Clinical Progress Note: Consolidated Guidelines on Management of Coagulopathy and Antithrombotic Agents for Common Bedside Procedures

Jessica A Blank, MD[1], Kyle K Peters, MD[2], Matt A O'Donnell, DO[3], André M Mansoor, MD[3]*

[1]*School of Medicine, Oregon Health & Science University, Portland, Oregon;* [2]*Internal Medicine Residency Program, Oregon Health & Science University, Portland, Oregon;* [3]*Department of Medicine, Oregon Health & Science University, Portland, Oregon.*

The practice of internal medicine includes bedside procedures such as paracentesis, thoracentesis, and lumbar puncture (LP). The American Board of Internal Medicine requires graduates of internal medicine residency programs to be competent in the cognitive components of procedural training (eg, indications, contraindications, complications) and considers it essential that trainees have opportunities to perform procedures relevant to their intended career direction.[1] Whether or not the performance of procedures is part of a given hospitalist's practice, it is necessary that hospitalists understand each procedure's risks and mitigation strategies to prevent a range of periprocedural complications, including clinically significant bleeding. Numerous recommendations and guidelines exist describing bleeding risk for common procedures. In this Progress Note, we summarize and consolidate this literature, covering a range of scenarios common to the hospital setting, including thrombocytopenia, elevated international normalized ratio (INR), and the use of medications such as antiplatelet and anticoagulant agents (Table 1 and Table 2). We performed electronic searches in PubMed, focusing on literature published since 2016. Key search terms included *paracentesis*, *thoracentesis*, *lumbar puncture*, *anticoagulant*, *antiplatelet*, *coagulopathy*, *INR*, *thrombocytopenia*, and *guideline*. In addition, we used the following MeSH terms: *spinal puncture* AND *blood coagulation disorders*, *spinal puncture* AND *platelet aggregation inhibitors*, *spinal puncture* AND *anticoagulants*, *paracentesis* AND *blood coagulation disorders*, *paracentesis* AND *platelet aggregation inhibitors*, *paracentesis* AND *anticoagulants*, *thoracentesis* AND *blood coagulation disorders*, *thoracentesis* AND *platelet aggregation inhibitors*, and *thoracentesis* AND *anticoagulants*.

TABLE 1. **Summary of Periprocedural Management of Coagulopathy for Paracentesis, Thoracentesis, and Lumbar Puncture, Stratified by Referenced Guidelines**

		Paracentesis and thoracentesis	Lumbar puncture
		Correction threshold	
INR	Without chronic liver disease	≤2.0-3.0[2] <2.0[3] <1.5[5a]	≤2.0-3.0[2] ≤1.5[4] <1.5[3]
	With chronic liver disease	No threshold[2,6b] <2.0[3]	No threshold[2] ≤1.5[4] <1.5[3]
Platelets (per μL)		No threshold[6b] >20,000[2,3] >50,000[5a]	≥20,000[2] >40,000[3,7c] ≥50,000[4]

[a]Specific to thoracentesis.
[b]Specific to paracentesis in the setting of chronic liver disease.
[c]If platelets are 20,000-40,000/μL, an additional risk-benefit discussion is encouraged.
Abbreviation: INR, international normalized ratio.

GENERAL CONCEPTS

Weighing Risks and Benefits

Proceduralists should discuss risks and benefits with patients and the referring service before attempting to mitigate bleeding risk by holding antithrombotic agents or reversing coagulopathy, as these actions come with risks outside the anticipated procedure, in particular, an increased risk of thrombosis. There are many factors that influence an individual patient's arterial thromboembolism and venous thromboembolism (VTE) risk, including surgical history, genetics, comorbidities, and the underlying indication for antithrombotic therapy. The American College of Chest Physicians updated their clinical practice guidelines describing perioperative thromboembolism risk stratification in 2012.[12] In general, higher-risk individuals include those with any mitral valve prosthesis, recent (within 6 months) stroke or transient ischemic attack (TIA), $CHADS_2$ score of 5 or 6, recent (within 3 months) VTE, or severe thrombophilia. Individuals at moderate risk include those with bileaflet aortic valve repair (AVR) with at least one major stroke risk factor, $CHADS_2$ score of 3 or 4, recent (within 3-12 months) or recurrent VTE, or active or recent (treatment within preceding 6 months) cancer. Finally, individuals at low risk include those with bileaflet AVR without major stroke risk factors, $CHADS_2$ score of 0 to 2, or VTE more than 12 months earlier. There are also patient-specific bleeding risk factors that should be considered, including hypertension, abnormal renal function, abnormal hepatic function, prior stroke, history of major bleeding

***Corresponding Author:** André M Mansoor, MD; Email: mansooan@ohsu.edu; Telephone: 503-494-8607; Twitter: @AndreMansoor.

