelatin, and thrombin compounds can be placed directly on the bleeding site to promote clot formation even in fully anticoagulated patients. Both topical and IV use of tranexamic acid has also been described in the management of epistaxis, but there is a lack of evidence-based data supporting its efficacy.[84–86] Recently a case report described the successful use of topical tranexamic acid in the management of rivaroxaban associated epistaxis after failure with a thrombin-soaked inflated nasal tampon.[87]

Nasogastric Tube Insertion

There is a lack of information available about the safety of placing a nasogastric tube (NGT) in the setting of anticoagulation. Severe coagulopathy is a commonly stated relative contraindication of NGT passage for risk of epistaxis without reference to evidence-based data.

Similarly, the often stated NGT placement contraindication of esophageal varices is unproven. Although mechanical or chemical irritation is thought to cause esophageal varices rupture and bleeding, there are no evidence-based data that stratifies the risk of NGT placement in this clinical setting. In an anesthesia study of patients undergoing hepatic transplantation with esophageal varices, 0 of 75 patients developed bleeding after NGT placement.[88] This further calls into question the link between NGT placement and causation of bleeding esophageal varices. Additional research is required to prove or disprove this link.

Thrombocytopenia is a common finding in cirrhosis and is a poor indicator for risk of future gastrointestinal hemorrhage.[89] Furthermore, routine coagulation assays are not reliable indicators of coagulation status in patients with cirrhosis.[89] Whereas platelet transfusion is commonly recommended prior to endoscopy for a platelet count of less than 30×10^9/L, there is no analogous recommendation for NGT insertion.[90]

Labor and Delivery

Delivery of a newborn in the ED is a relatively rare event. Postpartum bleeding and hemorrhage is a complication exacerbated by maternal factors such as anticoagulation and bleeding disorders.

Pregnant patients diagnosed with venous thromboembolism are typically treated with LMWH. In the final weeks of pregnancy obstetricians occasionally switch patients to unfractionated heparin to reduce time to normalization of coagulation studies when labor begins. However, fully anticoagulated patients may present with precipitous labor and develop postpartum hemorrhage. Reversal of anticoagulation may be necessary in the event of refractory bleeding. There is no recommendation for prophylactic reversal of anticoagulation for delivery.[91]

Patients with vWD are at increased risk for postpartum hemorrhage. These patients have a higher risk of delayed postpartum hemorrhage reported up to 2 to 3 weeks after delivery. According to case reports, postpartum hemorrhage may still occur despite prophylaxis with factor VIII, cryoprecipitate, FFP, and DDAVP. Expert opinion recommends that a von Willebrand factor activity of greater than or equal to 50 IU/dL should be achieved before delivery and maintained for at least 3 to 5 days afterward. Prophylaxis with DDAVP or von Willebrand factor concentrate should be given prior to childbirth if time permits.[92] However, there are no randomized trials that have studied DDAVP's efficacy to prevent or treat postpartum hemorrhage.[93]

Although a rare occurrence because of its X-linked nature, replacement of factors is recommended for pregnant women with severe hemophilia A or B in labor. Risk for bleeding begins when levels are below 30% of normal. Risk increases with severity of disease especially those with less than 1% normal factor activity.[94]

Wound Management

Control of Hemorrhage

Hemostasis is an essential step in wound management. Inadequate hemostasis can lead to the formation of a hematoma within a closed wound, which may cause dehiscence of wound edges, impaired healing, and increased risk for wound infection. Anticoagulated patients may come to the ED for prolonged or severe episodes of bleeding from an acute traumatic wound. Most bleeding wounds are effectively managed with routine application of direct pressure and elevation. However, anticoagulants may impair the integral mechanisms of hemostasis and prevent adequate spontaneous hemostasis.

There are multiple techniques that can be utilized to control a bleeding wound including compression, vessel crushing, ligation, electrocautery, or application of a vasoconstrictor or hemostatic agent. These traditional techniques are not specific to anticoagulated patients, but they may be useful in achieving hemostasis. There are a few topical hemostatic agents that have been shown effective in the setting of anticoagulation.

Chitosan is a complex carbohydrate derived from chitin that interacts with platelets and red blood cells to form a gel-like clot independent from coagulation factors. In a heparinized swine model, Millner showed chitosan granules (Omni-Stat, Medtrade Products Ltd., Crewe, United Kingdom) and dressings (Celox Gauze, Medtrade) were both efficacious in providing hemostasis over plain gauze compression.[95] The long-term stability of the clot is not well-established and therefore these products are used as temporary management if definitive therapy such as surgical intervention is required. Chitosan-based dressings (Hemcon, Tricol Biomedical, Portland, OR) have also been used externally for hemostasis in pediatric patients with bleeding tendencies from congenital or acquired bleeding disorders.[96]

Topical thrombin has also shown efficacy as a topical hemostatic agent in anticoagulated patients, in particular heparin and clopidogrel therapy.[97,98] These commercially available topical thrombin products aid in the production of fibrin in one of the final steps of the coagulation pathway to create a stable clot.

IV tranexamic acid has been shown to be efficacious in trauma patients especially when given early after injury.[99,100] However, anticoagulated patients were not included in the study. The use of topical tranexamic acid for the control of bleeding has been promising in many clinical scenarios but remains unproven especially in the setting of anticoagulation.

Incision and Drainage

There is no literature reporting complications in anticoagulated patients who undergo incision and drainage. Although bleeding is a risk with incision and drainage, local therapy alone is typically sufficient to provide hemostasis. EPs should make a case-based clinical decision weighing the risk of hemorrhage for patients requiring incision and drainage.

SUMMARY

Procedures in the setting of anticoagulation present a unique complexity in the ED. The EP should be mindful of potential bleeding complications and should be prepared to identify and treat these events. Reversal of anticoagulation is not always necessary prior to performing a procedure and the EP should be attentive to the risk of thrombosis. In some instances, the risk-benefit ratio may favor delaying a procedure until the patient's coagulation status returns to normal range with time, or the use of medications or blood products. Lastly, emergency procedures to correct an imminent life-threatening life-saving condition should never be withheld in the setting of anticoagulation.

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