

# Society of Interventional Radiology Consensus Guidelines for the Periprocedural Management of Thrombotic and Bleeding Risk in Patients Undergoing Percutaneous Image-Guided Interventions—Part II: Recommendations

Endorsed by the Canadian Association for Interventional Radiology and the Cardiovascular and  
Interventional Radiological Society of Europe

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## ABBREVIATIONS

AASLD = American Association for the Study of Liver Disease, aPTT = activated partial thromboplastin time, CI = confidence interval, CVC = central venous catheter, DAPT = dual antiplatelet therapy, DOAC = direct oral anticoagulant, DVT = deep vein thrombosis, FFP = fresh frozen plasma, INR = International Normalized Ratio, LMWH = low molecular weight heparin, NVAF = nonvalvular atrial fibrillation, PEG = percutaneous endoscopic gastrostomy, PT = prothrombin time, RCT = randomized controlled trial, VKA = vitamin K antagonist, VTE = venous thromboembolism

## INTRODUCTION

Part II of the consensus guidelines updates the recommendations for the periprocedural management of thrombotic and bleeding risks in patients who require image-guided interventions (**Appendices A and B**, available online on the article's **Supplemental Material** page at [www.jvir.org](http://www.jvir.org)). Class of recommendation and level of evidence have been assigned in accordance with the Society of Interventional Radiology (SIR) evidence grading methodology (1). In addition to patients with acquired coagulopathies and inherited bleeding disorders, it is estimated that approximately 10% of patients receiving long-term anticoagulation require surgery or another invasive procedure in a given year (2). However, data to guide interventionalists on the periprocedural management of patients with coagulopathies or those receiving anticoagulation and/or antiplatelet medications continue to be limited to retrospective series primarily focused on non-radiology-based procedures, with minimal availability of high-quality, randomized, controlled data. Nonetheless, clinical care decisions need to be made with the intent of minimizing risk and maximizing benefit for

patients. Therefore, similar to how other specialty societies have addressed this topic, these guidelines are consensus-based (3–6) and propose an algorithmic, multidisciplinary approach to the management of these patients to overcome the lack of specific data. These recommendations are not intended to supplant professional judgment, and a physician may deviate from these guidelines as necessitated by the individual patient, practice setting, or available resources. As such, interventional radiologists are encouraged to engage with one another and their multidisciplinary colleagues who have specific expertise in this clinical topic, such as cardiologists, hematologists, hepatologists, and vascular medicine and transfusion medicine specialists, to develop clinical management protocols that may provide better fits for their local institution (7). Last, the writing group recognizes that the majority of studies in the literature typically address only 1 coagulation derangement (eg, elevated International Normalized Ratio [INR] or thrombocytopenia in isolation) at a time and that no evidence exists to provide direction in patients who present with multiple coagulopathies.

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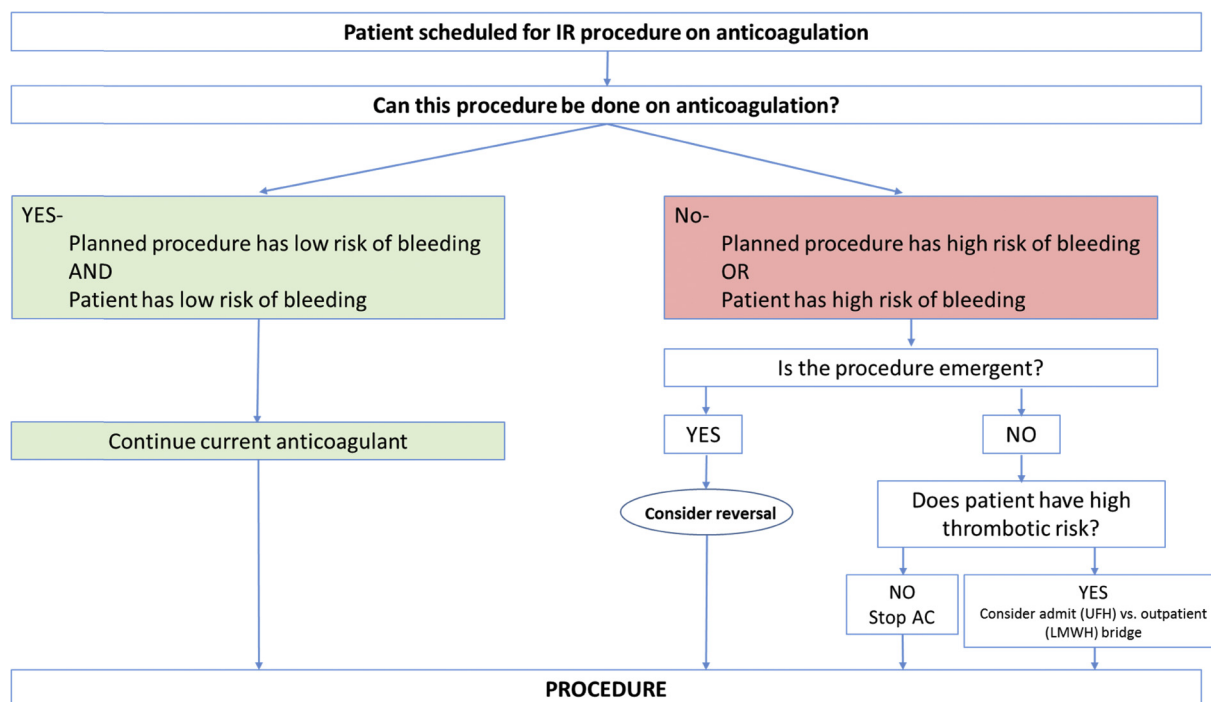
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**Appendices A and B** can be found by accessing the online version of this article on [www.jvir.org](http://www.jvir.org) and clicking on the **Supplemental Material** tab.

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**Figure 1.** Management of anticoagulation agents before a procedure (see [Table 6](#) for agent-specific recommendations). The management of anticoagulation agents before a procedure depends on the patient's overall clinical status, thromboembolic and bleeding risks, and the procedure-associated bleeding risk. For a patient who plans to undergo a procedure associated with a low bleeding risk with no or minimal bleeding risk factors, most anticoagulant agents can be continued. In this case, the patient's thromboembolic risk, whether high or low, does not influence the clinical decision. For a patient who plans to undergo a procedure associated with a high bleeding risk or a patient who has a high risk of bleeding, regardless of procedural risk, additional factors need to be considered. It should be noted that this figure is reflective of recommendations for patients receiving anticoagulation medication with the assumptions that no other coagulation defect is present and that no other drug that may affect coagulation status has been administered.

## ALGORITHMIC APPROACH TO PATIENT EVALUATION/ASSESSMENT

Any decision about periprocedural management should be based on a thorough assessment of a patient's overall clinical status, including the thrombotic and bleeding risks and the procedure-associated bleeding risk. This assessment should result in a recommendation regarding appropriate withholding and reinitiation of medications. Observance of the appropriate withholding and reinitiation recommendations by class of pharmaceutical agent, with or without the use of blood products, is essential. The following sections, [Figures 1–3](#), and [Tables 1](#) and [2](#) outline an algorithmic approach to the assessment of periprocedural thrombotic and bleeding risk.

## ASSESSMENT OF PATIENT THROMBOEMBOLIC RISK

Patients who have had a stroke or venous thromboembolic event or have an underlying malignancy or a significant cardiovascular disease history are particularly prone to thrombotic events ([Table 1](#)) (8–10). Thrombotic events are associated with significant fatality rates: 17.5% for mechanical heart valve thrombosis, 5%–10% for venous thromboembolism (VTE), and 37% for embolic stroke (6). Unfortunately, most relevant scoring systems often refer to long-term or annual thrombotic risk. It is therefore difficult to predict what the periprocedural thrombotic (11) or bleeding (12) risk would be for a particular patient, and extrapolation from annual risk to the periprocedural period has not been validated, nor is validation across multiple procedures likely to be developed.

### Stroke Risk

Considering these limitations, the CHA2DS2-VASc score ([Table 1](#)) has been validated to predict annual stroke risk in patients with nonvalvular

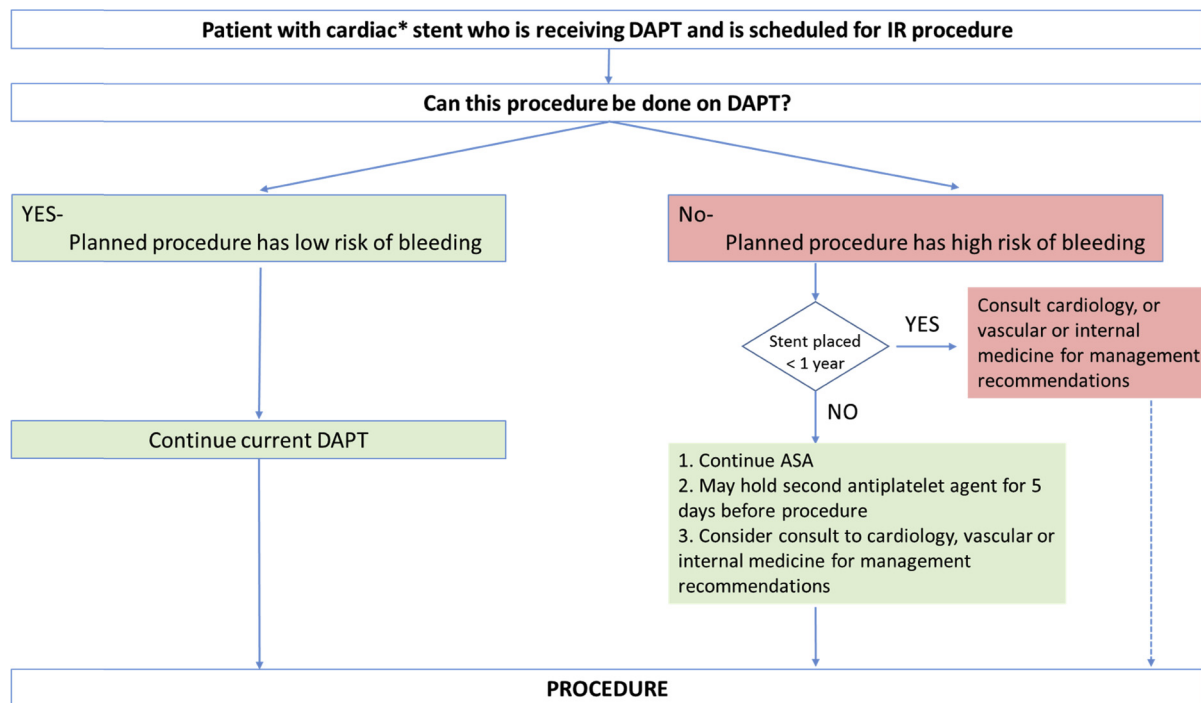
atrial fibrillation (NVAf) (13). The acronym represents underlying cardiovascular risk factors used to calculate the score: congestive heart failure (C), hypertension (H), age (A), diabetes (D), stroke/transient ischemic attack (S), and vascular diseases (VASc) such as peripheral arterial disease, previous myocardial infarction, and aortic atheroma. A score of < 4 is considered low, 5/6 moderate, and > 7 high. In addition, a stroke within the past 3 months is specifically considered a marker of high risk (3).