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TABLE 2. **Summary of Periprocedural Management of Antiplatelet and Anticoagulant Agents for Paracentesis, Thoracentesis, and Lumbar Puncture, Stratified by Referenced Guidelines**

	Paracentesis and thoracentesis		Lumbar puncture	
	Recommended hold time prior to procedure[a]	**Recommended restart time after procedure[a,b]**	**Recommended hold time prior to procedure[a]**	**Recommended restart time after procedure[a,b]**
Aspirin	Continue[2,5c]	Not applicable	Continue[2] Continue (if low dose)[4,7] 5 d (if high dose)[4]	No delay[7]
Clopidogrel	Continue[2,5c]		Continue[2] 5 d[4] 5-7 d[8] 7 d[7,9]	After 6 h[7] After 12-24 h[9] Next day[4]
Prasugrel	Continue[2,5c]		Continue[2] 7 d[7] 7-10 d[8,9]	After 6 h[7] After 24 h[9]
Ticagrelor	Continue[2,5c]		Continue[2] 5 d[9] 5-7 d[8] 7 d[7]	After 6 h[7] After 24 h[9]
Dipyridamole	Continue[2]		Continue[2,9] 24 h[7,8]	After 6 h[7,8]
Abciximab	24 h[2]	Not available	24 h[2,4] 24-48 h[8] 48 h[7] 2-5 d[9]	After 8 h[4] After 8-12 h[9] After 24 h[7]
Tirofiban, eptifibatide	4-8 h[2]		4 h[4] 4-8 h[2,7,8] 8-24 h[9]	After 8-12 h[9] After 24 h[7]
Warfarin	Continue[10] Continue if no patient-related risk factors for bleeding[11de] Continue with INR within patient's target range[3f] Hold to target INR ≤3.0[2] 3-5 d to target INR <2.0[3g] 5 d to target INR <1.5[5c]	After 12-24 h[3] After 24 h[11]	Hold to target INR ≤3.0[2] 3-5 d to target INR ≤1.5[4] 5 d[2,3,7] to target INR <1.5[3] or ≤1.4[7] 5 d to target a normal INR[8,9]	After 6 h[9] After 12 h[4,7] After 12-24 h[7] After 24 h[11]
LMWH				
Prophylactic dosing	Continue[3f] 12 h[3g]	After 6 h[3]	6-12 h[3] 12 h[7-9]	After 4 h[7] After 6-12 h[3] After 12 h[8] After 12-24 h[9]
Therapeutic dosing	One dose[5c] 24 h[3g]	After 6-12 h[3]	24 h[3,7-9]	After 4 h (after 24 h if traumatic)[7] After 12-24 h[9] After 24-72 h[3]
Either	Continue[2,10]	Not applicable	Continue[2] Last dose or 12 h[4]	After 24 h[4]

(especially within the preceding 3 months), and bleeding history with a similar procedure.[11]

Hepatic and Renal Dysfunction

In the setting of chronic liver disease, thrombocytopenia and elevated INR are generally not reliable indicators of bleeding risk.[13] The included recommendations for INR and platelet count thresholds in the setting of chronic liver disease are derived from the referenced guidelines and supplemental personal communication with the guideline authors. Many antiplatelet and anticoagulant medications are partially cleared or metabolized by the liver, suggesting that hepatic dysfunction may impact drug clearance, but this has not been well studied. Impaired renal function should also be considered when determining appropriate hold times for antithrombotic drugs that are partially renally cleared. The periprocedural hold and restart times outlined in Table 2 are specific to patients without clinically significant hepatic or renal dysfunction. For patients with these conditions, further information on hold time adjustment can be found in the individual references.

Bridging Therapy

The decision to use bridging therapy prior to a bedside procedure must be individualized and take into account

TABLE 2. **Summary of Periprocedural Management of Antiplatelet and Anticoagulant Agents for Paracentesis, Thoracentesis, and Lumbar Puncture, Stratified by Referenced Guidelines (continued)**

