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Chapter 4

BLEEDING DISORDERS IN SURGICAL PATIENTS

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A The first step to identifying potential bleeding abnormalities is a thorough history and physical examination. Patients who report prior episodes of significant bleeding after surgical, endoscopic, or dental procedures are likely to have underlying coagulation abnormalities. A history of easy bruising, petechia, gingival bleeding, epistaxis, hemarthrosis, and heavy menstrual flow in women also suggests an underlying bleeding disorder. Similarly, patients with a family history of hospitalizations secondary to life-threatening bleeding should arouse concern. Chronic renal and liver disease, malnutrition, leukemia, and autoimmune disorders are risk factors for surgical bleeding. Finally, the patient's prescribed medications, specifically, any oral anticoagulant or antiplatelet therapy, should be reviewed, and the most recent time of ingestion is critical. However, the most important step in a patient with a potential bleeding disorder is to determine if the patient is actively bleeding and needs an immediate intervention. Mechanical control of major bleeding is a priority, and waiting for coagulation results before taking the patient for definitive care will not benefit the patient. In this clinical scenario of a massive transfusion, the blood bank needs to be alerted, and early blood-based product resuscitation is needed. Conversely, preemptive transfusions in a hemodynamically stable patient with a presumed coagulation abnormality can be lethal. The decision to transfuse blood products into a patient in preparation for the operating room should be goal directed, with a laboratory-based assay with a defined threshold for each blood product administered that is coordinated with the timing of the operative intervention.

B A complete blood count (CBC) provides a gross measurement of the patient's circulating cellular components that contribute to coagulation. A normal CBC in a patient suspected to have ongoing bleeding does not rule out active bleeding and requires serial monitoring if there is a high clinical suspicion. The same is true for a low hemoglobin, which can suggest occult internal hemorrhage, chronic anemia resulting from an underlying disease, or potential bone marrow failure. Platelet counts provide a crude measurement of coagulation function. There is an increased risk for bleeding as platelet counts decrease below 100,000. However, it is not until patients reach a critical threshold of less than 20,000 that they are at risk for spontaneous bleeding. Also, a normal platelet count does not rule out platelet dysfunction. Conversely, in certain disease states, such as cirrhosis, an adaptive response to low platelet counts by the coagulation system develops, and the patient can be paradoxically hypercoagulable despite the abnormally low platelet count. It is also important to take into consideration that the patient's hematocrit can affect platelet function. The optimal hematocrit for platelets to function is 30%. This occurs through margination, a process in which the red blood cells push platelets to the periphery of vessels.

C The prothrombin time (PT), more commonly referred to as the international normalized ratio (INR), and activated partial thromboplastin time (PTT) are often used as first-line screening for bleeding risk. The PT was originally designed to measure the effects of warfarin or detect liver disease and the PTT to identify hemophilia A/B. However, these plasma-based assays reflect circulating levels of clotting factors in the extrinsic and intrinsic clotting pathways and thus do not represent the physiology of hemostasis in accordance with the now accepted cell-based concept of clotting. Consequently, changes in INR and PTT are relatively nonspecific when applied beyond the measurement of hereditary coagulation abnormalities and medically induced anticoagulation.

D Fibrinogen plays a critical role in hemostasis because it is the precursor to fibrin, which binds platelets. Fibrinogen is an acute-phase reactant, and levels are generally preserved even with liver failure. Low levels of fibrinogen are a result of massive blood loss, consumption, dilution, hyperfibrinolysis, or sustained metabolic acidosis. A fibrinogen level, measured by the Clauss assay, of less than 150 mg/dL is usually the threshold for treating active bleeding. Viscoelastic assays also have specific tests that can measure fibrinogen activity (TEG functional fibrinogen and ROTEM FIBTEM). Fibrinogen deficiency in the United States is treated with cryoprecipitate, whereas in Europe, a recombinant fibrinogen product is available.

E D-Dimers are a clinical assay to measure degradation products of fibrinolysis. Although an elevated level of D-dimer is concerning for overactivation of the fibrinolytic system (hyperfibrinolysis), this is a nonspecific finding. Any tissue injury related to operative interventions will elevate levels. As a result, they hold limited utility in the postoperative surgical patient. However, in certain circumstances, such as obstetrics and septic patients in the intensive care unit, a rising D-dimer level with concurrent fibrinogen depletion is concerning for disseminated intravascular coagulation, warranting further work-up. The treatment for this pathology is to treat the underlying cause and not give an antifibrinolytic.

