



Consensus Guidelines for Periprocedural Management of Coagulation Status and Hemostasis Risk in Percutaneous Image-guided Interventions

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ABBREVIATIONS

aPTT = activated partial thromboplastin time, DIC = disseminated intravascular coagulation, DTI = direct thrombin inhibitor, FFP = fresh frozen plasma, INR = international normalized ratio, LMWH = low molecular weight heparin, LP = lumbar puncture, NSAID = nonsteroidal antiinflammatory drug, PT = prothrombin time

PREAMBLE

The membership of the Society of Interventional Radiology (SIR) Standards of Practice Committee represents experts in a broad spectrum of interventional procedures from both the private and academic sectors of medicine. Generally, Standards of Practice Committee members dedicate the vast majority of their professional time to performing interventional procedures; as such, they represent a valid broad expert constituency of the subject matter under consideration for standards production.

Technical documents specifying the exact consensus and literature review methodologies, as well as the institutional affiliations and professional credentials of the authors of this document, are available upon request from SIR, 3975 Fair Ridge Dr., Suite 400 N., Fairfax, VA 22033.

METHODOLOGY

SIR produces its Standards of Practice documents by using the following process. Standards documents of relevance and timeliness are conceptualized by the Standards of Practice Committee members. A recognized expert is identified to serve as the principal author for the standard. Additional authors may be assigned depending on the magnitude of the project.

An in-depth literature search is performed by using electronic medical literature databases. Then, a critical review of peer-reviewed articles is performed with regard to the study methodology, results, and conclusions. The qualitative weight of these articles is assembled into an evidence table, which is used to write the document such that it contains evidence-based data with respect to content, complication rates, outcomes, and thresholds for prompting quality assurance reviews.

When the evidence of literature is weak, conflicting, or contradictory, consensus for the parameter is reached by a minimum of 12 Standards of Practice Committee members by using a modified Delphi consensus method (**Appendix**) (1). For the purposes of these documents, consensus is defined as 80% Delphi participant agreement on a value or parameter.

The draft document is critically reviewed by the Standards of Practice Committee members either by telephone conference calling or face-to-face meeting. The finalized draft from the Committee is sent to the SIR membership for further input/criticism during a 30-d comment period. These comments are discussed by the Standards of Practice Committee, and appropriate revisions made to create the finished standards document. Before its publication, the document is endorsed by the SIR Executive Council.

INTRODUCTION AND BACKGROUND

Hematologic management in the patient undergoing percutaneous image-guided intervention is complex because of the wide range of procedures and equally wide range of patient demographics and comorbidities. Concurrent increases in the use of short- and long-term anticoagulation, as well as the increasing use of antiplatelet agents, further complicates the periprocedural management of these patients. Despite the continuing increase in the volume of percutaneous image-guided procedures, there is a general paucity of data regarding the periprocedural management of the patient with abnormal coagulation parameters. In the absence of data, clinicians may respond to the patient with abnormal coagulation parameters by canceling or postponing the procedure, altering an otherwise indicated procedure, or infusing blood products such as fresh frozen plasma (FFP) or platelets. Recommendations from open surgical experience can be extrapolated, but may not be completely applicable to interventional procedures because, in open cases, the operator is typically able to directly visualize and promptly control any bleeding complications. Finally, medicolegal factors may influence the management of the patient, as clinicians feel the

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Table 1. Tests of Hemostasis

Test	Indication	Normal Range
INR/PT	Extrinsic pathway (I, II, V, VII, X) Oral anticoagulant therapy Liver disease	INR 0.9–1.1
aPTT	Intrinsic pathway (VIII, IX, XI, XII) Intravenous heparin therapy von Willebrand disease Factor VIII, IX, or XI deficiency	aPTT 25–35 s
Platelet count	Known or suspected thrombocytopenia	150,000–450,000/ μ L
Bleeding time	No current indication before image-guided procedures	—

aPTT = activated partial thromboplastin time, INR = international normalized ratio, PT = prothrombin time.

need to “correct” an abnormal coagulation factor, despite the fact that studies of bleeding complications in percutaneous procedures have not shown a correlation between mild to moderate abnormality of preprocedural coagulation parameters and a higher incidence of bleeding complications.

The coagulation status of patients undergoing image-guided interventions should be assessed whenever the procedure involves direct entry into the arterial or venous system as an anticipated part of the procedure or whenever there is a possibility of inadvertent entry into the arterial or venous system with significant-sized interventional devices or tools. Patients are at increased risk for delayed detection of postprocedural hemorrhage when the site of the intervention is not easily assessed and poorly controllable, such as percutaneous intraperitoneal procedures. Coagulation status is complex; components of the intrinsic and extrinsic coagulation cascade and platelet function figure integrally into human hemostasis. The components of coagulation are evaluated by multiple tests of hemostasis. These tests and the component of coagulation function they assess are described later in this document and are summarized in **Table 1**, along with normal values for each test.

DEFINITIONS

Coagulation Parameters

Prothrombin time. The prothrombin time (PT) test measures the clotting time upon activation of the extrinsic and common coagulation pathway. It is used for monitoring oral anticoagulant therapy and is now widely reported as an international normalized ratio (INR). The degree of prolongation of the clotting time correlates to the degree of deficiency or inhibition of extrinsic or common pathway clotting factors I (fibrinogen), II (prothrombin), V, VII, and X, which are synthesized by the liver. When any of these factors is deficient, the PT is prolonged and the INR is elevated. The PT in a healthy adult is approximately 11–14 s. There is variation depending on the reagent used in the test (2).

