Correction of Coagulopathy for Percutaneous Interventions

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ABSTRACT

Due to medical illness or pharmacotherapy, patients undergoing percutaneous interventions often have abnormal hemostasis. Its etiology may include alterations in the protein-based coagulation system, thrombocytopenia, deficient platelet function, or mixed deficits such as disseminated intravascular coagulation. In this article, the authors review the basic science of each of these etiologies, as well as their available methods of correction. They also review the evidence and guidelines regarding the assessment and treatment of coagulopathy in image-guided procedures. The periprocedural bleeding risk and the urgency of a given procedure guide the management of abnormal hemostasis in this patient population.

KEYWORDS: Anticoagulation, platelets, coagulopathy, disseminated intravascular coagulation, reversal

Objectives: Upon completion of this article, the reader should be able to recall the major coagulopathies encountered in the periprocedural setting and their appropriate management.

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Hemostasis is an elaborate process involving blood vessel walls, plasma enzymes, and platelets. These components interact in a highly regulated system to form a fibrin-rich platelet plug. Given its complex nature, it is not surprising that dysfunction of the clotting process is common. At the broadest level, hemostatic deficits can be placed into three categories: an insufficient number of platelets, deficient platelet function, and dysfunction of the protein-based coagulation system. Platelets and the protein-based coagulation system can be altered not only by medical illness but also by numerous pharmacotherapies. In many patients, these deficits coexist.

Patients with abnormal hemostasis are frequently encountered in the periprocedural setting. The appropriate management of these patients depends on the bleeding risk of the procedure, the urgency of the procedure, and the type and severity of the hemostatic abnormality. Even when these variables are known, there may be multiple options for correcting a clotting defect. In this article, we attempt to clarify these issues by reviewing the basic mechanisms of hemostasis, the alterations commonly seen in the periprocedural setting, and the available methods for correction. When possible, we incorporate evidence and guidelines regarding recommended treatment thresholds and therapies.

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Figure 1 The classic "cascade" model of coagulation. PK, prekallikrein; HMWK, high molecular weight kininogen; TF, tissue factor.

MODELING HEMOSTASIS: AN UPDATE

The coagulation "cascade," originally proposed in 1964, describes two discreet enzymatic pathways, the intrinsic and extrinsic, which come together to form a common pathway that converts prothrombin to thrombin (Fig. 1).^{1,2} Although this successfully models *in vitro* clotting, it inadequately predicts *in vivo* clotting phenomena. Subsequently, a cell-based system of hemostasis has been proposed that more accurately models *in vivo* coagulation (Fig. 2).³

In the cell-based model, a fibrin clot is formed through the activation of the extrinsic pathway, and is divided into initiation, amplification, and propagation phases. The initiation phase begins when injury brings blood into contact with tissue factor (TF), a lipoprotein expressed within vascular smooth muscle cells, adventitial fibroblasts, and leukocytes. Once a cell that expresses tissue factor is exposed to blood, the tissue factor on its surface binds and activates factor VII (VIIa). This forms a complex that in turn activates factor X (Xa) and factor IX (IXa). However, antithrombin (AT) and tissue factor pathway inhibitor (TFPI) rapidly inactivate factor Xa once it leaves the cell surface. The factor Xa that remains activates factor V (Va), and together they form a complex that converts small amounts prothrombin (factor II) to thrombin (factor IIa).

In the amplification phase, this small amount of factor IIa activates factors V, VIII, and XI, and increases platelet adhesion and activation. This is followed by the

propagation phase, in which thrombin is generated in large quantities. Once activated by factor IIa, factor VIIIa forms a complex with factor IXa on the platelet surface, with factor XIa providing additional factor IXa. The VIIIa/IXa complex generates factor Xa on the platelet surface, where it is insulated from the effects of antithrombin and TFPI. This leads to increased production of factor Xa, which binds factor Va and converts larger amounts of prothrombin to thrombin. In the last step of the clotting process, thrombin converts fibrinogen to fibrin.

To prevent uncontrolled clotting, the coagulation process contains several negative feedback loops. In the presence of thrombomodulin, an endothelial cell protein, thrombin activates protein C. Activated protein C forms a complex with protein S that inactivates factors Va and VIIIa. Antithrombin inactivates factors Xa, XIIa, XIa, and IIa, and TFPI inactivates the factor VIIa/TF complex.

