

Risk of Procedural Hemorrhage



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Patients who are critically ill and hospitalized often require invasive procedures as a part of their medical care. Each procedure carries a unique set of risks and associated complications, but common to all of them is the risk of hemorrhage. Central venous catheterization, arterial catheterization, paracentesis, thoracentesis, tube thoracostomy, and lumbar puncture constitute a majority of the procedures performed in patients who are hospitalized. In this article, the authors will discuss the risk factors for bleeding complications from each of these procedures and methods to minimize risk. Physicians often correct coagulopathy prior to procedures to decrease bleeding risk, but there is minimal evidence to support this practice.

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Invasive procedures are often part of the care plan for patients who are critically ill; therefore, operators must be familiar with indications, anticipated risks, and possible complications to establish informed consent and to perform the procedures competently. Common to most procedures is the risk of hemorrhage. Bleeding is associated with both short- and long-term morbidity and mortality, leading to increased length of hospitalization and costs.¹ There are several patient-specific factors that may influence risk of hemorrhage, including decreased ability to achieve hemostasis because of intrinsic or medication-related coagulation abnormalities, comorbidities such as renal disease, and abnormal anatomy. Several provider-related factors also relate to the risk of hemorrhage, such as inadequate procedural training, number of needle passes during a procedure, and the use of ultrasonography. The combination of these

factors leads to a unique risk profile for each patient. On top of this, consideration must be given to both the utility and risk associated with corrective interventions commonly used prior to procedures, such as transfusions in patients with hemostasis disorders. This review will focus on hemorrhagic risk for the more commonly performed critical care procedures (Table 1)²⁻¹⁷ with a special focus on the use of periprocedural fresh frozen plasma (FFP) and platelet transfusions.

Central Venous Catheterization

The use of central venous catheters (CVCs) is widespread in patients who are critically ill, with more than 5 million catheters inserted annually in the United States.² It is estimated that complications of central venous catheterization occur in up to 15% of patients, although with improvement in insertion techniques and the widespread use of ultrasound guidance this rate has been

ABBREVIATIONS: CVC = central venous catheter; FFP = fresh frozen plasma; INR = international normalized ratio; LP = lumbar puncture; PCC = prothrombin complex concentrate; PT = prothrombin time; PTT = partial thromboplastin time; TRALI = transfusion-related acute lung injury

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TABLE 1] Risk of Hemorrhagic Complications by Procedure Type

Procedure	No. of Procedures Annually	Bleeding Risk	Bleeding Risk Factors	Recommendations to Reduce Bleeding Risk
Central venous catheterization ²⁻⁴	5 million	0.5%-1.6%	<ul style="list-style-type: none"> ■ Anatomical abnormalities ■ No. of needle passes ■ Arterial puncture ■ Lack of operator experience ■ Lack of ultrasound guidance 	<ul style="list-style-type: none"> ■ Experienced operator ■ Real-time ultrasound guidance ■ Use of small-bore catheter if possible
Internal jugular		< 0.1%-2.2%		
Subclavian		0.4%-2.1%		<ul style="list-style-type: none"> ■ Lateral approach with axillary entry point to allow compressibility
Femoral		3.8%-4.4%		
Arterial catheterization ⁵	8 million	1.8%-2.6%	<ul style="list-style-type: none"> ■ Number of attempts ■ Lack of ultrasound guidance ■ Femoral artery: high entry site 	<ul style="list-style-type: none"> ■ Experienced operator ■ Real-time ultrasound guidance ■ Use of small-bore catheter
Thoracentesis ⁶⁻⁸	178,000	< 1%	<ul style="list-style-type: none"> ■ Renal disease ■ Small pleural effusion ■ Obesity ■ Complicated pleural space ■ Suboptimal patient position ■ Lack of operator experience ■ Lack of ultrasound guidance ■ Large-volume drainage 	<ul style="list-style-type: none"> ■ Experienced operator ■ Use of ultrasound guidance ■ Knowledge of chest wall anatomy ■ Entry site within safe zone (50%-70% of the way down the intercostal space)
Tube thoracostomy ^{9,10}	> 1 million	0.2%-1.4%		
Paracentesis ^{7,11-14}	150,000	0%-0.97%	<ul style="list-style-type: none"> ■ Renal disease ■ Therapeutic paracentesis ■ Lack of operator experience ■ Lack of ultrasound guidance 	<ul style="list-style-type: none"> ■ Experienced operator ■ Use of ultrasound guidance ■ Awareness of location of abdominal wall vessels
Lumbar puncture ¹⁵⁻¹⁷	400,000	< 0.1%	<ul style="list-style-type: none"> ■ CNS disease ■ Rapidly decreasing platelet count ■ Multiple procedural attempts ■ Traumatic lumbar puncture ■ Abnormal anatomy ■ Obesity 	<ul style="list-style-type: none"> ■ Experienced operator ■ Image guidance in patients at high risk ■ Close postprocedural monitoring for early signs of bleeding

reported at 4.6%.^{2,3,18} The risk of any bleeding complication ranges from 0.5% to 1.6%.¹⁹ These complications may manifest as insertional site bleeding, subcutaneous hematoma, mediastinal or retroperitoneal hematoma, or hemothorax. A database analysis of 16,721 CVC placements showed an incidence rate of 0.09 (per 1,000 catheter days) for severe bleeding

complications, typically defined as a decrease in hemoglobin requiring transfusion or causing hemodynamic instability.²⁰