### Venous Thrombosis Risk

Predicting VTE-related risk is challenging, and there are several factors to consider. First, the acuity of the clot is important, as most recurrence and embolization occur within 30 days of clot formation, with rate of clot recurrence decreasing after 3 months from the initial event (14). Clot type and location are also important to consider. A deep vein thrombosis (DVT) carries a higher risk of complications than a superficial vein clot, and a proximal lower-extremity DVT (ie, popliteal vein or more proximal vein) puts the patient at a higher risk for recurrence than a distal lower-extremity DVT (ie, calf) or an upper-extremity DVT. Most pulmonary emboli also carry a high risk of recurrence and complications, but the treatment of subsegmental pulmonary embolism should be considered on a per-case basis (15). Finally, other patient-related factors can affect risk: many types of cancer increase thrombosis risk (16), as do obesity, hormone-replacement therapy, long-term immobilization, or certain thrombophilias (eg, antiphospholipid antibody syndrome).

### Mechanical Heart Valves

The assessment of mechanical heart valve–related thrombosis risk is also not straightforward. In general, withholding anticoagulation in the presence of a mechanical heart valve, even for short periods of time, is considered to present high risk for thrombosis. However, data are contradictory, and not



**Figure 2.** Management of dual antiplatelet therapy (DAPT) before a procedure (see [Table 6](#) for specific recommendations). The management of antiplatelet agents before a procedure is dependent on the assessment of the patient's overall clinical status, thrombotic and bleeding risks, and the procedure-associated bleeding risk. For patients receiving DAPT scheduled to undergo a procedure associated with low bleeding risk, most antiplatelet agents can be continued. For patients receiving DAPT scheduled to undergo a procedure associated with high bleeding risk, the patient's thrombotic risk, which is related to the duration of DAPT and to the original indication (eg, cardiac vs peripheral stent), must be taken into consideration. Consultation with the care team managing the antiplatelet therapy (eg, cardiovascular practitioner) is recommended for patients who have had a cardiac stent placed within the previous 12 months. For cardiac stent recipients who have completed 12 months of DAPT, the recommendation is to continue aspirin while withholding the second antiplatelet agent, and involvement of a multidisciplinary care team for management recommendations may be helpful. It should be noted that this figure is reflective of recommendations for patients receiving dual antiplatelet agents with the assumption that no other coagulation defect is present and that no other drug that may affect coagulation status has been administered. (\*Patients who have a peripheral stent or bypass graft and who are receiving DAPT merit a separate discussion with their vascular provider.) ASA = acetylsalicylic acid.

all valves are the same. Reported annual thrombosis risk across indications, locations, and valve types vary and range from approximately 1%–5% to 7% (17,18). Factors including valve location, make, and age affect thrombosis risk (19). Prosthetic mitral valves or mechanical aortic valves that are a caged ball or tilting disc are considered to be associated with higher risk. However, even bioprosthetic heart valves and valves placed by the transcatheter approach are not devoid of thrombotic risk, especially when newly implanted (18).

### Coronary Artery Disease

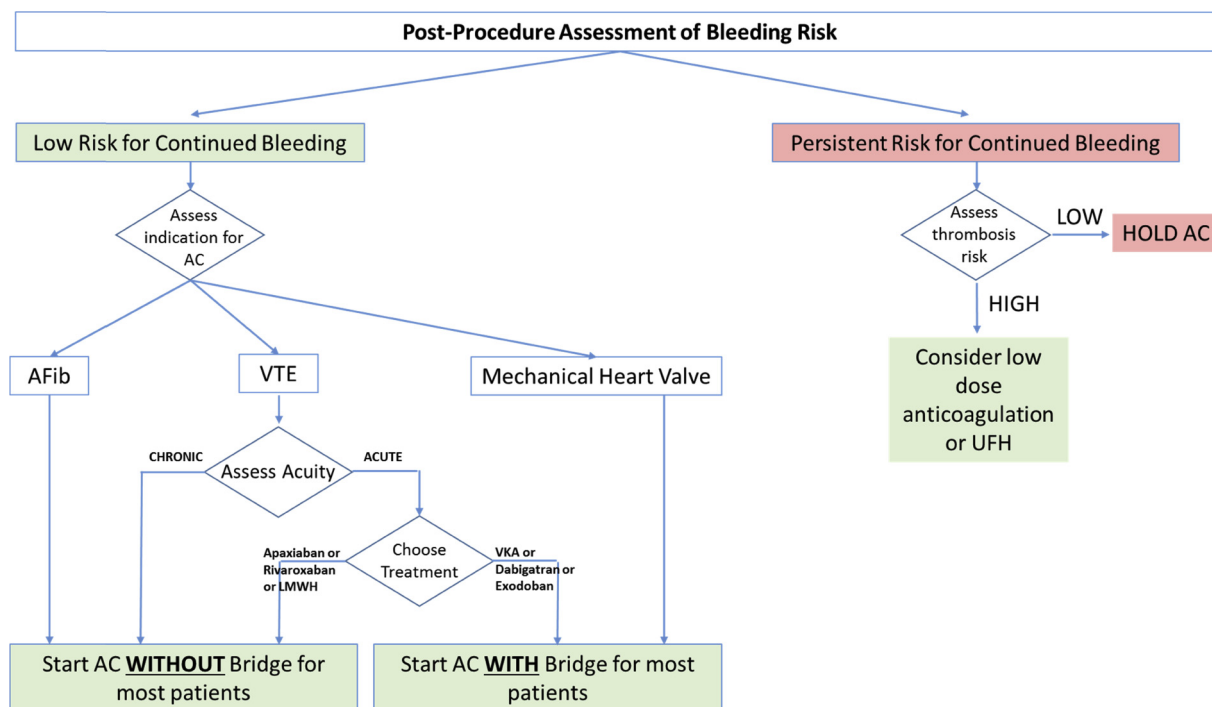
As discussed in part I of these guidelines, significant morbidity and potential for thromboembolic complications exist if such patients are mismanaged (20), particularly for patients who have had acute coronary syndrome or those with cardiac stents, especially if the stent implantation or cardiac event occurred within 1 year.

### ASSESSMENT OF PATIENT BLEEDING RISK

Patients with congenital bleeding diatheses, disseminated intravascular coagulation, sepsis, or renal dysfunction (3) have acquired coagulopathies that increase bleeding risk (Table 2) (3,21,22). Bleeding risk is also considered to be increased in patients who have had a bleeding episode within 3 months of a procedure, especially if it occurred during a similar procedure (3). In a study examining 1,293 incidents of warfarin interruption in 1,024 patients (23), the most common indications for anticoagulation were atrial fibrillation (n = 550), venous thrombosis within 4

weeks (n = 144), and mechanical mitral heart valve (n = 132; 40.9%). Only 0.7% of patients (95% confidence interval [CI], 0.3%–1.4%) experienced a thrombotic event within 30 days. Importantly, 0.6% of patients (95% CI, 0.2%–1.3%) experienced major bleeding, and an additional 1.7% of patients (95% CI, 1.0%–2.6%) experienced clinically significant nonmajor bleeding. The authors concluded that bleeding risk should be weighed against what seems to be a low thrombosis risk for most patients.

There are scoring systems that exist to try to predict bleeding risk over time (24–26) but have not been validated for periprocedural risk assessment. However, the Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly (HAS-BLED) score (Table 2) warrants specific discussion. This score has been validated to predict bleeding rate in patients with NVAF who are receiving long-term anticoagulation with vitamin K antagonists (VKAs) (27,28). The HAS-BLED score is based solely on patient characteristics and does not include procedure-related factors. The HAS-BLED score was evaluated in 1,000 patients who required anticoagulation interruption for invasive procedures (cardiac catheterization, n = 533; pacemaker implantation, n = 128; surgery, n = 194; other, n = 145) (29). During 30 days, there was an 0.4% incidence of thrombotic complications, 0.1% incidence of major bleeding episodes, and 3.5% incidence of clinically relevant bleeding. Predictors for bleeding were history of mechanical heart valve ( $P = .0002$ ) and HAS-BLED score  $\geq 3$  (hazard ratio, 11.8; 95% CI, 5.6–24.9). Importantly, HAS-BLED score showed only modest discriminatory performance for periprocedural bleeding (30).



**Figure 3.** Restarting anticoagulation after a procedure (see *Management of Anticoagulation and/or Antiplatelet Agents before and after a Procedure* for full details). After a procedure, the goal is to restart anticoagulation as quickly as possible. The timing of anticoagulation after a procedure depends mainly on procedural bleeding risk and bleeding-related complications. Typically, the person who performed the procedure is best equipped to decide when anticoagulation can be restarted. In patients who are considered to be at high risk for thrombotic events, but in whom procedure-related bleeding risk is perceived to be high, alternatives to full-dose anticoagulation with long-acting agents should be considered.

The BleedMAP score also warrants specific discussion. In a prospectively collected retrospective analysis (31), 2,182 patients who required interruption of anticoagulation were followed for 3 months. Bleeding was associated with “bridging,” active cancer, previous bleeding, and reinitiation of heparin within 24 hours of a procedure. The most common surgical procedures were gastrointestinal and orthopedic; interventional radiologic procedures as a general category represented 3% of the procedures studied and were uniformly categorized as low-risk. Multivariate analysis of the results permitted the authors to isolate 4 independent predictors of major bleeding. The BleedMAP score assigned 1 point for each of the following risk factors: history of bleeding (Bleed), mechanical mitral heart valve (M), active cancer (A), and low platelet count (P). For patients, including those receiving heparin therapy, the risk of major bleeding was noted to increase with increasing BleedMAP scores. At a score of 0, the major bleeding rates were 0.81% (95% CI, 0.35–1.6) for all patients and 0.75% (95% CI, 0.24–1.74) for patients receiving low molecular weight heparin (LMWH) for bridging. Rates of thromboembolic complications were 0.71% for all patients and 0.6% for those receiving bridging therapy. In contrast, at a score > 3, the major bleeding rates were 10% (95% CI, 2.79–23.66) for all patients and 12.12% (95% CI, 3.4–28.2) for patients receiving LMWH for bridging. There were no thromboembolic complications irrespective of bridging status. The bleeding rates varied more than 10-fold from highest to lowest BleedMAP risk scores.