The Extrinsic Pathway

BACKGROUND

The extrinsic pathway involves factors II, V, VII, and X as well as fibrinogen, and its integrity *in vitro* is measured by the prothrombin time (PT). The PT is then converted to an international normalized ratio (INR), which corrects for the sensitivity of the thromboplastin reagent used in the PT assay.

Figure 2 The cell-based model of coagulation. Dashed boxes represent complexes on the tissue-factor (TF) bearing cell during initiation. Solid boxes represent factors or factor complexes on the platelet surface during amplification and propagation.

Two of the most common causes of an elevated INR are liver disease and vitamin K deficiency. The liver synthesizes all coagulation factors except factor VIII, which is produced by endothelial cells; thus, hepatic dysfunction will affect both the intrinsic and extrinsic pathways. Vitamin K is a necessary cofactor for the hepatic production of factors II, VII, IX, and X, as well as proteins C and S. Therefore, vitamin K deficiency will also affect both the extrinsic and intrinsic pathways, although the extrinsic pathway is affected earlier. Vitamin K deficiency may be caused by inadequate intake, malabsorptions, or, at the tissue level, vitamin K antagonists (VKAs) such as warfarin. Although much less common, the INR can also be raised by deficiencies or inhibitors of any of the components of the extrinsic pathway.

CORRECTION OF INR

An elevated INR is frequently encountered in the periprocedural setting as a result of medical illness and/or VKAs. The best method to correct this coagulopathy depends on the etiology of the elevation and the rapidity of correction necessary. For elective procedures in those on VKA therapy, the American College of Chest Physicians (ACCP) guidelines recommend stopping the VKA

5 days prior to an elective procedure,⁴ as it can take up to 4 days for a patient's INR to decline to 1.5 from the therapeutic range of 2.0 to 3.0.⁵ For patients whose INR is still equal to or greater than 1.5 1 to 2 days before the planned procedure, the ACCP guidelines recommend administration of 1 to 2 mg of oral vitamin K (Fig. 3).⁴

In more urgent situations, reversal with vitamin K alone is often insufficient as its onset of action takes 24 hours when given orally and 4 to 6 hours when given intravenously (IV).⁶ Furthermore, the risks of reversing anticoagulation with vitamin K are not insignificant: in one study, 5.9% of patients treated with IV vitamin K experienced warfarin resistance, the inability to be reanticoagulated following the reversal of coagulation.⁷ Rarely, IV vitamin K causes anaphylactic reactions, with a reported incidence of 3 per 10,000 doses.⁸ However, the ACCP guidelines recommend that all patients needing rapid reversal (in less than 12 hours) of VKA-related anticoagulation receive 2.5 to 5 mg of oral or IV vitamin K.⁴ This is because vitamin K permanently neutralizes VKAs, preventing the reemergence of anticoagulant activity after more rapidly acting agents wear off. Subcutaneous (SQ) vitamin K is not recommended for this indication, as its efficacy is similar to that of placebo.⁹ Vitamin K repletion is

Figure 3 Reversal of vitamin-K antagonist (VKA) anticoagulation in the periprocedural setting. Recommendations are based on American College of Chest Physician guidelines.⁴ *rFVIIa is not approved by the Food and Drug Administration (FDA) for VKA reversal and dosing is widely variable. †Prothrombin complex concentrates (PCCs) available in the United States are not effective for VKA reversal and are not FDA-approved for this indication. Dosing is widely variable. INR, international normalized ratio.

also effective in correcting coagulopathy in patients with liver disease, as their endogenous stores are often depleted; however, its benefit is limited in patients with severe parenchymal injury.¹⁰

For patients requiring immediate correction of an elevated INR, direct replacement of coagulation factors is necessary. This can be accomplished by the administration of fresh frozen plasma (FFP), prothrombin complex concentrates (PCCs), or recombinant factor VIIa (rFVIIa). There are no randomized controlled trials comparing these three therapies, although ACCP guidelines specifically recommend FFP or “another prothrombin concentrate” for VKA reversal in the perioperative setting.⁴ No matter which agent is used, it should be given in combination with either oral or IV vitamin K.⁴