F Thromboelastography (TEG) or rotational thromboelastometry (ROTEM) are gaining prominence in the assessment of surgical bleeding because these devices reflect the individual components of the cell-based concept of hemostasis. Current indications primarily involve the assessment of abnormalities in the clotting cascade during active blood product replacement for significant bleeding. Measurements provided by TEG can guide ongoing transfusion needs. Specifically, an elevated activated clotting time (ACT > 128 secs) indicates the need for coagulation factors, and thus FFP should be administered. If the angle of the TEG tracing is decreased (<65 degrees), cryoprecipitate is given. If the maximal amplitude of clot is diminished (<55 mm), platelets should be administered. If the LY 30 is >5%, fibrinolysis is elevated, and tranexamic acid should be considered.

G Platelet mapping refers to a category of studies that assess the strength of the platelet plug and the contribution by a

Abstract

One of the most common indications for and complications of surgery is bleeding. Patients may be at an elevated risk for bleeding as a result of inherited abnormalities, chronic medical conditions, or pharmacologic therapies, and the apt surgeon should be able to identify and address each of these. Moreover, the tests to identify abnormalities in coagulopathy, either intrinsic or extrinsic, continue to advance with newer studies, such as thromboelastography and platelet aggregometry. With advancements in the assessment of coagulation, therapy for bleeding, in addition to surgical correction when indicated, has become more goal directed, with blood products and other medication given based on laboratory findings. Specifically, when bleeding is worsened by coagulopathy in trauma, the response is to correct the abnormalities in the different aspects of clot formation, such as replacing platelets when the platelet plug strength is diminished. As a result of the increasing specificity of the management of bleeding, an algorithm provides a roadmap to addressing underlying factors that may prolong or worsen bleeding before or after a surgical intervention is undertaken.

Keywords

bleeding
hemorrhage
resuscitation
coagulation
thromboelastography

variety of platelet receptors that are common drug targets. These are most commonly used to assess the response to a variety of antiplatelet medications, including aspirin and clopidogrel. Surgical services have begun implementing these studies to assess the risk for bleeding in a patient on these medications who requires urgent surgical intervention. A minority of patients are poor responders to these antiplatelet regimens and thus may not require a delay before surgery once confirmed by a platelet mapping study.

H For massively bleeding patients, early blood component therapy is essential. To prevent the development of a dilutional coagulopathy, red blood cell (RBC) transfusions should be administered in a ratio of 2 to 1 with fresh frozen plasma (FFP). FFP not only provides a myriad of clotting proteins but is also the optimal colloid to reverse shock. Early administration of platelets and cryoprecipitate is recommended, although the exact ratio of platelets to other products is of ongoing scientific debate. The ideal management now appears to be with the guidance of TEG or ROTEM.

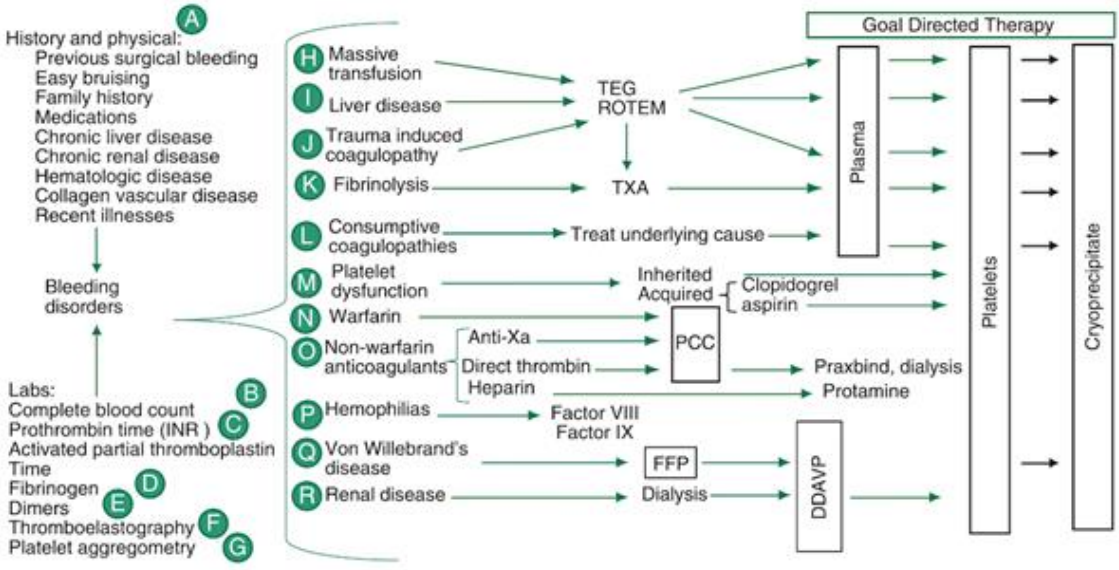
I Liver disease is frequently encountered among trauma and transplant services. This presents most often with an elevated INR but commonly coexists with other coagulation study abnormalities. Management of mild bleeding can begin with the administration of IV vitamin K, which leads to an effect in 8 hours. More rapid correction of the INR can occur with prothrombin complex concentrate (PCC), although data demonstrating a benefit are lacking in the setting of cirrhosis. In addition, FFP and cryoprecipitate can replace deficient factors and fibrinogen in a patient with poor hepatic synthetic function with ongoing bleeding.