International normalized ratio. The INR is an expression of the results of a PT in a standardized testing environment. It is calculated by using an international standard that corrects for laboratory variation. The INR allows for universal standardization anticoagulant therapy. In the following calculation, the ISI is the International Sensitivity Index of the thromboplastin reagent used in the assay: $INR = (\text{patient PT} / \text{control PT})^{ISI}$.

In this test, the patient’s plasma is mixed with PT reagent containing thromboplastin and calcium chloride. The time to clot formation is measured. The degree of prolongation of the clotting time correlates to the degree of deficiency or inhibition of extrinsic or common pathway clotting factors I (fibrinogen), II (prothrombin), V, VII, and X, which are synthesized by the liver. When any of these factors is deficient or inhibited, the PT is prolonged and the INR is elevated. The INR results from different kits can vary by an average of more than 0.7 (3). This variation results from differing sensitivities to the various coagulation factors (4). The INR in a normal patient not undergoing warfarin therapy is 0.9–1.1.

A prolonged PT and elevated INR occur with warfarin therapy, vitamin K deficiency, lupus anticoagulants, extrinsic pathway coagulation factor deficiencies, disseminated intravascular coagulation (DIC), bile duct obstruction, malabsorption, malnutrition, and other conditions. Hirudin, argatroban, and heparin may prolong the PT. Because the coagulation factors are synthesized in the liver, the PT is elevated with severe liver failure and acute liver injury (5,6).

Activated partial thromboplastin time. The activated partial thromboplastin time (aPTT) measures the clotting time upon activation of the intrinsic coagulation pathways. In this test, the patient’s plasma is mixed with reagent containing an activator, phospholipid, and calcium chloride. The time to clot formation is measured.

A normal aPTT in an adult is approximately 25–35 s. A therapeutic ratio of 1.5–2.5 times the control value is frequently employed in heparin therapy; however, this range varies depending on the reagent.

A prolonged aPTT occurs with factor deficiencies (especially of factors VIII, IX, XI, and/or XII), inhibitors (lupus anticoagulants), liver disease, DIC, vitamin K deficiency, or therapeutic anticoagulants such as heparin, hirudin, or argatroban). The aPTT is not useful in monitoring warfarin therapy (7). An isolated elevated aPTT is often the most common transient abnormal coagulation test result, with half of cases reverting to a normal result on subsequent testing (8). Furthermore, lupus inhibitors and factor XII deficiency are known to prolong the aPTT but do not cause excessive bleeding (8).

Thrombin time. Thrombin time provides an assay for fibrinogen concentration indirectly by measuring exogenous thrombin activated clotting times (9).

Bleeding time. Originally introduced in 1901 by Milian, bleeding time has been used to diagnose platelet disorders, assess patients for clinically significant bleeding tendencies before invasive procedures, and assess the effects of various therapies on bleeding tendencies and platelet function. The bleeding time is subject to reliability and reproducibility issues, with a number of studies showing that it is neither a specific nor a sensitive indicator of bleeding risk associated with surgery or other invasive procedures (10). Secondary to this, it has largely fallen out of favor in modern clinical practice as an assessment for bleeding tendencies because of conflicting data on its usefulness (11).

Platelet count. The platelet count is generally measured as a standard part of the complete blood count. It is commonly used to diagnose and follow bleeding disorders, thrombocytopenia, drug-induced thrombocytopenia, DIC, and neoplastic disorders, and to evaluate the response to platelet transfusions. The platelet count simply reflects the number of circulating platelets, not the platelet function. A normal adult platelet count is approximately 150,000–450,000 platelets per microliter of blood (12). A platelet count lower than 20,000/ μ L is a life-threatening event in which spontaneous bleeding may occur (12).

A small number of patients receiving heparin (including low-dose

heparin) develop thrombocytopenia secondary to an antibody mediated process (13). Drugs and chemicals associated with thrombocytopenia include chemotherapeutic agents, chloramphenicol, colchicine, H₂ blocking agents, heparin, hydralazine, indomethacin, isoniazid, quinidine, streptomycin, sulfonamide, thiazide diuretic agents, and tolbutamide (14). Estrogen and oral contraceptive agents may cause elevated platelet levels (15).

ANTICOAGULANTS

Warfarin

Warfarin (Coumadin) antagonizes the production of the vitamin K–dependent extrinsic pathway clotting factors (II, VII, IX, X) and protein C and S in the liver. The clinical effect is measured by the INR, which reflects antagonism of factor VII, which has the shortest half-life of approximately 6 h. Therapeutic INR values may vary by indication for anticoagulation, but most often range from 2.2 to 2.8. Patient comorbidities, concomitant medication use, as well as diet may significantly alter the effect of warfarin. Congestive heart failure, malignancy, malnutrition, diarrhea, unsuspected vitamin K deficiency, and concomitant antibiotic use may all enhance the response to warfarin. The half-life of warfarin (37 h) is dependent on the amount of circulating clotting factors, the most important of which is factor II (prothrombin half-life of 96 h) (16).

Heparin (Unfractionated)

Unfractionated heparin potentiates the action of antithrombin III by accelerating inhibition of factor Xa, and is dosed according to weight and usually administered by continuous intravenous infusion. Therapeutic response is monitored by aPTT, which is targeted at 1.5–2.5 times normal. Unfractionated heparin has a complex metabolism, with the half-life varying from 23 min to 2.48 h (17).

The platelet count should be monitored after the administration of heparin for the possibility of heparin-induced thrombocytopenia, which is defined as a platelet count of less than 150,000/ μ L or a 50% decrease in the platelet count within 5–10 d after the initiation of heparin therapy. There are two types: type I is a benign self-limited disorder in which the platelet count is rarely lower than 100,000/ μ L and type II is a possibly life-threatening disorder with platelet counts often lower than 75,000/ μ L and often seen in association with acute arterial and/or venous platelet-rich “white” thrombi.