Fresh frozen plasma is widely used for the immediate reversal of an elevated INR. It contains all of the noncellular components of human blood, and is derived from either donated whole blood or apheresis. Once administered, the half-life of FFP is 4 to 6 hours. The risks of FFP are similar to those of other blood products, and may include febrile reactions, urticaria (reported in 1–3% of cases), and rarely transfusion-induced acute lung injury (TRALI) or anaphylaxis.¹¹ The traditional dose for FFP is 10 to 15 mL/kg,¹¹ which in most adults is equivalent to at least three 180 to 300 mL bags of FFP. However, the efficacy of FFP decreases with milder elevations in INR. In a study of 174 FFP transfusions, significant changes in the INR were observed only in those patients with pretransfusion INRs greater than 1.7.¹²

Prothrombin complex concentrates are virally inactivated plasma products that contain all of the vitamin K dependent factors at concentrations up to 25 times higher than plasma levels.¹³ Although originally

developed for use in hemophilia, they have been found to be efficacious in the rapid reversal of anticoagulation due to warfarin.¹⁴ PCCs can be prepared and infused more quickly and in a much smaller volume than FFP, and carry no risk of TRALI.¹⁵ However, in the United States the three commercially available PCC products available contain primarily factor IX and are approved by the Food and Drug Administration (FDA) for hemophilia-related bleeding. All contain relatively lower levels of factor VII, which limits their efficacy in lowering the INR.¹⁵ The dosing of PCCs varies by manufacturer as well as indication, and the primary adverse event associated with PCC therapy is thromboembolism.¹³ The half-life of the factor IX in PCCs is 24 to 32 hours.

Recombinant factor VIIa is another option for the rapid correction of an abnormal INR. Like PCCs, it was developed for use in hemophilia, and can be given more quickly and in a smaller volume than FFP while carrying none of the inherent risks of blood products. Though only FDA-approved for hemophilia-related bleeding, numerous studies have reported off-label efficacy in a wide range of bleeding conditions.¹⁶ One case series found it to be safe and effective in reversal of excess warfarin-induced anticoagulation, including patients undergoing epidural catheter removal, Hickman catheter removal, and arterial sheath removal.¹⁷ Another case series indicated efficacy in controlling bleeding in patients with liver failure.¹⁸ However, a randomized controlled trial involving 245 patients with cirrhosis and upper gastrointestinal bleeding found no advantage to treatment with rFVIIa given in addition to standard therapies.¹⁹ Its half-life ranges between 1.7 and 3.1 hours, and like PCCs, there is a risk of thromboembolic events associated with its use.²⁰ When administered, the INR may be normalized as the PT is exquisitely sensitive to

Table 1 Treatment Thresholds and LMWH Guidelines Based On Periprocedural Bleeding Risk

Bleeding Risk	INR	UFH	Platelets	LMWH
Low	>2.0	NC	<50,000/ μ L	Hold one dose
Moderate	>1.5	NC*	<50,000/ μ L	Hold one dose
High	>1.5	Stop or reverse for PTT >1.5x control	<50,000/ μ L	Withhold for 24 h or up to two doses

*There was a trend toward recommending correcting for PTT >1.5 times control in moderate risk procedures amongst the consensus panel. INR, international normalized ratio; LMWH, low-molecular-weight heparin; NC, no consensus; PTT, partial thromboplastin time; UFH, unfractionated heparin.

Adapted from the SIR Consensus Guidelines for Periprocedural Management of Coagulation Status and Hemostasis Risk in Percutaneous Image-Guided Interventions.²⁷

factor VIIa levels. However, its dosing is widely variable and depends on the clinical situation, although typical doses are between 15 μ g/kg and 90 μ g/kg. PCCs and rFVIIa have only been directly compared in animal models²¹ and in vitro,²¹ and there are no clinical situations where either is clearly superior.²²