Arterial puncture occurs in 3% to 15% of CVC procedures, which, if unrecognized, can lead to severe hemorrhage and neurologic complications.² Hematoma

and arterial puncture vary by site of line insertion, occurring more commonly with femoral catheterization than in internal jugular or subclavian sites.² The complications associated with arterial needle puncture can be exacerbated if the artery is dilated and an indwelling catheter is inserted. Accordingly, it is recommended that confirmation of venous, rather than arterial, puncture be established before dilation is performed. This can be done with the use of real-time ultrasonography, transduction of the cannulated vessel prior to dilation, manometry, pressure waveform analysis, or venous blood gas analysis.⁴

Strategies to reduce the risk of mechanical complications of central line placement include recognition of risk factors such as prior surgery at a site, assistance of a more experienced operator, and use of real-time ultrasound guidance.² Sznajder et al³ demonstrated that a physician who has performed more than 50 procedures is one-half as likely to have a mechanical complication than is a physician who has performed fewer than 50. Additionally, the number of insertion attempts is associated with increasing risk.^{21,22} A recent systematic review showed that the use of ultrasound guidance in internal jugular catheter placement reduced the number of arterial punctures by 72% and hematoma formation by 73%.²³ Ultrasound guidance for subclavian catheter placement also significantly decreases the incidence of arterial puncture, hematoma formation, and hemothorax.²⁴ Studies of ultrasound-guided vs landmark technique show that a possible additional benefit of real-time ultrasound guidance for subclavian catheterization is the ability to move the site of vein entry more lateral (ie, the axillary vein) and, therefore, to a more compressible site should bleeding occur.²⁵ A meta-analysis showed that ultrasound guidance in femoral vein catheterization has not been shown to decrease bleeding risk but increases first-attempt success rate and decreases the overall complication rate.^{26,27} After the data for all three insertion sites has been pooled, the use of real-time ultrasound guidance significantly reduces the risk of arterial puncture, hematoma, and hemothorax.²⁸

There is minimal evidence to support routine prophylactic platelet or plasma transfusions to decrease bleeding risk prior to central line placement in patients with mild to moderate hemostasis disorders (international normalized ratio [INR] of 1.5 to 3 or platelet count of 25,000 to 50,000/ μ L). Two prospective studies examining CVC placement in patients with an INR \geq 1.5 or platelet count $<$ 50,000/ μ L showed

no association with bleeding complications.^{29,30} A large retrospective study examining the risk factors for bleeding due to CVC insertion also showed no association between hemorrhage and abnormal coagulation tests in 1,737 consecutive line insertions.¹⁹ An increased risk for bleeding complications with large-bore (11.5-13 F) catheters is described, but in a study of the placement of large-bore tunneled CVCs in patients with a platelet count between 25,000 and 50,000/ μ L or an INR of 1.5 to 2, there was no increase in bleeding complications.^{19,31} There is not a definitive cutoff value for CVC placement in the setting of thrombocytopenia, with some studies showing that a platelet count $<$ 50,000/ μ L is associated with mild bleeding complications (such as oozing at the insertion site), and other studies concluding that CVCs can safely be placed when the platelet count is \geq 20,000/ μ L.^{32,33} In a prospective study in patients with liver disease with a median INR of 2.4 and platelet count of 81,000/ μ L, there was no increase in major bleeding complications.³⁴ Additionally, no increased risk of major bleeding events has been observed in patients with cancer with hemostasis disorders.³⁵

The summary evidence available at this time indicates that CVC placement carries similar risk in patients with and those without hemostasis abnormalities. Accordingly, we recommend the following strategies for CVC placement to minimize risk of bleeding: (1) presence of an experienced operator, (2) use of real-time ultrasound guidance for all CVC placement, (3) use of a lateral approach to subclavian vein cannulation with axillary vein entry to allow vessel compression, (4) avoidance of routine prophylactic transfusions in mild to moderate hemostasis disorders.

Arterial Catheterization

An estimated 8 million arterial catheters are placed annually in the United States for hemodynamic and blood gas monitoring.⁵ The most common site of placement is the radial artery, followed by femoral, axillary, brachial, and dorsalis pedis sites. A review of the literature from 1978 to 2001 showed no difference in bleeding complications by site.⁵ In a study of 4,932 medical and surgical patients in the ICU, the risk of bleeding was between 1.8% and 2.6%.³⁶ Bleeding complications are often limited to oozing or hematoma formation. The development of a hematoma may increase the risk of vascular occlusion and ischemia. Femoral catheterization also carries the risk of retroperitoneal hematoma formation,

with higher femoral artery puncture increasing this risk.³⁷

The use of ultrasound guidance significantly reduces the overall complication rate in both radial and femoral arterial catheterization. The relative risk of hematoma formation is decreased by 86% when ultrasonography used in radial artery catheterization.³⁸ In the cardiology literature, the use of ultrasonography decreases the overall complication rate of femoral artery catheterization, including decreases in the risk of hematoma (relative risk, 0.51; $P = .14$), and improves the likelihood of first-pass success by 42%.³⁹