## PROCEDURE-ASSOCIATED BLEEDING RISKS

General procedure-related bleeding risk also needs to be considered, but is limited by the lack of data on bleeding risks for individual image-guided interventions, which prevents a determination of specific procedure-related bleeding risk (Table 3) (4,32–38). The original SIR consensus guidelines (39) divided procedures into 3 groups: low, moderate, and high bleeding risk. In the present update, we have recategorized procedures into those associated with low risk versus those associated with high risk for major bleeding. The concept of a 2-tier procedure-related bleeding risk categorization has been

described by other professional societies and authors (3,35,37,40–49) and has also been suggested by members of the radiology community (50). Procedures categorized as having low risk are those that are expected to rarely have hemorrhagic complications or are occurring in areas where bleeding is easy to diagnose and control. High bleeding risk procedures are those that may be expected to have hemorrhagic complications, are occurring in areas where bleeding will be difficult to diagnose or treat (eg, intraabdominal cavity, lung parenchyma, retroperitoneum), or involve procedures occurring in locations where even minor amounts of bleeding may have devastating consequences (eg, eye, spinal cord, brain) (35). Although there is no standard, accepted risk rate of major bleeding that defines a high procedure-related bleeding risk, definitions to delineate high from low procedure-related bleeding risk have been proposed, with high-risk procedures defined as having a > 1.5% rate of major bleeding versus low-risk procedures defined as having a < 1.5% rate of major bleeding (35) or high-risk procedures defined as having a 2-day risk of major bleeding of 2%–4% versus low-risk procedures defined as having a 2-day risk of major bleeding of 0%–2% (51). When assessing procedure-related bleeding risk, the absolute bleeding risk and the location and potential consequences of a bleeding complication need to be considered.

*Recommendation 1:* Given research developments in the thrombosis field and the complexity of patient risk assessment, we recommend a multidisciplinary, shared decision-making approach for planning periprocedural management in patients at high risk for thromboembolic or bleeding events. Specialists in cardiology, hematology, or vascular or internal medicine should be involved to ensure that patients at high risk receive optimal medical management in the periprocedural period. (Level of evidence, E; strength of recommendation, strong.)

## PREPROCEDURE LABORATORY TESTING

There are no high-quality data to guide whether preprocedural laboratory testing reduces periprocedural bleeding risk. The 2012 SIR consensus guidelines (39) did not recommend routine preprocedural assessment of

**Table 1.** Assessment of Patient Thrombotic Risk (8–10)

CHA2DS2-VASc Score		Thrombosis Risk	
Criterion	Points	High	Low
Male	0	• Any mitral valve prosthesis	• Bileaflet aortic valve prosthesis
Female	1	• Any caged-ball or tilting-disc aortic valve	• CHA2DS2-VASc score < 4
CHF history	1	• Stroke or TIA within 6 mo	• Provoked* VTE > 3 mo
Diabetes history	1	• CHA2DS2-VASc score > 7	• VTE at least 3 mo, with/without nonsevere thrombophilia (eg, heterozygous Factor V Leiden)
HTN history	1	• Rheumatic valvular heart disease	
Vascular disease history	1	• Recurrent idiopathic VTE	
Age 65–74 y	1	• VTE within 3 mo	
Age > 75 y	2	• VTE of any duration with severe thrombophilia (eg, homozygous factor V Leiden or positive antiphospholipid antibodies)	
History of stroke/TIA/thromboembolism	2	• Cancer-associated thrombosis	

CHF = congestive heart failure; HTN = hypertension; mo = months; TIA = transient ischemic attack; VTE = venous thromboembolism; y = years.

\*Unprovoked VTE may be associated with low or high risk after 3 mo and must be considered on a per-patient basis.

**Table 2.** Assessment of Patient Bleeding Risk (3,21)

HAS-BLED Score (Score > 3 Predictive of Bleeding Events)		Other Risk Factors for Bleeding
Criteria	Points	
Hypertension (systolic BP > 160 mm Hg)	1	• Prior bleeding within 3 mo
Abnormal renal function (dialysis, renal transplantation, serum Cr > 200 $\mu$ mol/L)	1	• Prior bleeding with similar type of procedure
Abnormal liver function (cirrhosis or bilirubin > 2 $\times$ ULN, AST or ALT > 3 $\times$ ULN)	1	• Platelet abnormality
Prior stroke	1	• INR above therapeutic range at time of procedure (VKA)
History of major bleeding or predisposition to bleeding (anemia)	1	• Prior bleeding with bridging therapy
Labile INR (VKA) defined as time in therapeutic range < 60%	1	• Mechanical mitral heart valve
Age > 65 y	1	• Active cancer
Concomitant use of antiplatelet agent or NSAID	1	
History of alcohol or drug use (> 8 drinks per week)	1	

Note—There are currently no well validated scoring systems that can be used to assess bleeding risk across interventional radiologic procedures. Similarly, the HAS-BLED score has not been designed to assess periprocedural bleeding risk. However, this score is often used in clinical practice as a general guide to aid clinicians in recognizing potential factors that may increase patient-specific bleeding risk and should be used for this purpose alone. History of bleeding, mechanical mitral heart valve, and active cancer are BleedMAP factors that may also indicate an increased propensity for a patient to experience bleeding; however, it should be noted that BleedMAP is not procedure-specific. Platelet counts lower than  $20 \times 10^9/L$  and lower than  $50 \times 10^9/L$  may be associated with increased risk of bleeding for low- and high-risk procedures, respectively (22).

ALT = alanine aminotransferase; AST = aspartate aminotransferase; BP = blood pressure; Cr = creatinine; mo = months; NSAID = nonsteroidal antiinflammatory drug; ULN = upper limits of normal; VKA = vitamin K antagonist; y = years.

platelet count or hemoglobin for patients undergoing procedures with low bleeding risk, and this panel concurs. However, for patients who have an inherently higher bleeding risk, such as those with hematologic disorders, patients receiving certain chemotherapies, or those who are receiving anti-coagulant therapy, preprocedural laboratory testing may be indicated, even if a procedure is considered to present a low risk for bleeding. This is a clinical decision that the physician performing the procedure must make based on patient comorbidities and any anticipated technical factors that may increase the complexity of what would typically be considered a low bleeding risk procedure. For high bleeding risk procedures, this panel supports the recommendation for routine preprocedural coagulation testing, which includes the assessment of hemoglobin, platelet count, and prothrombin time

(PT)/INR, with activated partial thromboplastin time (aPTT) or anti-Xa testing recommended for patients receiving unfractionated heparin. Fibrinogen level may be helpful for patients with cirrhosis. The presence of direct oral anticoagulants (DOACs) can be evaluated by using DOAC-specific assays or surrogate tests (table 3 in part I of these guidelines). In this update, the previous recommendations for aPTT testing have been removed as a result of a lack of supporting data. INR ranges, reflecting the upper limits of thresholds, have been provided in the recommendations, as the varying degrees of bleeding risk within procedural categories should be taken into consideration (ie, an INR < 1.8 may be acceptable for a liver biopsy but an INR < 1.5 may be preferred before an aortic intervention, as the strategies and success of controlling unanticipated bleeding differ between

the 2 procedure types). Recommendations for patients with cirrhosis differ and are specified in [Table 4](#) (52).

## Laboratory Parameters for Low Bleeding Risk Procedures

Although of low quality, evidence in the literature supports that low bleeding risk procedures can be safely performed at INRs  $> 1.5$  or platelet counts  $> 20 \times 10^9/L$  (53–57). These data are derived largely from retrospective studies of central venous catheter (CVC) insertion or removal, paracentesis, thoracentesis, and angiography. The data have been extrapolated to inform generalized recommendations for image-guided procedures classified as having low bleeding risk.

As noted in their review of 25 studies analyzing the ability of abnormal coagulation parameters to predict bleeding associated with invasive bedside or image-guided procedures, Segal and Dzik (58) noted that abnormalities in PT and INR are not associated with increased bleeding during CVC insertion. Several case series (59–64) have also demonstrated the absence of clinically significant bleeding in patients with elevated INRs who did not receive fresh frozen plasma (FFP) before CVC placement. Therefore, the use of an INR threshold above which FFP should be prophylactically transfused has been called into question. A 2016 Cochrane review (57) identified only very limited evidence from 1 randomized controlled trial (RCT) to inform the decision of whether to administer prophylactic FFP before CVC insertion for patients with INR  $> 1.5$ . In this RCT (65), there were no reported episodes of major bleeding within 24 hours of the procedure between the group who received FFP and the group who did not; therefore, it was not possible to recommend whether prophylactic FFP transfusion was beneficial or harmful.

Stecker et al (66) reported on 180 patients with tunneled cuffed central venous catheters requiring removal, concluded that preremoval laboratory evaluation was not warranted, and suggested that platelet dysfunction may be an important factor in prolonging time to hemostasis, but that the degree of prolongation was unlikely to be clinically relevant. A 2015 Cochrane review (55) identified no completed RCTs that could determine a platelet count threshold at which CVC insertion could be performed. The review did note that CVC placement is the most common intervention that requires prophylactic platelet transfusions to prevent bleeding in patients with hematologic disorders (67) and further noted that the platelet count threshold recommended before CVC insertion varied significantly between countries:  $50 \times 10^9/L$  in the United Kingdom (22),  $30 \times 10^9/L$  in Belgium (68),  $20 \times 10^9/L$  in the United States (69), and  $10 \times 10^9/L$  in Germany unless there are risk factors for bleeding (55). A number of nonrandomized studies (61,62,70,71) have demonstrated the safety of CVC insertion in patients with thrombocytopenia who did not receive prophylactic platelet transfusion. A 2015 review by the AABB (69) used 8 observational studies to inform its recommendation that prophylactic platelet transfusion be given if the platelet count is  $< 20 \times 10^9/L$  for patients undergoing elective CVC placement. This recommendation is supported by the American Society of Clinical Oncology (5), which states that “certain procedures, such as bone marrow aspirations and biopsies, and insertion or removal of [CVCs], can be performed safely at counts  $> 20 \times 10^9/L$ .”