Low Molecular Weight Heparin

Low molecular weight heparin (LMWH) inhibits factor Xa, and is administered subcutaneously and often dosed by weight. LMWH is poorly reversible with protamine and therefore does not prolong the aPTT, nor does it affect the INR (18). Therapeutic dosing (ie, treatment of acute deep vein thrombosis) is maintained at 12-h intervals whereas prophylactic dosing (ie, postoperative deep vein thrombosis prophylaxis) is kept at 24-h intervals. Drug therapy can be monitored by measuring anti-factor Xa activity; however, this is not the standard of practice in large part because of the short half-life of approximately 2–4 h with mild prolonged anticoagulant effect in patients with renal failure (18).

Fondaparinux

A synthetic pentasaccharide that acts as an indirect selective inhibitor of factor Xa, fondaparinux is administered subcutaneously and used in a similar fashion as LMWH. It has a linear pharmacokinetic profile with 100% absorption, independent of dose, and an approximate half-life of 17 h, allowing for once-daily dosing. Fondaparinux is almost completely excreted by the kidneys, thereby precluding its use in patients with renal dysfunction (19). Of note, because of its lack of affinity to platelet factor 4, the risk of heparin-induced thrombocytopenia is substantially lower compared with unfractionated heparin and LMWH (20).

Direct Thrombin Inhibitors

Direct thrombin inhibitors (DTIs) directly inhibits the enzyme thrombin, producing a more predictable anticoagulant response than heparin (21).

Bivalent DTIs such as hirudin, bivalirudin, and lepirudin block thrombin at the active site and exosite 1, whereas univalent DTIs such as argatroban bind only to the active site. Although no widely available therapeutic drug monitoring is available for DTIs, in contrast to unfractionated heparin (ie, aPTT) and warfarin (ie, INR), an ecarin clotting time would be the most appropriate test if needed (22).

HEMOSTATIC AGENTS

Fresh Frozen Plasma

FFP contains plasma proteins, including coagulation factors, that can be administered to correct coagulopathies secondary to clotting factor deficiency; however, the effect of FFP is variable because the variable concentration of vitamin K–dependent clotting factors. On average, at least 10 mL/kg is needed to effectively increase plasma protein levels. Common dose ranges are from 15 to 30 mL/kg. In practice, in the patient with an INR in the 2.5 range, 2 U of FFP may be effective in reversing the effect of warfarin. Patients with higher INR levels should receive doses accordingly, with possible concomitant use of vitamin K in the absence of significant liver disease (23–26).

Platelets

Platelets are fractionated blood product used in the setting of thrombocytopenia or platelet dysfunction. They are often dosed in increments of 4–6 U (from random donors) or as one single-donor unit (27).

Protamine

Protamine may be used in emergency situations when rapid reversal of heparin is needed before a procedure or when heparin reversal is desired before removing arterial catheters or sheaths. Protamine has a rapid onset of action within 10 min after administration. Its half-life, however, is short and ranges from 5 to 7.5 min, which can lead to “paradoxical” repeat anticoagulation after protamine administration. Protamine dosing strategies vary considerably. A “neutralizing dose” of protamine is 2 mg/kg. Protamine may also be dosed according to the amount of heparin given, at a 1 mg protamine/100 U heparin ratio. To reverse commonly given intraprocedural doses of heparin (3,000–5,000 IU), a total of 50 mg protamine is often given in adults. Protamine should be given by slow intravenous “push” or infusion over a period of 5 to 10 min. Side effects include hypotension, bradycardia, pulmonary artery hypertension, decreased oxygen consumption, and anaphylactoid reactions (28–32).

Vitamin K (Phytonadione)

Vitamin K (phytonadione) may be given orally, intravenously, or subcutaneously depending on the value of the INR and the desired time frame for anticoagulant reversal. The American College of Chest Physicians has published evidence-based guidelines for the use of vitamin K in managing elevated INRs and/or clinical bleeding in patients receiving oral anticoagulation (33). In stable, elective cases without active bleeding, oral administration (5–10 mg in adults) is preferred. Although intravenous administration of vitamin K is associated with a risk of anaphylactoid reaction, it has a more rapid effect than subcutaneous vitamin K and may be more effective in the truly emergent case. The United States Food and Drug Administration has issued a “black box” warning for the subcutaneous, intravenous, and intramuscular routes of administration as a result of reports of severe reactions, including fatalities (34,35).

Cryoprecipitate

Cryoprecipitate is used in acquired or hereditary deficiencies of fibrinogen. Ten units of cryoprecipitate will typically increase fibrinogen level by 75 mg/dL in a 70-kg patient (36).

Recombinant Factor VIIa

Recombinant factor VIIa is used in patients with hemophilia with inhibitors to factor VIII or in severe, non-hemophilia-related bleeding such as acute trauma (37).

Desmopressin

Desmopressin, or 1-deamino-8-D-arginine vasopressin, is a synthetic analogue of antidiuretic hormone. Desmopressin acts through an unclear mechanism to enhance the plasma levels of factor VIII and von Willebrand factor (38). A dose of 0.3 $\mu\text{g}/\text{kg}$ is given intravenously, usually diluted in 100 mL normal saline solution and infused over a period of 20–30 min. A single dose can be expected to increase the factor VIII level three to six fold. Adverse effects may include mild hyponatremia. Tachyphylaxis has been reported in patients who have received multiple treatments. There are case reports of vascular thrombosis and myocardial ischemia after intravenous administration (39).

