Chapter 23
Disorders of Hemostasis

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BACKGROUND

Assessing the risk of perioperative bleeding is a fundamental component of the preoperative evaluation. Early recognition and proper perioperative management of hemostatic disorders may prevent, or at least reduce the risk of, perioperative bleeding. This chapter focuses on the preoperative assessment of hemostatic disorders, and the management of von Willebrand disease, hemophilia, vitamin K deficiency, and acquired coagulopathies. See Chap. 22 for evaluation and management of platelet disorders.

PREOPERATIVE EVALUATION

HISTORY AND PHYSICAL EXAM

A preoperative hemostatic history is appropriate for all patients, regardless of the planned procedure [1–3]. Specific information to elicit from the patient includes:

- A personal history of abnormal bleeding, such as excessive bleeding associated with childbirth, menses, minor trauma, dental procedures, or surgery; bruising that occurs spontaneously or with minimal trauma [1]; and bleeding that required a blood transfusion
- Family history of bleeding disorders
- Past medical history of hepatic, renal, or hematologic disease
- Current medication use including aspirin, nonsteroidal anti-inflammatory drugs, antiplatelet medications, anticoagulants, and vitamins, supplements, or herbal preparations

M. B. Jackson et al. (eds.), *The Perioperative Medicine Consult Handbook*,
https://doi.org/10.1007/978-3-030-19704-9_23

Although many patients will not have abnormal exam findings, a preoperative physical exam supports the hemostatic history. Physical exam may:

- Suggest the presence of an undiagnosed hemostatic disorder (e.g., petechiae, purpura, ecchymoses)
- Demonstrate chronic findings of hemostatic disorders (e.g., joint deformity and muscle atrophy in hemophilia, although with early diagnosis and treatment, such findings are increasingly rare)
- Reveal signs of chronic conditions that result in hemostatic abnormalities (e.g., jaundice, ascites, and spider telangiectasias observed in cirrhosis; or pallor, lymphadenopathy, and splenomegaly observed in a variety of hematologic disorders)

TESTING

Routine preoperative laboratory testing, including platelet count, prothrombin time (PT/INR), and partial thromboplastin time (PTT), is generally not indicated in patients with a normal hemostatic history [1–4]. Numerous observational studies have demonstrated that an abnormal preoperative PT/INR and/or PTT alone or a bleeding time do not predict an increased perioperative bleeding risk [2, 5]. Preoperative testing is directed by the patient's history and exam and the procedural bleeding risk (see Table 23.1):

- For low-risk procedures and a reassuring history and exam, no further testing is required.
- For high-risk procedures, and to a lesser degree for moderate-risk procedures, a platelet count, PT/INR, and PTT may be considered in addition to history and exam [1, 6].
- Regardless of the procedure, a platelet count, PT/INR, and PTT are appropriate initial testing for patients with a suspected disorder of hemostasis.
- Consider obtaining a platelet count, PT/INR, and PTT if a patient cannot provide a history [3].

Depending on the results of initial testing, additional specialized testing or evaluation may be required. For prolonged PT/INR and/or PTT, the first step is to repeat testing. If repeat testing confirms the abnormal test and a cause is not readily apparent (see Table 23.2), then a referral to hematology for further evaluation is appropriate. Additional testing may include a mixing study to determine if the abnormality is due to factor deficiency (abnormality corrects with mixing) or a factor inhibitor (abnormality does not correct with mixing), lupus anticoagulants, DIC panel, thrombin time, or specific factor levels.