Similar nonrandomized data exist for paracentesis (56,72–74) and thoracentesis (53,75–78). The pooled data on patients with abnormal coagulation profiles (INR  $> 1.5$  and/or platelet count  $< 50 \times 10^9/L$ ) indicate a very low risk of major bleeding for paracentesis (0.2%, 5 of 2,113 patients) (56,72–74) and thoracentesis (0.5%, 7 of 1,505 patients) (75–78). Other retrospective reviews on thoracentesis suggest similar results: 17 bleeding-related complications after thoracentesis in 9,320 patients (0.18%), all of which occurred in patients with platelet counts  $> 50 \times 10^9/L$  (53); and no bleeding complications after thoracentesis in 32 patients with an INR  $> 3.0$  (77). Because of this very low risk of bleeding for paracentesis and thoracentesis, the need for prophylactic blood products before these procedures has been called into question (78,79).

There has been little new evidence to refute the findings of Darcy et al (54), who determined that abnormal PTs and partial thromboplastin times do not correlate with an increased risk of postangiographic hematoma in a prospective study of 1,000 patients undergoing femoral arterial puncture for

a diagnostic or therapeutic vascular procedure. There was, however, a correlation of a higher incidence of hematoma with platelet count  $< 100 \times 10^9/L$ . The study (54) concluded that, in the absence of an overt history of bleeding and an expected PT of less than 18 seconds, preprocedural testing with PT and aPTT measurement was not warranted. The 2012 American College of Cardiology/Society for Cardiovascular Angiography and Interventions consensus document (80) recommends that elective coronary angiography for patients receiving long-term warfarin be deferred until the INR is  $< 1.8$  for femoral artery access or  $< 2.2$  for radial artery access. The interventional cardiology literature considers coronary angiography and pacemaker or defibrillator placement to be low bleeding risk procedures, and studies (33,34) have demonstrated that these procedures can be safely performed in patients receiving VKA therapy with an INR within the range of 2.0–3.0 on the day of the procedure, with low bleeding complications.

**Recommendation 2:** For patients with minimal risk factors for bleeding, screening coagulation laboratory testing is not routinely recommended for procedures with low bleeding risk but may be considered for patients receiving warfarin or unfractionated heparin or those with an inherently higher risk of bleeding. The following laboratory value thresholds have been suggested: correct INR to within range of 2.0–3.0 or less, consider platelet transfusion if platelet count is  $< 20 \times 10^9/L$  ([Table 3](#)); for low bleeding risk procedures that require arterial access, the recommended INR threshold is  $< 1.8$  for femoral access and  $< 2.2$  for radial access. (Level of evidence, D; strength of recommendation, weak.)

## Laboratory Parameters for High Bleeding Risk Procedures

A platelet count of  $> 50 \times 10^9/L$  (5) and an INR  $< 1.5$  have been the standard threshold at which major surgery can be performed safely. An INR  $> 1.5$  demarcates the level above which the activity of some coagulation factors decrease to less than 50% (57). These surgical laboratory thresholds have been extrapolated to inform generalized recommendations for image-guided procedures classified as having high bleeding risk because there is a paucity of evidence to suggest alternatives.

The image-guided liver biopsy is a representative procedure within the high bleeding risk category in which factors influencing periprocedural bleeding have been studied. In a study involving direct visualization of the liver during laparoscopic biopsy, Ewe (81) was unable to correlate the duration of observed bleeding after biopsy with abnormalities in preprocedural coagulation parameters: 4.3% of patients with a PT longer than 13.5 seconds showed bleeding for more than 12 minutes after biopsy, compared with 4.6% of patients with normal coagulation parameters. Observational studies on liver biopsy (38,74,82,83) support the threshold of a platelet count  $> 50 \times 10^9/L$ . In a study of 291 consecutive patients who underwent a liver biopsy (74), a 3.4% incidence of clinically significant bleeding was noted among 175 patients with mild thrombocytopenia (platelet counts 50–99  $\times 10^9/L$ ), and this was not different from the bleeding incidence in patients with normal platelet counts (74). A retrospective analysis of 6,613 image-guided liver biopsies (82), in which 92 procedures were performed with a platelet count  $< 50 \times 10^9/L$ , reported a higher frequency of hemorrhage in patients with platelet count  $< 50 \times 10^9/L$  than in patients with higher platelet counts (2.2% vs. 0.5%;  $P = .04$ ). An analysis of 2,740 percutaneous liver biopsies performed in patients with hepatitis C–related fibrosis or cirrhosis (83) reported that bleeding occurred in 5.3% of the biopsies performed at a platelet count of  $< 60 \times 10^9/L$ , compared with  $< 1\%$  of biopsies performed in patients with higher platelet counts. Finally, in an observational study (38), 50 patients with hematologic malignancies and a mean preprocedural platelet count of  $17 \times 10^9/L$  underwent transjugular liver biopsy after platelet transfusion. The mean posttransfusion platelet count was  $38 \times 10^9/L$ , with 24 patients having platelet counts  $< 30 \times 10^9/L$ . There were no clinically significant bleeding complications, and the authors concluded that a platelet count of  $30 \times 10^9/L$  represented a safe threshold for transjugular liver biopsy (38). Similar studies are not available to establish an INR threshold for liver biopsy.

Bleeding anywhere within the central nervous system has the potential for devastating neurologic consequences; therefore, multiple societies have chosen to classify pain procedures such as vertebral augmentation and

procedures with risk of epidural bleeding as being associated with high bleeding risk (32), and the AABB has chosen to recommend a “fairly liberal” platelet count of  $50 \times 10^9/L$  as the threshold for lumbar puncture (69). This is supported by the C17 guidelines committee (84), which recommends transfusion at a platelet count threshold of  $50 \times 10^9/L$  for diagnostic lumbar puncture for newly diagnosed pediatric patients with leukemia and a threshold for transfusion of  $20 \times 10^9/L$  for pediatric patients in stable condition requiring lumbar puncture. Similar studies and recommendations are not available to establish an INR threshold.

Limited data are emerging to suggest that the continuation of single-agent antiplatelet agents may be safe for certain high bleeding risk procedures such as solid organ biopsy (50,85), percutaneous endoscopic gastrostomy (PEG) (86,87), and percutaneous nephrolithotomy (88). In a cohort of 15,181 percutaneous core biopsies performed at a single institution (50), the incidence of bleeding complications in patients who had taken aspirin within 10 days of the biopsy was 0.6% (18 of 3,195), and this was not different compared with patients who had not taken aspirin (0.4%; 52 of 11,986;  $P = .34$ ). The incidences of bleeding by biopsy site, inclusive of all patients, were as follows: liver, 0.5%; kidney, 0.7%; lung, 0.2%; pancreas, 1.0%; and others, 0.2% (50). A retrospective review of 63 patients who used clopidogrel within 5 days of undergoing percutaneous core biopsy in the liver, lung, kidney or abdominal/pelvic/retroperitoneal areas (85) revealed only 1 major bleeding complication that was related to injury to an intercostal artery during lung biopsy. Forty-eight patients of this group (76%) also took aspirin within 5 days of the procedure. Two recent retrospective series in the gastroenterology literature (86,87) indicate that aspirin, clopidogrel, or warfarin use is not associated with complications after PEG. In a group of 401 patients (86), use of aspirin, clopidogrel, or warfarin was not predictive of acute or chronic complications after PEG. Richter et al (87) reported on the periprocedural use of aspirin, clopidogrel, or serotonin reuptake inhibitors in 990 patients who underwent PEG. Multivariate analysis demonstrated no association between periprocedural use of aspirin or clopidogrel and bleeding after PEG; however, serotonin reuptake inhibitor administration within 24 hours of PEG was associated with increased odds of postprocedural bleeding (adjusted odds ratio, 4.1; 95% CI, 1.1–13.4;  $P = .04$ ) (87). In a retrospective review of 285 consecutive percutaneous nephrolithotomies (88), in which an interventional radiologist accessed the kidney at the time of the procedure, tract dilation was performed to 30 F, and a ureteral stent with a 16–18-F nephrostomy tube was placed at the end of the procedure, there were no

differences in outcomes and complications between patients who underwent the procedure while receiving low-dose aspirin ( $n = 67$ ) and those who did not receive aspirin ( $n = 207$ ). Although these procedure-specific reports are encouraging, it should be noted that the patient numbers remain very small in these studies.

**Recommendation 3:** Appropriate preprocedural coagulation testing should be obtained for patients undergoing procedures with high bleeding risk (Table 3). The following laboratory value thresholds have been suggested: correct INR to within range of 1.5–1.8 or less and consider platelet transfusion if platelet count is  $< 50 \times 10^9/L$  (Table 3). (Level of evidence, D; strength of recommendation, weak.)

## Laboratory Parameters for Patients with Chronic Liver Disease

The traditional laboratory parameters that have been used as thresholds for triggering the prophylactic transfusion of blood products to correct coagulopathy before an invasive procedure (Table 3) likely are not appropriate for patients with chronic liver disease (89). Because of the physiology of rebalanced hemostasis in cirrhosis, studies have repeatedly documented that abnormal screening coagulation test results, such as prolonged PT/INR and thrombocytopenia, do not correlate with bleeding in these patients (53,81,90). The American Association for the Study of Liver Disease (AASLD) has clearly stated that PT/INR in patients with cirrhosis does not correlate with bleeding, and any attempt to correct with plasma is ineffective and likely to be detrimental (91,92). In most patients with cirrhosis, splenomegaly also plays a central role in thrombocytopenia. As a result of the rapid sequestration of platelets within the enlarged spleen, these patients will exhibit a poor incremental response to platelet transfusions, which, if unrecognized, may lead to further transfusions, thereby increasing the risk for transfusion circulatory overload, elevation of portal pressures, and bleeding (93).