EVIDENCE AND GUIDELINES

Despite the wide range of therapeutic options available for the correction of an elevated INR, there is a relative paucity of evidence regarding acceptable INRs for image-guided procedures. The current literature includes mostly case studies and only one clinical study. Several studies of patients undergoing percutaneous procedures have found little relation between abnormal coagulation laboratory values and hemorrhagic complications. For instance, a retrospective study of 160 patients undergoing percutaneous nephrostomy compared those with an abnormal PT and partial thromboplastin time (PTT) with normal controls, and found no difference in hemorrhagic complications between the two groups.²³ Another study reviewed 658 central venous catheter placements in patients coagulopathic from liver disease, and despite median INRs of 2.4 in the subclavian group and 2.7 in the internal jugular group, only one major vascular complication occurred.²⁴ Similar results have been observed in patients undergoing tunneled central venous catheter removal²⁵ and angiography with access through the femoral artery.²⁶

The Society of Interventional Radiology (SIR) consensus guidelines regarding periprocedural management of coagulation recommend correction of INR based on the procedural bleeding risk.²⁷ For procedures with a low risk of bleeding, correction of the INR is recommended for values above 2.0, and for moderate and high risk procedures, the recommended threshold for correction is an INR above 1.5 (Tables 1 and 2).²⁷

The Intrinsic Pathway

BACKGROUND

In the classic cascade model of coagulation, the intrinsic pathway consists of factors XII, XI, prekallikrein (PK),

and high-molecular-weight kininogen (HMWK), known as the “contact” factors, as well as factors IX, VIII, X, V, and II (Fig. 1). Though its in vivo role is questionable,³ in vitro all components of this pathway are bioassayed by the partial thromboplastin time (PTT). Causes of an elevated PTT include antiphospholipid syndrome, severe liver disease, and hemophilia. PTT is effective in monitoring the anticoagulant activity of unfractionated heparin (UFH), as once heparin binds antithrombin the complex much more rapidly inactivates factors Xa, IIa, IXa, XIIa, and XIa. PTT is also effective in monitoring the activity of the direct thrombin inhibitors lepirudin and argatroban (Table 3), which are primarily used in the setting of heparin-induced thrombocytopenia (HIT). A third direct thrombin inhibitor, bivalirudin, is indicated for use in percutaneous coronary intervention in patients with HIT.

The low-molecular-weight heparins (LMWH) tinzaparin, dalteparin, and enoxaparin act with antithrombin to primarily inactivate factor Xa, as does the synthetic pentasaccharide fondaparinux (Table 3). These compounds have many advantages over UFH, such as the ability to be administered SQ, once- or twice-daily fixed dosing, and a greatly decreased risk of heparin-induced thrombocytopenia. However, as LMWH is renally excreted, its use is avoided in patients with a creatinine clearance less than 30 mL/min.²⁸

REVERSAL OF ANTICOAGULATION

In patients treated with the above anticoagulation agents, two questions arise in the periprocedural setting: Is the reversal of anticoagulation necessary, and, if necessary, how is it best achieved? For an elevated PTT, the SIR consensus guidelines again vary based on periprocedural bleeding risk.²⁷ There is no recommendation regarding management of an elevated PTT in low- and moderate-risk procedures, although there was a trend among the consensus panel toward recommending treatment for values greater than 1.5 times control in moderate-risk procedures. For those undergoing low- or moderate-risk elective procedures, one dose of LMWH should be held. For high-risk procedures, reversal of heparinization is recommended for PTT values 1.5 times greater than control. In high-risk

Table 2 Bleeding Risks Of Various Image-Guided Procedures

	Low Risk	Moderate Risk	High Risk
Vascular	<ul style="list-style-type: none"> • Dialysis access interventions • Venography • Central line removal • IVC filter placement • PICC line placement 	<ul style="list-style-type: none"> • Angiography and arterial intervention with access size up to 7F • Venous interventions • Chemoembolization • Uterine fibroid embolization • Transjugular liver biopsy • Tunneled central venous catheter • Subcutaneous port placement 	<ul style="list-style-type: none"> • Transjugular intrahepatic portosystemic shunt
Nonvascular	<ul style="list-style-type: none"> • Drainage catheter exchange • Thoracentesis • Paracentesis • Superficial aspiration and biopsy such as thyroid, or superficial lymph node • Superficial abscess drainage 	<ul style="list-style-type: none"> • Intraabdominal, chest wall, or retroperitoneal abscess drainage or biopsy • Lung biopsy • Transabdominal liver biopsy (core needle) • Percutaneous cholecystostomy • Gastrostomy tube placement • Straightforward radiofrequency ablation • Spinal procedures 	<ul style="list-style-type: none"> • Renal biopsy • Biliary interventions (new tract) • Nephrostomy tube placement • Complex radiofrequency ablation

IVC, inferior vena cava; PICC, peripherally inserted central catheter.