TABLE 23.1 RISK OF BLEEDING WITH SURGICAL OR INVASIVE PROCEDURES

Risk	Type of procedure	Examples
Low	Nonvital organs involved, exposed surgical site, limited dissection, percutaneous access	Lymph node biopsy, dental extraction, cataract extraction, most cutaneous surgery, laparoscopic procedures, coronary angiography
Moderate	Vital organs involved, deep or extensive dissection	Laparotomy, thoracotomy, mastectomy, major orthopedic surgery, pacemaker insertion
High	Bleeding likely to compromise surgical result, bleeding complications frequent	Neurosurgery, ophthalmic surgery, cardiopulmonary bypass, prostatectomy, bladder surgery, major vascular surgery, renal biopsy, bowel polypectomy

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TABLE 23.2 CAUSES OF ABNORMAL COAGULATION STUDIES [7]

PT/INR	PTT	Causes
Prolonged	Normal	Warfarin Vitamin K deficiency Liver disease Extrinsic factor deficiency or inhibitors
Normal	Prolonged	Heparin Von Willebrand disease Intrinsic factor deficiency or inhibitors Antiphospholipid syndrome
Prolonged	Prolonged	Direct oral anticoagulants (DOACs) Disseminated intravascular coagulation (DIC) Common pathway factor deficiency or inhibitors

If the history and physical exam are suggestive of a bleeding disorder but PT/INR and PTT are normal, platelet disorders (see Chap. 22) and von Willebrand disease should be considered, as well as referral to a hematologist.

PERIOPERATIVE MANAGEMENT

VON WILLEBRAND DISEASE

Von Willebrand disease (VWD) is the most common inherited bleeding disorder. The prevalence of VWD may be as high as 1% of the general population, but clinically significant VWD is much less common [8]. Von Willebrand factor (VWF) mediates the adhesion of platelets to damaged endothelium, and binds and stabilizes factor VIII. Von Willebrand disease (VWD) is caused by either a deficiency or dysfunction of VWF, which may also result in low factor VIII levels. There are 3 types of VWD [9]:

- Type 1 (mild) and 3 (severe) VWD represent a quantitative deficiency of VWF.
- Type 2 VWD represents a group of four subtypes that are characterized by dysfunctional VWF (qualitative disorder).

Clinical manifestations vary based on the VWD type, but typically include mucocutaneous and gastrointestinal bleeding. Bleeding typical of a coagulation defect (i.e., hemarthrosis, large ecchymoses) can be seen in Type 3 VWD and in some Type 2 subtypes. If a diagnosis of VWD is suspected, initial laboratory testing in addition to platelet count and PT/INR and PTT should include VWF antigen, VWF activity (e.g., ristocetin cofactor activity), and factor VIII activity levels. Platelet count, PT/INR, and PTT are typically normal, though PTT may be prolonged if factor VIII levels are low. Referral to a hematologist for more specialized testing and treatment is recommended if any studies are abnormal.

Surgical prophylaxis for patients with VWD involves either desmopressin (DDAVP), factor VIII/VWF concentrates, antifibrinolytic therapy (e.g., tranexamic acid), or some combination of the three. Consultation with a hematologist is recommended, as the treatment and monitoring may vary considerably depending on the VWD type.

- Desmopressin transiently increases VWF and factor VIII levels and is most effective for Type I VWD. It is typically reserved for low bleeding risk surgery. Patients should receive a test dose to establish responsiveness. The recommended IV dose is 0.3 μg/kg slowly infused 30 minutes prior to surgery. It can be administered every 12–24 hours if needed [8, 9]. Tachyphylaxis is common so factor VIII activity and VWF activity levels should be monitored if multiple doses are used. The main risks associated with desmopressin are hyponatremia and fluid overload. If repeat dosing is needed, water intake should be limited to 1,500 mL over the 24 hours following administration and serum sodium monitored [9].

- Factor VIII/VWF concentrates are recommended for surgical prophylaxis in the following situations: Patients with Type 3 VWD; patients with Type 2 VWD with an inadequate response to a DDAVP challenge; patients who have or are prone to developing volume overload or hyponatremia with desmopressin; and for any patient with VWD undergoing high bleeding risk surgery. For high bleeding risk surgery, VWF activity levels should be maintained >100 IU/dL during surgery and up to 36 hours after, then >50 IU/dL for a total of 7–10 days as needed. Dosing generally ranges from 50 to 60 IU/kg with repeated doses every 12–24 hours to maintain appropriate levels [8, 9].