Adherence to the traditional laboratory parameters to guide blood product administration for patients with chronic liver disease places these patients at risk for receiving unnecessary transfusion products and associated complications, and laboratory parameters to guide transfusion management that are specific to patients with chronic liver disease have yet to be definitively established. Additional research is clearly needed. Proposed laboratory parameter thresholds for prophylactic transfusion before invasive procedures in cirrhotic patients are based on survey data (89,94) or low-

**Table 3.** Procedure-Associated Bleeding Risk Categorization (4,32–38)

### Screening Coagulation

#### Laboratory Test

#### Low bleeding risk

PT/INR: not routinely recommended\*  
 Platelet count/hemoglobin: not routinely recommended  
 Thresholds<sup>†</sup>  
 INR: correct to within range of  $\leq 2.0$ – $3.0$ <sup>‡</sup>  
 Platelets: transfuse if  $< 20 \times 10^9/L$

### Procedures

Catheter exchanges (gastrostomy, biliary, nephrostomy, abscess, including gastrostomy/gastrojejunostomy conversions)  
 Diagnostic arteriography and arterial interventions: peripheral, sheath  $< 6$  F, embolotherapy<sup>‡</sup>  
 Diagnostic venography and select venous interventions: pelvis and extremities  
 Dialysis access interventions  
 Facet joint injections and medial branch nerve blocks (thoracic and lumbar spine)<sup>§</sup>  
 IVC filter placement and removal<sup>||</sup>  
 Lumbar puncture<sup>||</sup>  
 Nontunneled chest tube placement for pleural effusion  
 Nontunneled venous access and removal (including PICC placement)  
 Paracentesis  
 Peripheral nerve blocks, joint, and musculoskeletal injections<sup>§</sup>  
 Sacroiliac joint injection and sacral lateral branch blocks<sup>§</sup>  
 Superficial abscess drainage or biopsy (palpable lesion, lymph node, soft tissue, breast, thyroid, superficial bone, eg, extremities and bone marrow aspiration)  
 Thoracentesis  
 Transjugular liver biopsy<sup>#</sup>  
 Trigger point injections including piriformis<sup>§</sup>  
 Tunneled drainage catheter placement<sup>‡</sup>  
 Tunneled venous catheter placement/removal (including ports)<sup>‡</sup>

*continued*

**Table 3.** Procedure-Associated Bleeding Risk Categorization (4,32–38) (continued)

Screening Coagulation Laboratory Test	Procedures
<b>High bleeding risk</b>	
PT/INR: routinely recommended	Ablations: solid organs, bone, soft tissue, lung
Platelet count/hemoglobin: routinely recommended	Arterial interventions: > 7-F sheath, aortic, pelvic, mesenteric, CNS <sup>†,‡</sup>
Thresholds <sup>†</sup>	Biliary interventions (including cholecystostomy tube placement)
INR: correct to within range of ≤ 1.5–1.8	Catheter directed thrombolysis (DVT, PE, portal vein)**
Platelets: transfuse if < 50 × 10 <sup>9</sup> /L	Deep abscess drainage (eg, lung parenchyma, abdominal, pelvic, retroperitoneal)
	Deep nonorgan biopsies (eg, spine, soft tissue in intraabdominal, retroperitoneal, pelvic compartments)
	Gastrostomy/gastrojejunostomy placement
	IVC filter removal complex**
	Portal vein interventions
	Solid organ biopsies
	Spine procedures with risk of spinal or epidural hematoma (eg, kyphoplasty, vertebroplasty, epidural injections, facet blocks cervical spine) <sup>§</sup>
	Transjugular intrahepatic portosystemic shunt <sup>††</sup>
	Urinary tract interventions (including nephrostomy tube placement, ureteral dilation, stone removal)
	Venous interventions: intrathoracic and CNS interventions

CNS = central nervous system; DVT = deep vein thrombosis; INR = International Normalized Ratio; IVC = inferior vena cava; PE = pulmonary embolism; PT = prothrombin time.

\*Screening coagulation laboratory testing before low bleeding risk procedures should be considered for patients with risk factors for bleeding or those receiving warfarin or heparin drip if there is concern for supratherapeutic levels.

<sup>†</sup>Thresholds for laboratory parameters are based largely on scientific consensus established in the literature from limited-quality studies and the consensus of the Writing Group and Standards Committee volunteers. INR ranges, reflecting the upper limits of thresholds, have been provided in the recommendations, as the varying degrees of bleeding risk within procedural categories should be taken into consideration. For example, an INR < 1.8 may be acceptable for a liver biopsy but an INR < 1.5 may be preferred before an aortic intervention, as the strategies and success of controlling unanticipated bleeding differ between the 2 procedure types. Similarly, an INR < 2.0 may be preferred for catheter placement procedures in which a subcutaneous tunnel is planned. Recommendations for patients with cirrhosis differ and are specified in [Table 4](#).

<sup>‡</sup>Low bleeding risk procedures involving percutaneous and venous access have been performed safely at INRs within the range of 2.0–3.0 (32–34). For low bleeding risk procedures that require arterial access, the recommended INR thresholds are < 1.8 for femoral access and < 2.2 for radial access (4). Interventions involving the creation of a subcutaneous tunnel (eg, pacemaker insertion, pleural or venous catheter placement) have traditionally been grouped into the low bleeding risk category (35–37). Preprocedure DOAC interruption > 24 h vs < 24 h was not identified as a potential risk factor for major bleeding events (36).

<sup>§</sup>Injection and pain-management procedures follow the classification outlined by the American Society of Regional Anesthesia and Pain Medicine, the European Society of Regional Anesthesia and Pain Therapy, the American Academy of Pain Medicine, the International Neuromodulation Society, the North American Neuromodulation Society, and the World Institute of Pain (32). These guidelines consider spine procedures with risk of spinal or epidural hematoma to be high bleeding risk procedures given that bleeding in this area could be difficult to manage and be associated with morbid consequences for the patient.

<sup>||</sup>IVC filter placements and uncomplicated IVC filter removals would fall into the low bleeding risk category. For IVC filter removal, consider the anticipated technical complexity of the procedure (ie fractured legs, legs penetrating outside of IVC, tilt) and dwell time.

<sup>¶</sup>See discussion in text: *Laboratory Parameters for High Bleeding Risk Procedures and Recommendation 3*.

<sup>#</sup>Ref. 38 sets a platelet threshold of > 30 × 10<sup>9</sup>/L for transjugular liver biopsy.

\*\*Clinical and technical nuances involved in catheter-directed lysis procedures and complex IVC filter retrieval cases should govern the target thresholds for INR and platelet count on an individual patient basis. For example, the INR target for complex IVC filter retrieval may be higher for patients in whom the interventionalist chooses to maintain anticoagulation medications during the case. Similarly, the bleeding risk for planned overnight lysis with lytic agents may be different than the bleeding risk in which only mechanical removal of clot is planned. However, both procedures are listed in the high bleeding risk category given that advanced techniques and/or medications will be used that may increase the complexity and procedural bleeding risk.

<sup>††</sup>Transjugular intrahepatic portosystemic shunts are classified as high bleeding risk procedures, as tearing of the portal vein may be a fatal complication. Most patients who undergo transjugular intrahepatic portosystemic shunt creation will have chronic liver disease, and the suggested laboratory parameters for this patient population are listed in [Table 4](#).

quality evidence. The 2013 AASLD revised practice guideline for the management of adult patients with ascites caused by cirrhosis (91) determined that the routine administration of blood products before paracentesis in patients with cirrhosis and coagulopathy is not data-supported (56). This recommendation, categorized as weak and supported by consensus opinion, case studies, or standard of care (91), was based on a study of 1,100 large-volume paracenteses performed in patients with cirrhosis in which there were no reported hemorrhagic complications despite the lack of prophylactic transfusions, platelet counts as low as 19 × 10<sup>6</sup>/L (54% of procedures

performed with platelet counts < 50 × 10<sup>6</sup>/L, 4.5% of procedures performed with platelet counts < 30 × 10<sup>6</sup>/L), and elevated INRs (75% of procedures performed with INR > 1.5 and 26.5% with INR > 2.0) (56). Furthermore, in a survey of 95 physician attendees of a symposium on coagulation in liver disease (89), 50% indicated that they never transfused plasma before a procedure or used plasma only if the INR was > 2.5 before paracentesis. With respect to high bleeding risk procedures, such as liver biopsy, 81% of respondents indicated that they would transfuse platelets for a count below 30 × 10<sup>6</sup>/L and 50% of respondents would transfuse plasma



**Table 4.** Suggested Laboratory Thresholds for Performance of a Procedure in Patients with Chronic Liver Disease (52)

Procedure Risk	INR*	Platelet Count ( $\times 10^9/L$ ) <sup>†</sup>	Fibrinogen (mg/dL) <sup>‡</sup>
Low	NA	> 20	> 100
High	< 2.5	> 30	> 100

Note—The suggested laboratory thresholds and strategies for correction are based on expert opinion (52). The addition of a fibrinogen level to laboratory testing for patients with chronic liver disease who plan to undergo a procedure may be helpful. INR = International Normalized Ratio; NA = not applicable.

\*Recommendation: give 10 mg slow intravenous infusion of vitamin K if INR > 2.5.

<sup>†</sup>Recommendation: administer a dose of platelets in patients with a large spleen if platelet count is below suggested thresholds.

<sup>‡</sup>Recommendation: administer 1 dose (body weight < 80 kg) or 2 doses (body weight > 80 kg) of cryoprecipitate.

in cases of INR > 1.5 (89). In the absence of clear consensus, the AASLD 2009 position paper on liver biopsy (91) concluded that there is “no specific PT-INR and/or platelet count cutoff at or above which potentially adverse bleeding can be reliably predicted” and that “the decision to perform liver biopsy in the setting of abnormal laboratory parameters of hemostasis should continue to be reached as the results of local practice(s).”

Although PT/INR and platelet count have been shown to be poorly predictive of bleeding risk in patients with chronic liver disease, hyperfibrinolysis as a cause for bleeding is an emerging concept (52), and the assessment of fibrinogen levels in patients with chronic liver disease undergoing procedures may be of value. The AASLD cautions that the presence of hyperfibrinolysis (3-dimensional ecchymosis/hematoma) or clinically evident disseminated intravascular coagulation should preclude an invasive procedure (91). Given that these observations have yet to be validated in large-scale clinical trials and that there are no societal practice statements on this particular patient population, transfusion strategies for the management of patients with chronic liver disease are currently based on expert opinion. Table 4 summarizes the current expert consensus view in regard to prophylaxis and treatment recommendations for patients with chronic liver disease who undergo invasive procedures. Interventional radiologists are encouraged to engage hepatologists, hematologists, and transfusion medicine specialists in determining whether specific practice suggestions as outlined in Table 4 may be pertinent for their institution.