Adapted from the SIR Consensus Guidelines for Periprocedural Management of Coagulation Status and Hemostasis Risk in Percutaneous Image-Guided Interventions.²⁷

elective procedures, LMWH should be held for 24 hours or up to two doses (Table 1).²⁷

Reversal is the most straightforward with UFH. The PTT will normalize in 3 to 4 hours as the half-life of heparin is 60 to 90 minutes. For emergent procedures, heparinization can be reversed with protamine, which ionically binds and neutralizes heparin. One milligram of protamine neutralizes 100 units (U) of heparin, and the total amount of heparin in the body is approximated by the total amount given in the preceding 2 to 3 hours.²⁹ Thus, in a patient receiving 1000 U/h of heparin, the protamine dose will be 20 to 30 mg. Its onset of action is immediate, and the activity of protamine is monitored by the PTT, which is expected to normalize. Given its half-life of 10 minutes,

repeated infusions may be required. However, the maximum dose of protamine is 50 mg, which is administered over 10 minutes because protamine infusion may cause histamine release leading to bronchoconstriction and hypotension.¹³ Protamine also carries a risk of anaphylaxis. The risk is elevated in those with fish allergies (protamine is derived from fish sperm) and diabetics exposed to neutral protamine Hagedorn (NPH) insulin.²⁹ Decreasing the rate of infusion of protamine lessens the likelihood of its provoking an allergic response. Protamine is associated with several other significant adverse reactions including bradycardia, pulmonary hypertension, and acute lung injury.³⁰ In excess doses, protamine inhibits platelet function and may cause paradoxical anticoagulation.³⁰

Table 3 Characteristics and Reversal Agents for Subcutaneous and Intravenous Anticoagulants

Drug	Mechanism of Action	t _{1/2}	Assay	Reversal Agent
Heparin (UFH)	Increases AT protease activity	60–90 min	PTT	Protamine
Enoxaparin	Factor Xa inhibitor*	4.5–7 h	Anti-factor Xa	Protamine (partial); rFVIIa [†]
Dalteparin	Factor Xa inhibitor*	3–5 h	Anti-factor Xa	Protamine (partial)
Tinzaparin	Factor Xa inhibitor*	3–4 h	Anti-factor Xa	Protamine (partial)
Fondaparinux	Factor Xa inhibitor	17–21 h	Anti-factor Xa	rFVIIa [†]
Argatroban	Directly inhibits thrombin	39–51 min	PTT	None
Lepirudin	Directly inhibits thrombin	90–120 min	PTT	None
Bivalirudin	Directly inhibits thrombin	25 min	PTT	None

*LMWH also has less significant anti-factor IIa activity.

[†]Based on case reports; rFVIIa is not FDA-approved for this indication.

[‡]Reversal of fondaparinux with rFVIIa has only been studied in healthy volunteers. rFVIIa is not FDA-approved for this indication.

AT, antithrombin; PTT, partial thromboplastin time; UFH, unfractionated heparin.

The monitoring of LMWH and fondaparinux is more challenging, as is their reversal. Although routine monitoring is not recommended,³¹ the level of activity of LMWH and fondaparinux can be assessed by an antifactor Xa assay. This test is typically measured 4 hours after dosing, and the therapeutic range depends on the anticoagulant used as well as its dosing schedule. The reversal of LMWH is more difficult as protamine reverses the anti-factor IIa activity of LMWH, but not its more significant antifactor Xa activity.^{29,32} ACCP guidelines suggest using 1 mg of protamine for every 100 antifactor Xa units administered in the prior 8 hours, with 100 antifactor Xa units defined as 1 mg of enoxaparin.²⁸ If bleeding continues, 0.5 mg of protamine per 100 antifactor Xa units can be administered.²⁸ However, this is an unproven use of protamine²⁸; in one small case series, protamine was unable to stop abnormal bleeding in two-thirds of patients taking LMWH.³²