	Paracentesis and thoracentesis		Lumbar puncture	
	Recommended hold time prior to procedure[a]	**Recommended restart time after procedure[a,b]**	**Recommended hold time prior to procedure[a]**	**Recommended restart time after procedure[a,b]**
Unfractionated heparin infusion	Continue[2,10] 4 h[3] 4-6 h[5c]	After 6 h[3]	Continue[2] 4 h[3,4] 4-6 h[2,7,8] 6 h[9]	After 1 h[4,7] After 2 h (after 24 h if traumatic)[9] After 24 h[3]
Fondaparinux				
Prophylactic dosing	Continue[3f] 36 h[3g]	After 6-12 h[3]	36 h[3,7]	After 6-12 h[3,7]
Therapeutic dosing	48 h[3]	After 6-12 h[3]	48 h[3] Avoid LP[7]	After 6-12 h[3] Avoid LP[7]
Either	Continue[2,10] 24 h[5c]	Not applicable Not available	Continue[2] 48 h[4]	After 48 h[4]
Argatroban	Continue[2,10] 4 h[3] 48 h[5c]	After 6 h[3]	Continue[2] 4 h[3,4]	After 1 h[4] After 48-72 h[3]
Dabigatran	Continue[2,3f,10] ≥24 h[11d] 24-48 h[3g] ≥48 h[5c,11c]	After 6 h[3] Next day[11d] After 48-72 h[11c]	Continue[2] ≥48 h[11] 48-72 h[3,7] 72 h[8] 4 d[9]	After 6 h[7,8] After 24 h[9] After 48-72 h[3,11]
Rivaroxaban	Continue[2,3f,10] ≥24 h[5c,11d] ≥48 h[3g,11c]	After 6 h[3] Next day[11d] After 48-72 h[11c]	Continue[2] 24 h[7] 24-48 h[3] 24-72 h[4] ≥48 h[11] 72 h[8,9]	After 6 h[7,8] After 24 h[4,9] After 48-72 h[3,11]
Apixaban	Continue[2,3f,10] ≥24 h[5c,11d] 24-48 h[3g] ≥48 h[11c]	After 6 h[3] Next day[11d] After 48-72 h[11c]	Continue[2] 24 h (5 mg/d dose)[7] 24-48 h (20 mg/d dose)[7] 24-48 h[3] ≥48 h[11] 72 h[8,9]	After 6 h[8] After 6 h (5 mg/d dose)[7] After 6-24 h (20 mg/d dose)[7] After 24 h[9] After 48-72 h[3,11]

[a]For patients with clinically significant renal dysfunction, please see individual references for periprocedural hold and restart times.

[b]Assuming postprocedure hemostasis has been achieved.

[c]Specific to thoracentesis.

[d]Specific to paracentesis.

[e]Patient-specific bleeding risk factors include, but are not limited to, hypertension, abnormal renal function, abnormal hepatic function, prior stroke, history of major bleeding (especially within the preceding 3 months), and bleeding history with a similar procedure.

[f]For patients with high risk of thrombosis, consider continuing anticoagulation.

[g]For patients with low risk of thrombosis, consider either continuing anticoagulation or holding anticoagulation prior to the procedure for the duration listed.

Abbreviations: INR, international normalized ratio; LMWH, low molecular weight heparin; LP, lumbar puncture.

patient-specific factors. However, there is mounting evidence that bridging therapy is associated with higher risk of bleeding with no difference in the risk of thromboembolic events.[2,3,14] If the decision has been made to use bridging therapy with a heparin infusion prior to a bedside procedure, recommendations for hold and restart times can be found in Table 2.

Resuming Therapy

Another key consideration for procedures, especially those associated with a higher risk of bleeding, such as LP, is when to restart medications that have been held prior to the procedure. Table 2 provides a summary of the recommended postprocedural restart times for a variety of agents.

Other Considerations

Some guidelines referenced in this article are based on data collected on procedures performed by interventional radiologists, which may or may not accurately reflect the bleeding risks of bedside procedures performed by hospitalists. In the case of LP, we included some regional anesthesia and pain procedure guidelines based on the assumption that certain procedures are analogous to LP and associated with similar bleeding risks. Some of the guidelines referenced do

not provide specific periprocedural INR and platelet thresholds (reported as "No threshold" in Table 1), instead offering statements that elevated INR and thrombocytopenia are not contraindications to bedside procedures and periprocedural transfusion of blood products is generally not recommended, based on the overall low risk of bleeding and lack of evidence for the efficacy of interventions intended to improve INR values and platelet counts in these situations. Patients undergoing paracentesis, thoracentesis, or LP may be on multiple antithrombotic agents, such as dual antiplatelet therapy. There are limited guidelines and studies on how to manage these agents in the periprocedural context; however, one guideline recommends continuing dual antiplatelet therapy for paracentesis, thoracentesis, and LP in patients who have cardiac stents.[2] There are also limited guidelines on how to handle patients on simultaneous antiplatelet and anticoagulant therapy.

PARACENTESIS

Paracentesis is a common procedure that can be performed safely at the bedside. The overall rate of serious complications is low (1%-2%), with severe hemorrhage accounting for the majority of those complications (0.97%).[15] Bleeding usually occurs from puncture of an abdominal wall vein, a mesenteric varix, or an inferior epigastric artery. Certain techniques may help to mitigate serious bleeding, including the use of ultrasound to avoid overlying vessels. Paracentesis is frequently performed in patients with cirrhosis, a population at increased risk for coagulopathy, although INR and platelet counts may not reflect aggregate bleeding risk in patients with cirrhosis. The American Association for the Study of Liver Diseases released new guidelines in 2021, stating that elevated prothrombin time or thrombocytopenia is not a contraindication to paracentesis.[6] The most liberal guidelines for patients without chronic liver disease suggest correcting to an INR of 2.0 to 3.0, with multiple societies suggesting that a platelet count as low as 20,000/μL is safe.[2,3] As shown in Table 2, most guidelines recommend continuation of antiplatelet agents such as aspirin and thienopyridines (eg, clopidogrel, prasugrel), whereas recommendations vary regarding continuation of anticoagulant agents.