Desmopressin may be indicated before image-guided procedures in patients with hemophilia or von Willebrand disease and as a potential treatment option in patients with acquired platelet disorders as a result of uremia, liver disease, or antiplatelet agents (40,41).

REFUSAL OF BLOOD PRODUCTS

There are currently no interventional radiology specific guidelines for handling hemorrhage or preventing bleeding complications in patients who refuse administration of blood products for religious or other reasons. As such, we currently recommend to consult and coordinate care for these patients closely with the hematology department of the respective hospital. Administration of erythropoietin and desmopressin can be strongly considered before the start of procedures that are likely to cause significant bleeding or in patients with active bleeding at the time of, or as a result of, the interventional procedure. Other procedures acceptable to the elders of Jehovah's Witness include apheresis, hemodialysis, plasma-derived fractions (immunoglobulins, vaccines, antivenins, albumin, cryoprecipitate), hemostatic products containing blood fractions (fibrin glue and/or sealant), and hemostatic bandages containing plasma fractions and thrombin sealants (42,43).

TRANSFUSION MANAGEMENT

Fresh Frozen Plasma

The most common intervention before image-guided procedures is transfusion of FFP. In the United States, more than 3 million units of FFP are transfused each year (44,45). Dzik and Rao reported in a 3-mo audit of FFP use at the Massachusetts General Hospital that the most common reason for prescribing FFP was to prepare a patient with an elevated INR for an invasive procedure. This indication accounted for one third of all requests for FFP (46). Stanworth et al (47) reported a review of 57 randomized controlled trials investigating the efficacy of FFP to prevent hemorrhagic complications over a wide variety of indications and clinical settings, including cardiac surgery. They found the data insufficient to recommend or refute the prophylactic use of FFP. Because of the lack of data, percutaneous procedures were not included in this comprehensive review (47). There is a clear need for additional investigation of the use of FFP with image-guided procedures (47).

Segal and Dzik (48) recently reported a review of 25 studies analyzing the ability of abnormal coagulation parameters to predict bleeding associated with invasive bedside or image-guided procedures. Of the 25 studies available for analysis, one was a clinical trial (comparison of transjugular liver biopsy vs percutaneous biopsy with tract plugging) (49). The remainder of the studies were case series. The studies included patients undergoing bronchoscopy with biopsy, central vein cannulation, femoral angiography, liver biopsy, kidney biopsy, paracentesis, thoracentesis, and lumbar puncture (LP). Overall, the authors concluded that elevated coagulation parameters provide little to no predictive value for bleeding complications from image-guided interventions. They assert that, in the absence of randomized, controlled studies, mild to moderate elevation of coagulation times should neither be assumed to represent an increased risk for periprocedural bleeding nor be used as an indication for transfusion of FFP or clotting factor concentrates.

The use of FFP in nonbleeding cases before image-guided interventions must be weighed against the potential risks of transfusion. An increasingly recognized and often life-threatening complication, transfusion-

related acute lung injury, has an insidious onset characterized by hypoxia, dyspnea, and volume overload, occurring after transfusion of approximately 1 in 8,000–60,000 U of FFP (50). The ability of patients with congestive heart failure or other similar conditions to handle the volume and rate at which transfusions may occur are limited and should be addressed accordingly. Other important transfusion-related complications include allergic or anaphylactic reactions, transmittal of infectious diseases including HIV, hepatitis B, and hepatitis C, albeit rarely, and acute hemolysis secondary to anti-A or anti-B antibodies (50).

Literature data on preprocedural coagulation testing for specific procedures are summarized later.

Angiography

In a prospective study of 1,000 patients undergoing arteriography via common femoral artery access, Darcy et al (51) identified 85 patients with abnormal coagulation parameters, defined as a PT greater than 15 s (range, 15–20.8 s; normal, 13 s). Major bleeding, defined as a groin hematoma greater than 4 cm, was found in 1.2% of patients (one of 85) with abnormal coagulation parameters and 1.6% of patients (15 of 915) with normal coagulation parameters. The majority of procedures were performed with 5-F catheters (72%) or 6–7-F catheters (23%). There was, however, a correlation of a higher incidence of hematoma with a platelet count less than 100,000/ μL ($P = .002$). The study concluded that, in the absence of an overt history of bleeding and an expected PT of less than 18 s, preprocedural testing with PT and aPTT measurement is not warranted (51).

Liver Biopsy

In a laparoscopic study, Ewe (52) was able to directly visualize the liver biopsy site for bleeding. The author found that 4.3% of patients with a PT longer than 13.5 s showed bleeding for more than 12 min after biopsy, compared with 4.6% of patients with normal coagulation parameters. It should be noted that embolization of the biopsy tract was not performed on any patients. The author was unable to draw any correlation between the degree of abnormality of preprocedural coagulation parameters and the duration of observed bleeding (52).

Central Venous Catheter Placement

Fisher and Mutimer (53) evaluated 580 patients with an INR greater than 1.5 undergoing central venous catheterization. All procedures were performed with a 16- or 18-gauge needle. The majority of patients (83%) had a platelet count less than 150,000/ μL . One patient had major bleeding (0.2%) as a result of inadvertent puncture of the carotid artery. The authors concluded that central venous access can be performed safely by experienced physicians in the presence of abnormal coagulation parameters (53). Other studies have reported similar results (54–58).