J Trauma-induced coagulopathy is often seen in severely injured patients. This is best managed by a TEG-guided resuscitation strategy as described previously. Of note, in patients with an abnormal TEG but without signs of active hemorrhage, product administration may not be required.

K Fibrinolysis historically was managed by fibrinogen replacement with cryoprecipitate administration while treating the underlying cause. The newer agents tranexamic acid and aminocaproic acid can shut down fibrinolysis and thus provide an early treatment strategy when fibrinolysis is ongoing. Identifying which patients require antifibrinolytic therapy can be accomplished with TEG. If the lysis at 30 minutes is 5% or greater, antifibrinolytic therapy should be initiated in trauma. However, during elective surgery, the indications for using antifibrinolytics are different. Preemptive tranexamic acid (TXA) has been demonstrated to reduce surgical bleeding in high-risk obstetric, cardiac, and orthopedic surgery.

L The most important management of bleeding in the setting of consumptive coagulopathies such as disseminated intravascular coagulation (DIC) begins with treatment of the underlying cause (e.g., sepsis, pancreatitis, etc.). These patients often face platelet, fibrinogen, and coagulation factor deficiencies and thus should receive transfusions of platelets, FFP, and cryoprecipitate as indicated by laboratory and clinical studies (e.g., platelet number, fibrinogen level, TEG studies). Specifically, patients with platelets < 50k should receive a platelet transfusion, and those with fibrinogen level < 100 should receive cryoprecipitate.

M Platelet dysfunction is often a confounder because of the common use of antiplatelet agents for cardiovascular disease. Dual antiplatelet therapy (aspirin and clopidogrel) is now routine for most endovascular stents. Chronic renal and liver disease impairs platelet function, and there are rare inherited platelet deficiencies. Heparin-induced thrombocytopenia is another cause of thrombocytopenia in postoperative patients, presenting with a decrease in platelet count of 50% or more and a total platelet



count < 150k. This typically occurs between 5 and 10 days after heparin administration.

N Warfarin therapy remains common and acts through the reduction of liver-produced vitamin K–dependent factors II, VII, IX, and X. Thus vitamin K is used for slow reversal of warfarin, and FFP provides a more rapid effect. However, active bleeding warrants direct replacement with four-component PCC.

O Newer oral anticoagulants and heparin derivatives present a challenge in the bleeding surgical patient. Patients receiving unfractionated heparin may receive protamine if emergent reversal of anticoagulation is necessary. Protamine is less efficacious with low-molecular-weight heparin but may still be given for severe bleeding. Patients receiving direct Xa inhibitors such as apixaban and rivaroxaban can be reversed with PCC, although this practice has not been demonstrated to be efficacious is clinical studies. Moreover, surgeons should use this judiciously because PCC increases the risk for thrombosis in these patients. Currently only dabigatran, a direct thrombin inhibitor, has a reversal agent (idarucizumab). This reversal agent has a prohibitive cost and infrequent availability, and thus PCC or dialysis may be used to reverse the anticoagulant effects as well.

P Patients with hemophilia A and B should receive factor concentrates when available. In settings where such agents are unavailable, FFP may be administered; however, large volumes are required for the desired effect. Cryoprecipitate may be used in hemophilia A, but again, a large volume is required.

Q Patients with milder forms of Von Willebrand's disease (types 1 and 2) with bleeding often respond well to 1-desamino-8-D-arginine-vasopressin (DDAVP) administration. In patients with a complete absence of Von Willebrand's factor (type 3 disease), the first-line treatment in bleeding patients is Von Willebrand's factor where available. Alternatively, cryoprecipitate provides high levels of FVIII, or FFP may be used for factor replacement.

R Platelet dysfunction secondary to renal failure frequently responds to DDAVP, although the mechanism behind the rescue of uremic platelets is unknown. Although infrequently used, cryoprecipitate is known to improve platelet function in uremia, presumably via an endothelial mechanism. Dialysis should be initiated as early as possible in bleeding uremic patients because this will correct the underlying cause.

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