THORACENTESIS

Akin to paracentesis, thoracentesis is generally considered to be a safe bedside procedure, with an incidence of thoracentesis-associated bleeding of less than 1%.[15] Certain techniques may help to mitigate serious bleeding, including the insertion of the needle over the superior aspect of the rib in an effort to avoid the intercostal neurovascular bundle, which runs along the inferior aspect of each rib. Various clinical societies have proposed INR and platelet thresholds at which the risk of bleeding from thoracentesis is thought to be acceptable. The most liberal guidelines include a target INR of 2.0 to 3.0, although one group recommended an INR of <1.5.[2,5] Thoracentesis is commonly performed in patients with cirrhosis who develop hepatic hydrothorax. In this population, the Society of Interventional Radiology (SIR) guidelines state that there is no INR threshold that necessitates reversal strategies prior to the procedure.[2] For platelet count, there are multiple recommendations for greater than 20,000/μL and one for greater than 50,000/μL.[2,3,5] The recommendations for continuation or suspension of antiplatelet and anticoagulant medications prior to thoracentesis are similar to those for paracentesis. In general, continuing antiplatelet agents is felt to be safe, whereas there are mixed recommendations for anticoagulants, as described further in Table 2.

LUMBAR PUNCTURE

Compared to thoracentesis and paracentesis, LP is generally considered to be a higher-risk procedure owing to the rare possibility of spinal hematoma with associated neurologic compromise. In one retrospective review of more than 49,000 patients without coagulopathy who underwent LP, the risk for developing a spinal hematoma by 30 days post procedure was 0.20%.[16] Certain techniques may help to mitigate serious bleeding, including the use of image guidance in patients with large body habitus or those with difficult anatomy. Compared with paracentesis and thoracentesis, guideline recommendations for safe INR and platelet thresholds in patients undergoing LP are based on a more limited body of evidence. Guidelines also suggest a target INR of anywhere from ≤1.5 to the most liberal suggestion of 2.0 to 3.0.[2-4] The SIR guidelines categorize LP as a low–bleeding risk procedure, with a platelet threshold of 20,000/μL but note that most other societies and guidelines regard LP as a high–bleeding risk procedure with more conservative platelet thresholds.[2] The Association of British Neurologists (ABN), however, allows platelets to be 40,000/μL or greater than 20,000/μL with an additional risk-benefit discussion.[7] In contrast to paracentesis and thoracentesis, recommendations regarding hold times of antithrombotic medications prior to LP are more variable and sometimes more conservative. For example, some guidelines indicate that the thienopyridines can be continued, whereas others recommend holding them for up to 1 week prior to LP.[2,4,7]

GAPS IN KNOWLEDGE

A theme throughout the recent literature and recommendations from clinical societies is that it is uncommon for there to be one unifying recommendation for every situation, especially regarding LP. Recent guidelines remain largely based on studies that are decades old. With bedside ultrasound becoming more accessible and established in daily practice, the risk of bleeding has been decreasing, potentially making periprocedural coagulopathies and antithrombotic agents less of a concern. For example, in a retrospective study of 69,859 paracenteses, ultrasound guidance reduced the risk of bleeding complications by 68%, an odds ratio of 0.32 (95% CI, 0.25-0.41).[17] More research is needed to assess procedural bleeding risks in the context of current practice standards. This article focuses on a subset of bedside procedures most commonly performed by hospitalists. Similar references for other common bedside procedures, such as arthrocentesis, central venous catheter, and arterial line placement, would be helpful.

Finally, this article does not capture such nuances as needle gauge, operator experience, availability of (and comfort with) ultrasound, and variations in patient anatomy, all of which are factors that can contribute to the complexities and risks of these bedside procedures.

CONCLUSION

Although not every internal medicine physician performs bedside procedures in their practice, it is vital that all understand the cognitive aspects of common bedside procedures. This necessitates the understanding of periprocedural risks and possible complications and applying that to individual patients. Correcting coagulopathy and stopping or reversing antithrombotic agents are mitigation strategies that are associated with risk. It is therefore important to understand when coagulopathy should be corrected and when antithrombotic agents should be held and for how long. With multiple existing and sometimes conflicting guidelines regarding periprocedural management of coagulopathy and antithrombotic agents, we hope that providing consolidated tables with this information will increase efficiency, aid in risk-benefit discussions between patients and care teams, and enhance patient safety.

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