Morado et al (59) reported a case series of 15 pediatric patients with hemophilia and inhibitors who underwent a total of 34 catheter insertions. The mean age was 8.8 y (range, 16 mo to 39 y); all patients had factor VIII/IX inhibitors. Pericatheter bleeding was seen in seven catheter insertions in six patients, which required substantive treatment for several days (59).

Central Venous Catheter Removal

There is some controversy and lack of consensus regarding the management of patients undergoing removal of tunneled catheters. There is no evidence of the value of preremoval coagulation parameters or platelet count in the management of these patients. Stecker et al (60) reported a study of 180 patients with tunneled cuffed central venous catheters. Time to hemostasis was 5 min for 166 patients, with 14 patients requiring more than 5 min of manual compression at the insertion site (range, 10–35 min). Only one patient required more than 15 min of pressure. In the 14 patients with prolonged (> 5 min) time to hemostasis, statistically significant factors included use of antiplatelet agents, renal failure, high-flow hemodialysis catheter, and experience of the operator. They concluded that preremoval laboratory evaluation was not warranted and that platelet dysfunction was a more important factor than platelet number in prolonging time to hemostasis, but that the degree of prolongation was unlikely to be clinically relevant (60).

Nephrostomy Tube Placement

Martin et al (61) reported a series of 160 patients who underwent percutaneous nephrostomy tube placement by an experienced operator. A total of 153 patients had normal coagulation tests results; seven patients had an abnormal PT or aPTT (mean PT, 13.9 s; mean aPTT, 30.3 s). No patients in the study experienced bleeding complications associated with nephrostomy tube placement. The authors concluded that screening coagulation studies are not necessary in patients before nephrostomy tube placement (61,62).

PLATELET TRANSFUSIONS

Severe thrombocytopenia may result in an increased bleeding risk with image-guided interventions and open surgery, although the recommended threshold for platelet transfusion varies among procedures. As with the use of FFP, the literature data for platelet use are mostly from case series, retrospective case reviews, and consensus data (63–67). There are many etiologies of thrombocytopenia and significant variation in platelet function associated with patient comorbidities and medication use. For example, thrombocytopenia caused by platelet consumption is generally less likely to cause bleeding at any given platelet count, compared with thrombocytopenia caused by decreased platelet production, because circulating platelets in consumptive thrombocytopenia tend to be larger and relatively hyperfunctional (68). Conversely, in the presence of uremia, platelet function must be taken into account when considering the bleeding risk associated with thrombocytopenia (69). The decision for platelet transfusion before percutaneous procedures is therefore based on multiple variables, including platelet count, etiology of thrombocytopenia, platelet function, type of procedure, operator expertise and experience, and concurrent coagulopathies and other comorbidities.

Shiffer et al (70) reported recommendations for platelet transfusions in patients with cancer. With respect to periprocedural management, the authors concluded that, based on several consensus statements, in the absence of coexisting coagulation abnormalities, a platelet count of 40,000–50,000/ μL is sufficient for the safe performance of major invasive procedures. The consensus statements included data from major operative procedures such as laparotomy or craniotomy and more minor invasive procedures such as central catheter placement, transbronchial biopsy, and bone marrow biopsies. They noted that certain procedures, such as bone marrow aspiration and biopsy, are routinely performed safely at platelet levels of 20,000/ μL or lower (70). There were some data suggesting that coexisting coagulopathies resulted in higher periprocedural blood loss in the setting of thrombocytopenia. They noted the relative lack of studies evaluating the safety and efficacy of invasive procedures in patients with thrombocytopenia. Posttransfusion platelet count measurements were strongly recommended in all patients receiving platelet transfusions before invasive procedures (70).

Similar to the plasma-rich product FFP, platelets are also associated with a multitude of risks, including transfusion-related acute lung injury, anaphylaxis, and viral/bacterial contamination. Slichter et al (71) reported that, with increasing number of platelet transfusions, the effectiveness progressively decreased, even when lymphocytotoxic antibody-positive patients were removed from the analysis. The judicious use of platelet transfusion may reduce the overall benefit in a time of need, such as in the setting of active bleeding (71).

Literature data on periprocedural bleeding risks in the setting of thrombocytopenia for specific procedures are summarized later.

Liver Biopsy

With respect to percutaneous transabdominal liver biopsy, McVay and Toy (72) reported an incidence of clinically significant bleeding of 3.4% in 291 consecutive patients with mild thrombocytopenia as defined by platelet counts between 50,000/ μL and 99,000/ μL . There was no difference in bleeding incidence in comparison with patients with normal platelet counts. Underlying malignancy appeared to be an independent risk factor for bleeding (72). Wallace et al (73) reported a series of 50 patients with hematologic malignancies with moderate to severe thrombocytopenia who underwent transjugular liver biopsy. The mean preprocedure, pretransfusion platelet count was 17,000/ μL . Patients received prophylactic platelet

transfusions before the procedure, with posttransfusion platelet counts ranging from 5,000/ μL to 105,000/ μL (mean, 38,000/ μL), and lower than 30,000/ μL in 24 patients. Patients received a mean of 11 U of platelets. No clinically significant bleeding was encountered. The authors concluded that a platelet count of 30,000/ μL represented a safe level for transjugular liver biopsy (73).

Ewe (52) reported a series of 200 consecutive patients in whom liver bleeding time was observed by laparoscopy after percutaneous biopsy. Liver bleeding time and patient outcome did not correlate with preprocedural coagulation parameters or platelet count. The author concluded that standard measures of evaluation of coagulation and platelet count were not useful in determining bleeding risk associated with percutaneous liver biopsy (52).