*Recommendation 4:* Because of rebalanced hemostasis in patients with chronic liver disease, the transfusion of plasma and platelets should be used judiciously given the potential for increased portal pressure and transfusion-related adverse events. It is likely that future research will result in specific laboratory parameters for patients with chronic liver disease to guide the use of blood products in this patient population. For patients with chronic liver disease undergoing an invasive procedure, consider adjusting INR and platelet count thresholds higher and lower, respectively, than in the general population to minimize unnecessary transfusions. Measuring fibrinogen level may be useful, with replacement with cryoprecipitate if the level is low (Table 4). (Level of evidence, E; strength of recommendation, weak.)

## BLOOD COMPONENTS AND OTHER HEMOSTATIC AGENTS USED IN TRANSFUSION MANAGEMENT

The administration of blood components, such as red blood cells, plasma, platelets, cryoprecipitate, and other plasma derivatives, may be necessary to correct for coagulopathies in the periprocedural setting. Our knowledge regarding the impact of transfusion of plasma or platelets in the periprocedural setting is equivocal and is derived from small observational

studies, retrospective case reviews, and consensus data (58,95–101). An exhaustive review of individual blood components and their mechanisms of action is beyond the scope of this paper; however, the properties of commonly used blood products are summarized in Table 5 (102). A discussion of the risks versus benefits of the transfusion of blood components is required for the patient to give informed consent. Some patients may refuse blood products for religious or nonreligious reasons.

Jehovah's Witness patients may not accept any blood components or may accept certain products such as plasma, cryoprecipitate, albumin, or plasma-derived factor concentrates (eg, prothrombin complex concentrate or fibrinogen concentrate). It is essential to document the patient's preferences in the medical records. Intravenous vitamin K can be used to correct preprocedural prolonged PT/INR as a result of vitamin K deficiency or VKA anticoagulation. In a Jehovah's Witness patient experiencing bleeding, some of the hemostatic options that could be used include recombinant factor VIIa (20  $\mu\text{g}/\text{kg}$  every 2–4 h), desmopressin, or 4-factor prothrombin complex concentrate (103,104). Desmopressin (1-deamino-8-D-arginine vasopressin) is a synthetic analogue of antidiuretic hormone and enhances the plasma levels of factor VIII and von Willebrand factor (105). A single dose, 0.3  $\mu\text{g}/\text{kg}$  diluted in 100 mL normal saline solution and infused intravenously over 20–30 minutes every 12 hours (maximum 6 doses), is expected to increase the factor VIII and von Willebrand factor levels by 3–6 fold. In addition, desmopressin may be indicated before image-guided procedures in patients with mild hemophilia A or type 1 von Willebrand disease (105,106) or in patients with congenital or acquired platelet disorders as a result of uremia or antiplatelet agents (106,107).

Very serious transfusion-related complications are known to arise, such as allergic reactions, nonhemolytic febrile reactions, acute hemolytic reactions, sepsis from bacterial contamination, transfusion-related acute lung injury, and transfusion-associated circulatory (ie, volume) overload (108). Packed red blood cells and platelets are often leukoreduced before storage to avoid adverse effects of white blood cells, including cytokine-induced nonhemolytic febrile reactions, cytomegalovirus, or alloimmunization to human leukocyte antigens. However, fatal graft-versus-host disease is preventable only by irradiation of these blood products for immunocompromised (not immunosuppressed) patients. Transfusion-associated circulatory overload, which can cause death, is the most common adverse effect of plasma transfusion and is often underrecognized and underreported (109). Because of its high protein content, plasma has a very high oncotic pressure and draws water from extravascular space into the circulatory system, and can therefore increase portal pressure rapidly, which may lead to adverse outcomes, particularly in patients with cirrhosis. These potential adverse events should be considered before administration of any blood products.

## MANAGEMENT OF ANTICOAGULATION AND/OR ANITPLATELET AGENTS BEFORE AND AFTER A PROCEDURE

### Timing of Anticoagulation and/or Antiplatelet Agent Withholding before a Procedure

Determining whether to hold anticoagulation and/or antiplatelet agents before a procedure, and the duration of the hold, depend on the patient's overall clinical status, including thrombotic and bleeding risks; on procedural bleeding risk; and on the pharmacologic characteristics of the medication being held (Figs 1–3). The goal of holding anticoagulation and/or antiplatelet agents before a procedure is to minimize medication-related bleeding complications, but also carries a theoretical risk for thrombosis as a result of undertreatment. Therefore, the timing of withholding of medications is a balance between patient thrombosis risk and procedural bleeding risk. Patient comorbidities (eg, renal function) should be taken into account, and, for patients who present with complex medical comorbidities, multidisciplinary shared decision-making with the patient's cardiovascular specialist or hematologist is recommended for the management of antithrombotic agents, including bridging options, in the periprocedural period. Table 6 (32–34,36,110–128) summarizes agent-specific recommendations for periprocedural medication interruption and reinitiation, including recommendations for patients with renal impairment (39,43,129–137). The recommendations are extrapolated from a compilation of expert consensus recommendations from the cardiology, anesthesia, interventional, and surgical literature

**Table 5.** Summary of Commonly Used Blood Components (102)

Blood Component	Approximate Volume of 1 Dose (mL)	Source	Storage/Shelf Life	Expected Degree of Correction	Total Approximate Cost to Transfuse and Other Considerations
PRBCs	300	Centrifuged whole blood or apheresis method	Up to 42 d at 1–6°C	1 U PRBC increases hemoglobin by 1 g/dL in normal-sized adult	\$1,200/unit; patients receiving chronic transfusions (eg, sickle-cell anemia) may develop multiple alloantibodies, making it difficult to identify matched unit
Plasma	250	Supernatant of centrifuged whole blood	FFP is frozen at –18°C within 8 h of collection, stored for 1 y; frozen plasma is frozen within 24 h, stored for 1 y; thawed plasma, stored at 1–6°C for ≤ 5 d	Any plasma can be used to treat multiple factor deficiency; adequate dose of plasma 10–15 mL/kg to manage coagulopathy	\$1/mL; FVIII reduced significantly except in FFP; contraindicated for VKA reversal due to availability of 4F-PCC (102)
Platelets	250–300	90% of platelets derived from single-donor apheresis procedures; 10% derived from whole-blood donation (platelets from 4–6 donors pooled to constitute dose equivalent to apheresis unit, $3 \times 10^{11}$ platelets per dose)	Stored at room temperature (20–24°C); 5-d expiration period due to risk of bacterial contamination, making platelets often in short supply	One dose of platelets* (one unit of apheresis or 4–6 pooled from whole blood donors) increases the platelet count by $25\text{--}50 \times 10^9/\text{L}$ in normal-sized patient without splenomegaly	\$1,000/unit of apheresis or pooled platelets
Cryoprecipitate	100–200	Derived from thawing FFP at 4°C when certain proteins precipitate out (supernatant cryopoor, plasma removed) and refrozen (volume 10–20 mL) at –18°C; 1 dose of cryoprecipitate consists of pooling from 10 donors (volume 100–200 mL)	Stored at –18°C for 1 y; when thawed, should be used within 4–6 h	Adult dose provides $\geq 3$ g of fibrinogen and can increase fibrinogen by 100 mg/dL in normal-sized person; 1 dose of cryoprecipitate also contains ~1,000 U of VWF and factor VIII	\$1,000/dose; rich source of fibrinogen (2–4 g per dose)

d = days; 4F-PCC = 4-factor prothrombin complex concentrate; h = hours; PRBC = packed red blood cell; VKA = vitamin K antagonist; VWF = von Willebrand factor; y = years.

\*One dose of platelets is equivalent to 4–6 U or 250–300 mL.

(3,6,36,50,138). It should be noted that, in patients who are deemed to be at very high risk for thrombosis (eg, patients who have experienced recurrent antiphospholipid antibody–related thrombotic events), minimizing the time off anticoagulation by transitioning the patient to short-acting parenteral agents such as unfractionated heparin as inpatients may be advised.

## Bridging

Determining whether bridging is needed differs slightly before and after a procedure. Before a procedure, bridging is necessary if the thrombosis risk is deemed very high to minimize time off anticoagulation: a parenteral agent, typically heparin, is given after the effect of an oral agent, usually warfarin, has waned. Bridging after a procedure involves giving a parenteral agent while the oral anticoagulant effect of warfarin is taking effect or before a DOAC is given. Whether to bridge postprocedurally depends on the indication for anticoagulation, thrombosis and bleeding risk, and the type of anticoagulant agent the patient is receiving. Warfarin, dabigatran, and edoxaban are typically preceded by a parenteral agent for the indication of acute VTE.

There are several studies that have addressed bridging in the peri-procedural context, and it should be noted that bridging can be associated

with excess bleeding. The Bridge or Continue Coumadin for Device Surgery Randomized Controlled trial (33) compared a strategy of not withholding a VKA versus holding the VKA and bridging with heparin in patients undergoing implantation of pacemakers or implantable cardioverter defibrillators. This study demonstrated that patients in whom therapeutic anticoagulation with a VKA was maintained (INR goal < 3 on the day of procedure) experienced significantly less bleeding than those who were randomized to undergo temporary interruption of VKA agent and bridging with heparin (odds ratio, 0.91;  $P < .001$ ) (33). Results from the Role of Coumadin in Preventing Thromboembolism in Atrial Fibrillation Patients Undergoing Catheter Ablation trial (34) showed similar results, with patients who continued VKA anticoagulation (INR goal of 2–3) experiencing lower rates of minor bleeding ( $P < .001$ ) and thromboembolic events ( $P < .001$ ) than patients who underwent anticoagulation interruption and bridging with LMWH before catheter ablation for atrial fibrillation. Another study (139) compared various bridging strategies (none, prophylactic-dose heparin, full-dose heparin) in patients in whom warfarin was interrupted for a procedure. Patients in this study received anticoagulation for various reasons, most commonly atrial fibrillation or VTE. Most procedures were categorized as minor (62.7%), general abdominal (12.6%), or angiographic (11.8%).

Within 30 days, the rate of thrombosis was 0.8% and the rate of bleeding was 3.2% in the 492 patients. Full-dose heparin or LMWH was associated with increased bleeding risk. Finally, a study compared bridging versus no bridging for 1,178 patients receiving warfarin for secondary prevention of VTE undergoing 1,812 procedures (140). The most common procedures were gastrointestinal endoscopy (37.1%) and orthopedic (13.6%) and spinal or intracranial procedures (9.7%). Bleeding within 30 days occurred in 2.7% and 0.2% of patients with and without bridging, respectively, representing a 17-fold higher risk of bleeding for the patients receiving bridging. Recurrent venous thrombosis did not differ between the groups (0 vs 3;  $P = .56$ ).