Factor VIIa may hold promise as an antidote to LMWH and fondaparinux. A review of the literature from January 2000 to December 2009 reports that factor VIIa has been used to reverse bleeding after enoxaparin and fondaparinux therapy in 7 and 2 cases respectively.³³ It was effective/partially effective in all the enoxaparin cases but only in one of the fondaparinux cases.³³ Factor VIIa given 2 hours after administration of fondaparinux to healthy volunteers normalized the PT and PTT in all subjects.³⁴ Although the direct thrombin inhibitors have relatively short half-lives (39–50 minutes and 80 minutes for argatroban and lepirudin, respectively), they do not yet have a proven antidote (Table 3).¹³

Thrombocytopenia and Platelet Dysfunction

THROMBOCYTOPENIA

Platelets play an essential role in normal hemostasis, both helping to physically form the clot as well as providing a phospholipid surface on which the major clotting reactions take place. They are produced by the cytoplasmic fragmentation of megakaryocytes, and typically survive 10 days after leaving the bone marrow. As with any cellular component of blood, a decrease in the number of circulating platelets reflects impaired production, increased destruction, or both. Conditions that adversely affect the production of platelets include drug-related bone marrow suppression, aplastic anemia, alcohol, and malignancies, whereas conditions that increase platelet destruction include autoimmunity, infections, and microangiopathic hemolytic anemia. Platelets may also be sequestered in patients with hepatosplenomegaly.

In thrombocytopenic patients undergoing percutaneous interventions, it is important to define the

platelet count necessary for hemostasis in a given procedure. Central venous catheter insertions and transjugular liver biopsies have all been studied in patients with differing degrees of thrombocytopenia. Haas et al reviewed 3,170 tunneled central venous catheter insertions, including 428 where the platelet count was less than 50,000/ μ L.³⁵ Only three patients experienced bleeding complications, and none of those patients were thrombocytopenic. In a prospective trial, Ray et al compared patients with platelet counts of less than 50,000/ μ L, 50 to 100,000/ μ L, and greater than 100,000/ μ L undergoing radiologically placed central venous catheter insertions.³⁶ There were no significant differences in complications among the three groups, although patients with platelets less than 50,000/ μ L received platelet transfusions during the procedure. Wallace et al reviewed 51 transjugular liver biopsies in patients with postbiopsy platelet counts of 5 to 105,000/ μ L and reported no hemorrhagic complications, despite 24 patients having platelet counts of 30,000/ μ L or lower. The authors concluded that 30,000/ μ L was a safe threshold for transjugular liver biopsy.³⁷ However, the SIR consensus guidelines recommend transfusion for all patients undergoing image-guided interventions and a platelet count less than 50,000/ μ L (Table 1).²⁷

When transfusing platelets, the dose is based on the degree of correction required. Platelets are given either as pools prepared from the concentrated platelets of four to eight random donors, or as a single donor apheresis pack. Each random donor platelet concentrate should increase the platelet count by 5,000 to 10,000/ μ L. Thus, the facility-specific number of random donor concentrates in a pooled dose of platelets determines the expected increase in platelet count. One apheresis pack, equivalent to 6 to 8 random donor concentrates, is expected to increase the platelet count by $\sim$ 30,000/ μ L. Patients receiving multiple transfusions may become refractory to transfused platelets; the use of leukoreduced platelets helps prevent refractoriness,³⁸ and once present, crossmatched or HLA-matched platelets may be effective.³⁹

PLATELET FUNCTION

The contribution of platelets to hemostasis is not only dependent on their number, but also how well they function. There are several rare inherited defects that affect platelet function, the most common of which is von Willebrand disease (which can also be acquired). More common is acquired platelet dysfunction due to medical conditions such as renal or liver failure, or drugs such as aspirin or clopidogrel. Bleeding time was formerly the primary screen for platelet dysfunction, but it has largely been supplanted by the platelet function analyzer (PFA-100[®], Siemens Healthcare Diagnostics, Deerfield, IL). However, in the periprocedural setting, it is not useful to routinely assess platelet function in those

without a history of abnormal bleeding.⁴⁰ Due to lack of evidence, the SIR guidelines do not address the measurement of platelet function by bleeding time before percutaneous interventions.²⁷