Central Venous Catheter Placement

Multiple studies have evaluated the risk of bleeding with the placement of central venous access devices in the setting of thrombocytopenia. In a prospective study of 105 patients, Ray and Shenoy (74) evaluated the effect of various levels of thrombocytopenia on the incidence of bleeding complications necessitating intervention. Patients were divided into three groups: (i) moderate thrombocytopenia (< 50,000/ μL), (ii) mild thrombocytopenia (50,000–100,000/ μL), and (iii) thrombocyte counts greater than 100,000/ μL . Patients in the first group received platelet transfusions during the procedure, although the mean increase in platelet count was only 11,500/ μL . There were no significant bleeding complications requiring intervention in patients with thrombocytopenia (74). Other studies have shown similar results in patients with thrombocytopenia and an elevated INR, with a low incidence of bleeding complications (ranging from 1% to 6%) and no deaths caused by periprocedural bleeding complications (36,56–58).

Lumbar Puncture

Multiple studies have investigated the incidence of bleeding complications with LP in the setting of thrombocytopenia. Edelson et al, in 1974 (75), reported spinal subdural hematomas after LP in eight patients with thrombocytopenia, five of whom had platelet counts lower than 20,000/ μL . Breuer et al, in 1982 (76), reported significant spinal subarachnoid hematomas in two of 13 patients with platelet counts lower than 20,000/ μL who did not undergo preprocedural platelet transfusion. None of the seven patients with this degree of thrombocytopenia who received platelet transfusions developed significant bleeding complications. Howard et al, in 2000 (77), retrospectively reviewed the results of 4,309 LPs performed on 959 children with acute lymphocytic leukemia. A total of 378 procedures were performed on patients with platelet counts less than 25,000/ μL . There were no significant bleeding complications in any patients, although a higher incidence of traumatic LP appeared to be associated with worsening thrombocytopenia. Vavricka et al (78) reported the results of 195 LP procedures on 66 adult patients with acute leukemia. There were no significant bleeding complications, although the authors reported a statistically significant trend in the occurrence of traumatic procedures in patients with the lowest platelet counts (78). Each of these authors recommended a threshold level of 20,000/ μL for platelet transfusion before LP, and most noted the effect of increased operator experience in reducing hemorrhagic complications and traumatic procedures.

Nephrostomy Tube Placement

Many of the authors of studies reviewed here have expressed the opinion that severe coagulopathies and severe thrombocytopenia should be corrected before percutaneous nephrostomy tube placement, although specific recommendations for threshold values vary and are not specified in many cases.

ANTIPLATELET AGENTS AND MANAGEMENT

Aspirin

Aspirin irreversibly inhibits platelet cyclooxygenase, a key enzyme in production of thromboxane A₂, which acts as a mediator of platelet activation and aggregation (79). In patients with normal bone marrow function and reserve, platelet lifespan is approximately 10 d. Taking into

Table 2. Category 1: Procedures with Low Risk of Bleeding, Easily Detected and Controllable**Procedures****Vascular**

- Dialysis access interventions
- Venography
- Central line removal
- IVC filter placement
- PICC placement

Nonvascular

- Drainage catheter exchange (biliary, nephrostomy, abscess catheter)
- Thoracentesis
- Paracentesis
- Superficial aspiration and biopsy (excludes intrathoracic or intraabdominal sites): thyroid, superficial lymph node
- Superficial abscess drainage

Preprocedure laboratory testing

INR: routinely recommended for patients receiving warfarin anticoagulation or known or suspected liver disease

aPTT: routinely recommended for patients receiving intravenous unfractionated heparin

Platelet count: not routinely recommended

Hematocrit: not routinely recommended

Management

INR > 2.0: threshold for treatment (ie, FFP, vitamin K)

PTT: no consensus

Hematocrit: no recommended threshold for transfusion

Platelets: transfusion recommended for counts < 50,000/ μ L

Clopidogrel: withhold for 5 d before procedure

Aspirin: do not withhold

LMWH (therapeutic dose): withhold one dose before procedure

There was an 80% consensus on each of these recommendations unless stated otherwise. The management recommendations for each coagulation defect and drug assume that no other coagulation defect is present and that no other drug that might affect coagulation status has been administered. 1-Deamino-8-D-arginine vasopressin may be indicated before image-guided procedures in patients with hemophilia and von Willebrand's disease (38–41). aPTT = activated partial thromboplastin time, FFP = fresh frozen plasma, INR = International Normalized Ratio, IVC = inferior vena cava, LMWH = low molecular weight heparin, PICC = peripherally inserted central catheter, PTT = partial thromboplastin time.

account variabilities in drug clearance, withholding antiplatelet agents for 5 d will therefore result in approximately 30%–50% of platelets at the time of the procedure to have normal function.

Thienopyridines

Thienopyridines include clopidogrel, ticlopidine, and prasugrel. All medications within the thienopyridine family act by inhibiting adenosine diphosphate–dependent binding to platelet receptors thereby inhibiting activation of the glycoprotein IIb/IIIa pathway. Similar to aspirin, thienopyridines inhibit platelet aggregation for the entire lifespan of the platelet (approximately 7–10 d) (79,80). However, the effective half-life is approximately 4 h and, if exogenous administration of platelets is performed 6–8 hours after the last dose, it may be possible to restore some level of hemostasis as the newly transfused circulating platelets will not undergo inhibition (81).

Nonsteroidal Antiinflammatory Drugs

The effect of nonsteroidal antiinflammatory drugs (NSAIDs) on platelet aggregation, unlike aspirin, is reversible and will decay along with clearance of drug levels from the circulation. In general, NSAIDs do not cause significant bleeding problems except in patients with existing coagulopathies, such as hemophilia, von Willebrand disease, or severe thrombocytopenia. Paradoxically, NSAIDs tend to diminish the antiplatelet effect of aspirin when given concomitantly, and therefore should not be given to patients receiving aspirin therapy for cardiovascular disease (82,83).