### Timing of Anticoagulation and/or Antiplatelet Agent Administration after a Procedure

Resuming treatment with a prophylactic or therapeutic dose of an anticoagulant or antiplatelet agent following an invasive procedure should be based on the presumed risk of postprocedural bleeding weighed alongside the patient's risk for a thromboembolic event. Options for antiplatelet agents and anticoagulants include restarting at a low dose, starting immediately on a maintenance dose, or adding a loading dose. Although average bleeding risk estimates are available, in practice, assessment of bleeding risk for a particular patient is often based on subjective operator report. Therefore, resuming a therapeutic dose may require a delay until the bleeding risk has been minimized or controlled. For some medications, a loading dose may be recommended (eg, clopidogrel), but this often depends on clinical circumstances. The reinitiation dose should be determined in conjunction with the patient's cardiovascular clinician before the procedure.

DOACs take effect within a few hours, and care must therefore be given to deciding when to restart them. By using an algorithm to reinitiate dabigatran after a procedure, one study (141) reported low bleeding (1.8%) and VTE (0.2%) rates. After low bleeding risk procedures, dabigatran was resumed at a reduced dose of 75 mg on the night of the procedure (at least 4 h after neuraxial anesthesia), and the full dose was started the following morning. After high bleeding risk procedures, dabigatran was resumed at full dose at least 48 hours after the procedure. Although similar data regarding specific regimens do not exist for rivaroxaban (142) and apixaban (143), both have been shown to be equally safe when interrupted and resumed periprocedurally. DOACs currently carry a black box warning with respect to their use in patients undergoing neuraxial anesthesia. Recent multisociety consensus guidelines (32) recommend the discontinuation of a DOAC before neuraxial procedures (factor Xa inhibitors, 3–5 d; dabigatran, 4–5 d) and reinitiation of a DOAC 24 hours after the procedure. This is a cautious strategy, as the drug-free interval time is longer than typical recommendations, and, for patients with a high thrombotic risk, consideration of a bridging strategy may be warranted (3,36).

Reinitiation suggestions in Table 6 generally apply to patients with normal body weight and organ function. Clinical judgment should be used when treating children and patients of advanced age, patients with decreased renal function (creatinine clearance < 50 mL/min), or patients with high or low body mass index. The metabolism of many antiplatelet and

anticoagulant agents is dependent on liver or renal function, which therefore needs to be taken into account when considering how to dose the medication, when to interrupt a medication, and when to restart a medication at the appropriate dose. In addition, as renal function may be labile, especially in the periprocedural period, it should be monitored closely during this time. Caution is required if a patient is receiving more than 1 anticoagulant agent or concomitant medications that may interact with the anticoagulant or antiplatelet agent. Consideration for increasing the time interval to restarting anticoagulants or antiplatelet agents may be needed after traumatic procedures or procedures in locations in which even minor bleeding may be catastrophic (ie, neuraxial procedures). Close monitoring is recommended in the postprocedural period after restarting these medications.

### Considerations for Specific Common Clinical Conditions Requiring Anticoagulation

**Atrial fibrillation.**—In 2017, the American College of Cardiology issued a consensus decision pathway (31), which should be followed regarding anticoagulation interruption in patients with NVAF who require procedures. Typically, patients at low risk will not receive bridging anticoagulation, whereas those at high risk, including those with recent stroke (within 3 mo), will. Patients at intermediate risk may benefit from multidisciplinary management with individualized decisions based on stroke and bleeding risk assessment. Anticoagulation should not be interrupted in low bleeding risk procedures and in the absence of patient-related bleeding risk factors (3). The CHA2DS2-VASc score is useful for determining which patients with NVAF will benefit from bridging anticoagulation (3). Most patients with NVAF receiving anticoagulation will not require bridging (144), as bridging has been associated with increased postoperative bleeding risk (145). However, in patients who are treated with warfarin and who are considered to be at high risk for thrombosis, even with short gaps in anticoagulation, a bridge should be considered. When only 1 patient-related bleeding risk factor exists, the authors suggest a case-by-case discussion.

**VTE.**—The approach to patients who have experienced a venous thromboembolic event depends on acuity (more or less than 3 mo) in the context of the circumstance of the event (provoked vs unprovoked), as well as location (proximal vs distal DVT or pulmonary embolism). After a procedure, patients who have experienced an acute (within 3 mo) venous thromboembolic event should resume rivaroxaban or apixaban or receive bridging anticoagulation if they are being treated with warfarin (146), dabigatran, or edoxaban. The theoretic risk for warfarin-induced thrombosis should be considered in the context of postprocedural bleeding risk in patients with remote venous thrombosis. Therefore, although full-dose anticoagulation would typically be given in tandem with warfarin that is being started, some have advocated for prophylactic-dose anticoagulation in this setting (146). Notably, it is not clear whether a loading dose is required for rivaroxaban or apixaban (as would be the case in newly diagnosed VTE).

**Mechanical heart valves.**—Patients who have prosthetic heart valves will most likely be receiving anticoagulation with a VKA. Unfortunately,

**Table 6.** Management Recommendations for Anticoagulant and Antiplatelet Agents (32–34,36,110–128)

Medication	Low Risk for Bleeding	High Risk for Bleeding*
<b>Anticoagulants</b>		
<b>UFH</b>		
Withholding	Do not withhold	Withhold IV heparin for 4–6 h before procedure; check aPTT or anti-Xa level; for BID or TID dosing of SC heparin, procedure may be performed 6 h after last dose
Reinitiation	NA	6–8 h
<b>LMWH: enoxaparin (Lovenox), dalteparin (Fragmin)</b>		
Withholding	Do not withhold	Enoxaparin, withhold 1 dose if prophylactic dose is used; withhold 2 doses or 24 h before procedure if therapeutic dose is used; check anti-Xa level if renal function impaired; dalteparin, withhold 1 dose before procedure
Reinitiation	NA	12 h

*continued*

**Table 6.** Management Recommendations for Anticoagulant and Antiplatelet Agents (32–34,36,110–128) (continued)

Medication	Low Risk for Bleeding	High Risk for Bleeding*
Fondaparinux (Arixtra)		
Withholding	Do not withhold	Withhold 2/3 d (CrCl ≥ 50 mL/min) or 3–5 d (CrCl ≤ 50 mL/min)
Reinitiation	NA	24 h
Argatroban (Acova)		
Withholding	Do not withhold	Withhold 2–4 h before procedure <sup>†</sup> ; check aPTT
Reinitiation	NA	4–6 h
Bivalirudin (Angiomax)		
Withholding	Do not withhold	Withhold 2–4 h before procedure <sup>†</sup> ; check aPTT
Reinitiation	NA	4–6 h
Warfarin (Coumadin)		
Withholding	Target INR ≤ 3.0 <sup>‡</sup> ; consider bridging for high thrombosis risk cases	Withhold 5 d until target INR ≤ 1.8; consider bridging for high thrombosis risk cases; if STAT or emergent, use reversal agent
Reinitiation	NA or same-day reinitiation for bridged patients	Resume day after procedure; high thrombosis risk cases may benefit from bridging with LMWH and multidisciplinary management especially if reversal agent used along with vitamin K
Apixaban (Eliquis)		
Withholding	Do not withhold <sup>‡</sup>	Withhold 4 doses (CrCl ≥ 50 mL/min) or 6 doses (CrCl < 30–50 mL/min); if procedure is STAT or emergent, use reversal agent (andexanet alfa); consider checking anti-Xa activity or apixaban level especially with impaired renal function
Reinitiation	NA	24 h
Betrixaban (Bevyxxa)		
Withholding	Do not withhold <sup>‡</sup>	Withhold for 3 doses (113); if procedure is STAT or emergent, use reversal agent (andexanet alfa); consider checking anti-Xa activity especially with impaired renal function
Reinitiation	NA	24 h
Dabigatran (Pradaxa)		
Withholding	Do not withhold <sup>‡</sup>	Withhold 4 doses (CrCl ≥ 50 mL/min) or 6–8 doses (CrCl < 30–50 mL/min); if procedure is STAT or emergent, use reversal agent (idarucizumab); consider checking thrombin time or dabigatran level with impaired renal function
Reinitiation	NA	24 h
Edoxaban (Savaysa)		
Withholding	Do not withhold <sup>‡</sup>	Withhold for 2 doses; if procedure is STAT or emergent, use reversal agent (andexanet alfa); consider checking anti-Xa activity especially with impaired renal function
Reinitiation	NA	24 h
Rivaroxaban (Xarelto)		
Withholding	Do not withhold <sup>‡</sup>	Defer procedure until off medication for 2 doses (CrCl ≥ 50 mL/min), 2 doses (CrCl < 30–50 mL/min), or 3 doses (CrCl < 15–30 mL/min); if procedure is STAT or emergent, use reversal agent (andexanet alfa); consider checking anti-Xa activity or rivaroxaban level especially with impaired renal function
Reinitiation	NA	24 h
Antiplatelet agents: thienopyridines		
Clopidogrel (Plavix)		
Withholding	Do not withhold	Withhold for 5 d before procedure <sup>§</sup>
Reinitiation	NA	Reinitiation can occur 6 h after procedure if using 75-mg dose but should occur 24 h after procedure if using a loading dose (300–600 mg) <sup>  </sup>
Ticagrelor (Brilinta)		
Withholding	Do not withhold	Withhold for 5 d before procedure
Reinitiation	NA	Resume the day after procedure
Prasugrel (Effient)		
Withholding	Do not withhold	Withhold for 7 d before procedure
Reinitiation	NA	Resume the day after procedure
Cangrelor (Kengreal)		
Withholding	Defer procedure until off medication; if procedure is emergent, withhold 1 h before procedure; multidisciplinary discussion with cardiology suggested (118)	
Reinitiation	Patients receiving cangrelor are undergoing PCI or are within immediate periprocedural period from cardiac intervention; multidisciplinary, shared decision making recommended	

continued

**Table 6.** Management Recommendations for Anticoagulant and Antiplatelet Agents (32–34,36,110–128) (continued)

Medication	Low Risk for Bleeding	High Risk for Bleeding*
Antiplatelet agents: NSAIDs <sup>#</sup>		
Aspirin		
Withholding	Do not withhold	Withhold 3–5 d before procedure <sup>¶</sup>
Reinitiation	NA	Resume the day after procedure
Aspirin/dipyridamole (Aggrenox) (119,120)		
Withholding	Do not withhold	Withhold 3–5 d before procedure <sup>¶</sup>
Reinitiation	NA	Resume the day after procedure
Short-acting NSAIDs (half-life 2–6 h): ibuprofen, diclofenac, ketoprofen, indomethacin, ketorolac		
Withholding	Do not withhold	No recommendation
Reinitiation	NA	NA
Intermediate-acting NSAID (half-life 7–15 h): naproxen, sulindac, diflunisal, celecoxib		
Withholding	Do not withhold	No recommendation
Reinitiation	NA	NA
Long-acting NSAIDs (half-life > 20 h): meloxicam, nabumetone, piroxicam		
Withholding	Do not withhold	No recommendation
Reinitiation	NA	NA
Antiplatelet agents: glycoprotein IIb/IIIa inhibitors		
Long-acting abciximab (ReoPro)		
Withholding	Withhold 24 h before procedure**	
Reinitiation	Patients receiving glycoprotein IIb/IIIa inhibitor are undergoing PCI or within immediate periprocedural period from cardiac intervention; multidisciplinary, shared decision making recommended	
Short-acting: eptifibatide (Integrilin), tirofiban (Aggrastat)		
Withholding	Withhold 4–8 h before procedure**	
Reinitiation	Patients receiving a glycoprotein IIb/IIIa inhibitor are undergoing PCI or within immediate periprocedural period from cardiac intervention; multidisciplinary, shared decision making recommended	
Other		
Cilostazol (Pletal) (127,128)		
Withholding	Do not withhold	Do not withhold
Reinitiation	NA	NA