ACQUIRED DISORDERS OF COAGULATION

Acquired disorders of coagulation including liver disease, vitamin K deficiency (see below), and anticoagulants are common. Perioperative management of patients with liver disease and anticoagulants are discussed in Chaps. 17 and 26, respectively.

VITAMIN K DEFICIENCY

In the appropriate clinical context (inadequate dietary intake or TPN, alcohol dependence, antibiotics, disease of malabsorption, liver disease), suspect vitamin K deficiency when an elevated PT/INR corrects with 1:1 mixing study. If the clinical suspicion is high, a 1:1 mixing study is not necessary and patients may be given vitamin K for both diagnosis and management.

- For elective surgeries, oral vitamin K (5–10 mg daily for 3 days) is recommended with repeat PT/INR prior to surgery.
- For more urgent or emergent surgeries, intravenous vitamin K (1–2.5 mg IV once) is usually sufficient, but correction with fresh frozen plasma (FFP) may be necessary.

EFFECT OF FRESH FROZEN PLASMA TRANSFUSIONS

One unit of FFP is the plasma collected from a unit of whole blood or apheresis plasma. It contains all coagulation factors in normal or mildly reduced concentrations. The volume of one unit of FFP is roughly 200–300 mL [10].

- FFP transfusion may be used to correct preoperative coagulopathy (e.g., INR > 2), bleeding due to multiple factor deficiencies (e.g., cirrhosis, DIC), as part of a massive transfusion protocol to prevent dilutional coagulopathy, or for urgent warfarin reversal in the setting of serious bleeding when prothrombin complex concentrates are not available. In rare

instances, FFP may be used in emergent situations to manage factor deficiencies when specific factor replacement is not available [11].

- FFP transfusion may not be appropriate for a mildly elevated INR (e.g., INR < 2) as mild elevations are not predictive of increased bleeding and FFP does not significantly change INRs in this range [12].
- The recommended dose of FFP is 10–15 mL/kg. Since one unit of FFP is ~ 250 mL, 3–5 units of FFP are generally necessary for therapeutic effect when indicated [10]. A post-transfusion PT/INR and/or PTT may be measured 15–30 minutes after transfusion to assess the response.

HEMOPHILIA

Inherited factor deficiencies are relatively uncommon, especially when compared with acquired coagulopathies. Hemophilias are the most common of the inherited factor deficiencies. Hemophilia A (factor VIII deficiency) and hemophilia B (factor IX deficiency) together have an estimated incidence of 1:10,000 male births, with Hemophilia A making up ~80% of the cases [13]. Although some patients with mild factor deficiency may be diagnosed in adulthood, most patients with hemophilia are diagnosed as children and are managed by a hematologist. However, a negative family history does not rule out hemophilia with approximately one-third of cases due to de novo mutations [13]. Female carriers of hemophilia A or B may have bleeding symptoms, although usually less severe than in males. Patients with hemophilia undergoing surgery should be managed in consultation with a comprehensive hemophilia treatment center.

- Develop a specific plan with the patient's hematologist for the entire perioperative period which may include additional infusions or monitoring after discharge.
- The dose of factor replacement for surgical prophylaxis depends on the severity of hemophilia, the type of surgery, patient's response to replacement in the past, and the presence of an inhibitor.
- In general, preoperative normalization of factor activity levels with factor replacement is recommended for patients undergoing major surgery [13].
- Perioperative monitoring of factor levels with factor replacement is necessary.

KEY CLINICAL PEARLS

- Obtaining a preoperative PT/INR, PTT, and platelet count is indicated when the history and/or exam are suggestive of a bleeding disorder.
- If history and exam suggest a bleeding disorder but PT/INR and PTT are unrevealing, consider platelet disorders or von Willebrand disease.
- Desmopressin for bleeding prophylaxis is only appropriate in patients with type 1 or type 2 von Willebrand disease when the bleeding risk from surgery is low and they have established a safe response to desmopressin.

ACKNOWLEDGMENTS

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