Glycoprotein IIb/IIIa Inhibitors

Glycoprotein IIb/IIIa inhibitors act as antagonists to the integrin complex glycoprotein IIb/IIIa, found on platelets, thereby inhibiting platelet aggregation. These are administered intravenously, have a short half-life, and include abciximab, eptifibatide, and tirofiban (84).

Efficacy and Complications

Antiplatelet therapy has been shown to be effective in patients with coronary artery disease. Because of the prevalence of coronary artery disease, antiplatelet agents are commonly on the list of medications of patients presenting for noncardiac image-guided procedures. Two of the most commonly prescribed medications include aspirin and clopidogrel (Plavix; Bristol-Myers Squibb, New York, New York). Atwell et al (85) reported, after a retrospective review of 15,181 image-guided percutaneous core biopsies, the low risk of bleeding with recent aspirin therapy. The incidence of bleeding, irrespective of the organ that undergoes a biopsy, in patients taking aspirin within 10 d of the scheduled biopsy was 0.6%, compared with 0.4% in patients not taking aspirin ($P = .34$; not statistically significant) (85). Fox et al (86) reported the results of the Clopidogrel in Unstable Angina to Prevent Recurrent Ischemic Events trial in which 12,562 patients with unstable angina were randomized to receive clopidogrel or placebo. Of the study patients undergoing bypass surgery ($n = 1,015$), the rates of life-threatening hemorrhage were 4.2% in the placebo group and 5.6% in the clopidogrel group (relative risk, 1.30; not significant). The authors reported an excess of seven patients requiring transfu-

Table 3. Category 2: Procedures with Moderate Risk of Bleeding**Procedures****Vascular**

Angiography, arterial intervention with access size up to 7 F
 Venous interventions
 Chemoembolization
 Uterine fibroid embolization
 Transjugular liver biopsy
 Tunneled central venous catheter
 Subcutaneous port device

Nonvascular

Intraabdominal, chest wall, or retroperitoneal abscess drainage or biopsy
 Lung biopsy
 Transabdominal liver biopsy (core needle)
 Percutaneous cholecystostomy
 Gastrostomy tube: initial placement
 Radiofrequency ablation: straightforward
 Spine procedures (vertebroplasty, kyphoplasty, lumbar puncture, epidural injection, facet block)

Preprocedure laboratory testing

INR: recommended

aPTT: recommended in patients receiving intravenous unfractionated heparin

Platelet count: not routinely recommended

Hematocrit: not routinely recommended

Management

INR: correct to < 1.5

aPTT: no consensus (trend toward correcting for values > 1.5× control, 73% consensus)

Platelets: transfusion recommended for count < 50,000/ μ L

Hematocrit: no recommended threshold for transfusion

Clopidogrel: withhold for 5 d before procedure

Aspirin: do not withhold

LMWH (therapeutic dose): withhold one dose before procedure

aPTT = activated partial thromboplastin time, INR = international normalized ratio, LMWH = low molecular weight heparin.

sion and a trend for four patients to experience a life-threatening hemorrhage in the clopidogrel group. They recommended stopping clopidogrel for 5 d before coronary artery bypass graft for nonemergent surgery (86). There have been reports of serious and, in one case, fatal bleeding following lumbar sympathetic block in patients undergoing lumbar block procedures (87). Hussain et al (88) reported a case-control study of 40 patients undergoing endoscopic sphincterotomy. Most of their study patients who were receiving antiplatelet therapy were taking aspirin. The authors concluded that, after adjustment for elevated INR and cholangitis, antiplatelet agents do not increase the risk of clinically significant bleeding associated with endoscopic sphincterotomy (88). As for glycoprotein IIb/IIIa inhibitors, cessation of abciximab should occur at least 12 h before surgery, with 24 h being preferred when possible. On the contrary, tirofiban can be stopped at the moment of incision without any increased bleeding risks (89).

RECOMMENDATIONS FOR PREPROCEDURE TESTING AND MANAGEMENT

Assessment and preparation of the patient before image-guided procedures will vary according to the procedure to be performed in conjunction with a comprehensive assessment of the patient's comorbidities. Although image guidance is likely to make minimally invasive procedures more accurate, for example, in their ability to target lesions or to put effector devices such as needles or catheters in optimal position, by their very

nature, these procedures preclude the operator from direct visualization of postprocedural bleeding. The lack of available randomized, controlled studies specific to image-guided percutaneous procedures has resulted in considerable variety in clinical practice. In addition, it is doubtful that one can extrapolate the results from open surgical procedures to minimally invasive procedures because of the aforementioned separation of the operator from direct assessment of bleeding (and the associated ability to control it) at the site of the procedure.