Note—There was an 100% 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 unless otherwise noted. Recommendations may not pertain to emergency or highly urgent procedures in which the risk of procedural delay may outweigh the potential hemorrhagic risk.

ACT = activated clotting time; aPTT = activated partial thromboplastin time; ASA = acetylsalicylic acid; BID = twice daily; CrCl = creatinine clearance; d = day; h = hour; INR = International Normalized Ratio; IV = intravenous; LMWH = low molecular weight heparin; NA = not applicable; PCI = percutaneous coronary intervention; SC = subcutaneous; TID = three times per day; UFH = unfractionated heparin.

\*Clot stabilization occurs at approximately 6–8 h (32). Suggested reinitiation times assume that the periprocedural risk of bleeding has resolved. However, in addition to resolution of procedural bleeding risk, the reinitiation of any antiplatelet or anticoagulant medication is dependent on individual patient comorbidities (eg, chronic liver disease, chronic renal failure), and, for patients at high risk, multidisciplinary discussion may be warranted.

<sup>†</sup>Intravenous direct thrombin inhibitors are used in PCIs for only 24 h but longer for patients with heparin-induced thrombocytopenia. Reinitiation should be similar to UFH, 4–6 h (110).

<sup>‡</sup>Data suggest the safety of performing low bleeding risk procedures in the presence of a therapeutic INR (INR < 3). Preprocedural DOAC interruption > 24 h vs < 24 h was not identified as a potential risk factor for major bleeding events (36). For patients requiring arterial access, the target is INR < 1.8 for femoral puncture and < 2.2 for radial artery access. For patients who are at high risk for a thromboembolic event (Table 1), bridging therapy may be considered, and multidisciplinary, shared decision-making may be helpful. For patients in whom the target therapeutic INR range is > 3 (ie, patients with mechanical heart valves), evaluation of laboratory parameters and withholding warfarin and/or bridging may be necessary. Multidisciplinary shared decision-making is recommended. If warfarin is withheld, reinitiation can occur on the procedure day as the anticoagulant effects of warfarin are delayed (33,34,111,112).

<sup>§</sup>Consider checking drug effect because as many as 30% of patients can be poor responders and may not have to wait the full 5 d for withholding (114–116).

<sup>||</sup>Time to peak effect of clopidogrel is 24 hours but if a loading dose is used, then time to peak effect shortens to 4–6 h (117).

<sup>¶</sup>Withholding strategies for aspirin require a patient-specific approach (Fig 2, Table 1) in which the indication for aspirin therapy, thrombotic risk, and expected periprocedural bleeding risk should be considered. For high-risk or complex cardiovascular cases, multidisciplinary shared decision-making may be helpful. Complete recovery of platelet function can occur in as many as 50% of healthy men taking 325 mg ASA every other day for 14 d by the third day of discontinuation (121).

<sup>#</sup>Non-ASA NSAIDs have weak antiplatelet effects. Discontinuation of the agent for 5 half-lives should be sufficient to mitigate NSAID effect on platelet function (32). Selective cyclooxygenase-2 inhibitors, such as celecoxib, do not interfere with normal mechanisms of platelet aggregation and hemostasis (122,123). There are insufficient data to generate a recommendation. Discontinuation of these drugs is unlikely to affect cardiac or cerebral thromboembolic risk.

\*\*Glycoprotein IIb/IIIa inhibitors are often used in conjunction with heparin during PCI procedures. The following aPTT and ACT values reflect the recommended values before femoral arterial sheath removal per Food and Drug Administration drug insert: abciximab, aPTT < 50 s, ACT < 170 s; eptifibatide/tirofiban, aPTT < 45 s, ACT < 150 s (124–126).

data to support periprocedural anticoagulation management are based mainly on case series that are often outdated (15). Importantly, thromboembolic- and anticoagulation-related problems, and not structural failure, are by far the most frequent complications of mechanical valves. The American Heart Association and American College of Cardiology issued guidelines regarding the management of mechanical heart valves (10): the management of antithrombotic therapy should take into account valve type, location, and number of valves in the periprocedural period, especially for patients who have prosthetic, versus bioprosthetic, valves. Anticoagulation should not be stopped for low bleeding risk procedures. If a high bleeding risk procedure is required, consultation with the patient's cardiologist should be undertaken whenever possible, with options including a brief hold of anticoagulation versus a periprocedural bridging strategy.

## SUMMARY STATEMENT

Decision-making for the periprocedural management of thrombotic and bleeding risk should be patient-specific, as recommendations can be medication- and clinical condition-specific. The algorithmic approach endorsed in this document advocates for an individualized, per-patient decision-making process. The following is a summary of the main considerations.

- Determination of whether to hold anticoagulation and/or antiplatelet agents before a procedure and the duration of the hold depend on the patient's thrombotic and bleeding risks, procedural bleeding risk, and the pharmacologic characteristics of the medication being held. Specific attention should be given to the patient's liver and renal function. Clinical condition-specific recommendations (eg, atrial fibrillation, VTE, stroke, mechanical heart valves, coronary stents) require specific risk stratification.
- Determination of whether bridging is needed differs before and after a procedure. Before a procedure, bridging is necessary if the thrombosis risk is deemed very high to minimize time off anticoagulation. After a procedure, whether to administer bridging depends on the indication for anticoagulation, thrombosis and bleeding risk, and also on the anticoagulant agent the patient is receiving. Warfarin, dabigatran, and edoxaban are typically preceded by a parenteral agent for the indication of acute VTE. Bridging can be associated with excess bleeding.
- Determination of when to resume treatment with a prophylactic or therapeutic dose of an anticoagulant or antiplatelet agent following an invasive procedure should be based on the presumed risk of post-procedural bleeding (determined by the interventionalist) weighed alongside the patient's risk for a thromboembolic event (determined by the patient's cardiovascular or hematology physician). Resumption of a therapeutic dose of antiplatelet medication or anticoagulation may require a delay until the bleeding risk has been minimized.

## CONCLUSIONS

The periprocedural management of thrombotic and bleeding risks in patients undergoing invasive procedures is complex. It is important to acknowledge that the evidence informing many of the recommendations is of low quality and usually addresses only 1 coagulation abnormality at a time (elevated INR or thrombocytopenia), and additional research is needed to generate higher-quality evidence to guide future updates. Therefore, the recommendations herein should not be interpreted as being authoritative, but, rather, they should be used to aid in pragmatic clinical decision-making.

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## APPENDIX A: EXECUTIVE SUMMARY

### Guideline Question

What are the current recommendations for percutaneous image-guided periprocedural anticoagulation and antiplatelet management for percutaneous image-guided procedures?

### Target Population

Patients who require image-guided vascular or nonvascular interventions.

### Target Audience

Interventional radiologists and other clinicians who provide care for patients defined by the target population.

### Methods

A multidisciplinary expert panel was assembled to update the 2012 and 2013 Society of Interventional Radiology (SIR) consensus guidelines (1,2). A systematic review of the literature was performed, and relevant evidence was evaluated for inclusion into this updated document. Evidence was rated according to the updated SIR evidence grading system (3). The panel met face to face at the SIR 2018 Annual Meeting and held multiple subsequent telephone conferences to draft the document. Modified Delphi methodology was used to achieve consensus.

### New Recommendations

- Bleeding and thrombotic risks of each patient are dependent on medical comorbidities and need to be considered as part of periprocedural management.
- For high-risk or complex cases, a multidisciplinary, shared decision-making process is encouraged for periprocedural management recommendations to optimize patient outcomes.
- Algorithms are incorporated to provide a framework to guide the periprocedural management of patients who are receiving anticoagulation and/or antiplatelet agents.
- Laboratory parameters specific to patients with chronic liver disease have been suggested predicated on the concept of rebalanced primary and secondary hemostasis in this patient population.
- Procedure-associated bleeding risks for image-guided interventions have been reclassified into low risk versus high risk for major bleeding.
- Recommendations for timing of postprocedural reinitiation of anticoagulant or antiplatelet medications have been added.

### Updated Recommendations

- Revision of laboratory parameter recommendations:
  - a. No data to support activated partial thromboplastin time recommendations. Recommendations removed.
  - b. Recommended minimum platelet threshold of  $20 \times 10^9/L$  for low bleeding risk procedures.
  - c. Recommended correction of International Normalized Ratio (INR) to within range of 2.0–3.0 or less for low bleeding risk procedures. If

arterial access is required, correction of INR to  $< 1.8$  for femoral access and  $< 2.2$  for radial access.

- d. Recommended correction of INR to within range of 1.5–1.8 or less for high bleeding risk procedures.

### Unchanged Recommendations

- Routine screening coagulation laboratory testing (prothrombin time/INR, platelet count, hemoglobin) not recommended for procedures with low bleeding risk.
- Routine screening coagulation laboratory testing (prothrombin time/INR, platelet count, hemoglobin) recommended for procedures with high bleeding risk.
- Recommended minimum platelet threshold of  $50 \times 10^9/L$  for high bleeding risk procedures.

### Qualifying Statements

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