The main pharmacologic intervention for platelet dysfunction is the administration of desmopressin (DDAVP, 1-deamino-8-D-arginine vasopressin), a synthetic analogue of the hormone vasopressin. Although its exact mechanism of action is unknown, it increases serum levels of factor VIII, von Willebrand factor, and tissue plasminogen activator, and in vitro enhances platelet aggregation.⁴¹ It is useful in controlling bleeding in patients with hemophilia A and von Willebrand disease type 1, as well as in those with acquired platelet dysfunction, including uremia and cirrhosis.⁴² Desmopressin can be administered IV, intranasally, or SQ, although IV is usually the route of choice when given for hemostasis.⁴² The typical dose is 0.3 µg/kg, and it reaches maximal effect 30 to 60 minutes after administration. Tachyphylaxis quickly develops, and common side effects include facial flushing and fluid retention. Myocardial infarction has been associated with DDAVP administration in several case reports,^{43,44} but a review of 31 trials of patients undergoing major surgical procedures found no increase in arterial or venous thrombosis in those who received DDAVP as compared with placebo.⁴⁵

Periprocedurally, DDAVP has been most extensively studied in cardiac surgery. A meta-analysis of 17 placebo-controlled studies found that desmopressin only significantly reduced perioperative blood loss in those operations where there was excessive bleeding.⁴⁶ Desmopressin is the treatment of choice for patients with von Willebrand disease or mild hemophilia A undergoing surgery.⁴⁷ However, data for its routine use in patients undergoing percutaneous interventions is lacking, and the SIR consensus guidelines do not recommend the use of DDAVP even in procedures with significant bleeding risk.²⁷

A Mixed Defect: Disseminated Intravascular Coagulation

Disseminated intravascular coagulation (DIC) is a consumptive coagulopathy characterized by thrombocytopenia and a prolonged PTT and INR. It most frequently occurs in severe illness such as metastatic cancer, massive trauma, or bacterial sepsis. These abnormalities all expose tissue factor to blood, whether through necrosis, direct tissue injury, or increased cellular expression of tissue factor. Diffuse microvascular clotting results, which leads to end-organ damage. It also depletes platelets and coagulation factors in the circulating blood, causing a bleeding diathesis. Other laboratory abnormalities seen in DIC include elevated levels of D-dimer, a degradation product of cross-linked fibrin, and low levels

of fibrinogen. Microvascular clotting can also cause microangiopathic hemolytic anemia, characterized by schistocytes on the peripheral blood smear.

The periprocedural management of DIC is complex. Overall, the most important goal of management is treating the underlying cause. However, support with blood products is indicated in patients needing an invasive procedure or with active bleeding.⁴⁸ Platelets and FFP may be used to correct thrombocytopenia and coagulation factor deficiencies, respectively. For patients with platelet counts less than 50,000/µL, transfusion is indicated.⁴⁹ When fibrinogen levels fall to less than 50 mg/dL, cryoprecipitate should be used to increase levels to above 100 mg/dL. Cryoprecipitate is a concentrate of the fibrinogen, fibronectin, von Willebrand factor, factor VIII, and factor XIII found in FFP. Six units of cryoprecipitate should increase the fibrinogen level by 50 mg/dL in a 70 kg adult.⁴⁹ The risks of cryoprecipitate administration are similar to those of other blood products.⁵⁰ Despite the presence of microvascular clotting, heparin is only beneficial in patients with malignancy-related chronic DIC with thrombotic manifestations.⁵¹

CONCLUSION

The production of the platelet-filled fibrin clot is adversely affected by a diverse number of conditions and medications. However, whether the defect is due to the number of platelets, platelet function, or dysfunction in the coagulation pathways, the same issues arise in the periprocedural setting: defining when correction is indicated, and how it is best achieved. By integrating the clinical parameters of the bleeding risk of the procedure as well as its urgency, a comprehensive strategy for the management of coagulation defects in those undergoing image-guided procedures can be developed.

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