Recommendations for patient evaluation and general indications for the use of blood products and other hemostatic agents are outlined in **Tables 2–4**. Where reliable data were lacking, recommendations were derived by Delphi consensus of a panel of expert practitioners (1). **Tables 2–4** represent the results of the Delphi consensus panel, which were derived for the management of a patient with a single hemostatic defect. A total of 18 Certificate of Added Qualification–certified interventional radiologists participated in a four-round Delphi process. Although representative procedures were placed into one of three categories of risk, as outlined in **Tables 2–4**, the panel believed there was significant potential variability in risk from procedure to procedure within each category, depending on the individual patient comorbidities and possible multiple concomitant hemostatic defects. It must be stressed, therefore, that specific assessment of bleeding risk and considerations for the use of blood products or other hemostatic agents must be individualized to the patient at the total discretion of the performing physician, who must, at the time of the procedure, make clinical decisions based on an often complex array

Table 4. Category 3: Procedures with Significant Bleeding Risk, Difficult to Detect or Control**Procedures**

Vascular

TIPS

Nonvascular

Renal biopsy

Biliary interventions (new tract)

Nephrostomy tube placement

Radiofrequency ablation: complex

Preprocedure laboratory testing

INR: routinely recommended

aPTT: routinely recommended in patients receiving intravenous unfractionated

Heparin infusion: no consensus on patients not receiving heparin

Platelet count: routinely recommended

Hematocrit: routinely recommended

Management

INR: correct to < 1.5

aPTT: stop or reverse heparin for values > 1.5× control)

Platelets < 50,000: transfuse

Hematocrit: no recommended threshold for transfusion

Clopidogrel: withhold for 5 d before procedure

Aspirin: withhold for 5 days

Fractionated heparin: withhold for 24 h or up to two doses

There was an 80% consensus on each of these recommendations unless stated otherwise. The management recommendations for each coagulation defect and drug assume that no other coagulation defect is present and that no other drug that might affect coagulation status has been administered. 1-Deamino-8-D-arginine vasopressin may be indicated before image-guided procedures in patients with hemophilia and von Willebrand's disease (38–41). aPTT = activated partial thromboplastin time, INR = international normalized ratio, TIPS = transjugular intrahepatic portosystemic shunt.

of patient variables, comorbidities, and concomitant hemostatic defects. With respect to the categories in **Tables 2–4**, any individual procedure might possibly be treated at a higher risk level, depending on these individual patient factors. In addition, for the purposes of this document, the Delphi consensus panel treated the procedures as elective, with a single hemostatic defect. Emergency indications, multiple concomitant hemostatic defects, and the use of topical or intravascular/perivascular closure devices were not specifically addressed. Numerous maneuvers and modifications, such as needle tract embolization, have been employed to potentially reduce bleeding risks; however, there is no concrete evidence-based research showing their added efficacy, and therefore they will not be further delineated. Emergency or highly urgent procedures, in which the risk of procedural delay may outweigh the potential hemorrhagic risk, may not afford the time for equivalent correction of hemostatic defects as may be achieved in elective procedures. The physician must take into account pathophysiologic, psychosocial, medicolegal, and religious variables in coming to an overall assessment of the patient. For example, periprocedural management for percutaneous liver biopsy may vary significantly between one patient with an INR of 1.7 with no comorbidities and a second patient with INR of 1.7 and concomitant renal failure and cirrhosis.

As there is no evidence to support the use of bleeding times before minimally invasive procedures, the Delphi consensus panel did not

address the use of this test. In addition, the use of recombinant factor VIIa was not addressed. NSAID use was not specifically addressed by the panel. As mentioned earlier, although NSAIDs can inhibit platelet function, the effect is reversible with clearance of the drug. Furthermore, NSAIDs tend to cause bleeding mostly in patients with preexisting coagulopathies. LMWH was considered by the panel with respect to therapeutic dosing.

SUMMARY

In this document, we attempt to summarize some of the available literature regarding periprocedural surveillance and management of hemostatic defects in patients undergoing percutaneous image-guided procedures. Because of the lack of randomized controlled studies or other high-level evidence on this topic, a Delphi panel of experts constructed a set of consensus guidelines to hopefully serve as a reference for the practicing interventionalist in constructing their individual practice guidelines. Although it is likely that individual practice parameters will vary from this document, each practitioner should monitor outcomes and look for trends, both positive and negative, which may suggest modifications or adjustments to these parameters. Outlining bleeding complication rates for specific procedures is beyond the scope of this document and, in many cases, may be difficult or impossible to accurately accomplish because of the lack of high-level data. Where external benchmarks are not available, practitioners may choose to benchmark against their own historical data as part of an overall quality improvement program.

The periprocedural management of patients undergoing image-guided procedures is a continually evolving paradigm. Local factors such as procedure types and patient selection will influence management. In addition, advances in technology and image guidance will potentially significantly impact periprocedural management. The use of closure devices, smaller-gauge catheters and biopsy devices, adjunct hemostatic measures such as postbiopsy tract plugging, use of color-flow ultrasound or computed tomographic fluoroscopy all have the potential to impact the incidence of periprocedural bleeding complications, although further studies will be needed to accurately assess their impact.

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APPENDIX A: SIR STANDARDS OF PRACTICE COMMITTEE CONSENSUS METHODOLOGY

Consensus guidelines reported in this document were obtained using a modified Delphi technique (1). Eighteen Certificate of Added Qualifications–certified members of the SIR Standards of Practice Committee participated through four rounds of the Delphi to reach consensus as reported.

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SIR DISCLAIMER

The clinical practice guidelines of the Society of Interventional Radiology attempt to define practice principles that generally should assist in producing high quality medical care. These guidelines are voluntary and are not rules. A physician may deviate from these guidelines, as necessitated by the individual patient and available resources. These practice guidelines should not be deemed inclusive of all proper methods of care or exclusive of other methods of care that are reasonably directed towards the same result. Other sources of information may be used in conjunction with these principles to produce a process leading to high quality medical care. The ultimate judgment regarding the conduct of any specific procedure or course of management must be made by the physician, who should consider all circumstances relevant to the individual clinical situation. Adherence to the SIR Quality Improvement Program will not assure a successful outcome in every situation. It is prudent to document the rationale for any deviation from the suggested practice guidelines in the department policies and procedure manual or in the patient's medical record.