There are no data regarding the bleeding risk of arterial catheterization in patients with abnormal hemostasis who are critically ill. The cardiology literature suggests that arterial access carries no increased risk of bleeding with mild elevations in INR, particularly for the radial approach.^{40,41} In a small, observational study of arterial puncture for endovascular procedures, there was no difference in bleeding complications in patients with an INR of 2.3 than in patients with an INR of 1.1.⁴²

Thoracentesis

It is estimated that 178,000 thoracenteses are performed annually in the United States.⁶ The reported incidence of bleeding associated with thoracentesis is $< 1\%$.⁷ Given the rarity of this complication, there is minimal evidence describing the risk factors for bleeding. One observational study showed that renal disease, defined as a creatinine level > 6 mg/dL, may increase the risk of hemorrhagic complications.⁴³ Traditionally, coagulopathy and thrombocytopenia are implicated as risk factors. Other factors that increase the overall complication rate for thoracentesis include small effusions, obesity, complicated effusions in the pleural space, suboptimal patient positioning, lack of operator experience, lack of ultrasonography use, and large-volume drainage.⁴⁴

The strategies to decrease the risk of thoracentesis are most commonly examined in the context of reducing the rates of pneumothorax. There is much less evidence regarding reduction of hemorrhagic complications. One strategy for risk reduction may include increasing provider education to focus on improved understanding of the pleural and chest wall anatomy. For example, Wraight et al⁴⁵ described remarkable variation in the anatomic location of the intercostal neurovascular bundle on cadavers. The neurovascular bundle was not always tucked under the superior rib in the subcostal groove, as

is classically taught. Particularly noteworthy was the finding of a total of 83 inferior collateral intercostal arteries of a total of 148 interspaces evaluated. These inferior collateral intercostal arteries were not in the subcostal groove 90% of the time. On the basis of these findings, the authors recommended a safe zone between 50% to 70% of the way down an intercostal space to avoid the varyingly positioned superior intercostal neurovascular bundle and the inferior collateral artery.⁴⁵ This recommendation should apply to both thoracentesis and tube thoracostomy.

Additional cadaveric and imaging studies have also demonstrated variation in the course of the posterior intercostal artery but reveal that, in general, its location is closer to the undersurface of the rib as it travels more laterally from the spine.⁴⁶⁻⁴⁹ Therefore, in addition to familiarity with the aforementioned safe zone, these cadaveric and imaging studies suggest choosing a location at least 6 cm lateral from midline when performing a posterior thoracentesis, although this has not been studied in clinical practice. Knowledge of an individual's chest wall and pleural anatomy can be gained by the use of ultrasound guidance, which decreases the overall complication rate of thoracentesis.⁵⁰ A review of 19,339 thoracenteses found a 38.7% reduction in the likelihood of hemorrhage when using ultrasound guidance ($P = .071$).⁵¹

Many studies have examined coagulopathy and the use of prophylactic blood product transfusions to reduce the bleeding risk from thoracentesis. McVay and Toy⁴³ found no increased bleeding in patients who were undergoing thoracentesis and had mild to moderate coagulopathy defined as prothrombin time (PT) or partial thromboplastin time (PTT) up to twice the midpoint normal range or mild (50,000 to 99,000/ μ L) to moderate (25,000 to 49,000/ μ L) thrombocytopenia. A retrospective review of 1,076 ultrasound-guided thoracenteses showed no bleeding complications despite a preprocedural INR > 2.0 in 139 cases and platelet count $< 50,000/\mu$ L in 58 cases.⁵² A cohort study of 9,320 thoracenteses also showed no associations between bleeding and INR, PTT, or platelet counts.⁸ Puchalski et al⁵³ defined potential risk factors for bleeding as INR > 1.5 , platelet count $< 50,000/\mu$ L, therapeutic low-molecular-weight heparin or unfractionated heparin, and renal disease defined as a creatinine level > 1.5 mg/dL or use of renal replacement therapy. In their observational study in 312 patients, 42% of whom had a potential risk factor for bleeding, there was no difference in

pre- and postprocedural hematocrit levels.⁵³ Similarly, a retrospective review of 1,009 ultrasound-guided procedures in patients with an INR > 1.6 or platelet count < 50,000/ μ L showed no difference in bleeding complications in patients who had received FFP or platelets prior to the procedure compared with those who had not.⁹ In a retrospective study in 100 patients with hematologic malignancy who were undergoing thoracentesis, hemothorax occurred only 2% of the time, with none occurring in patients with abnormal clotting test results.¹⁰ The observational data available at this time do not support the routine use of prophylactic transfusions prior to thoracentesis to correct a mild to moderately abnormal INR or platelet count.

Tube Thoracostomy

Chest tube insertion (tube thoracostomy) is also a common procedure performed in patients who are critically ill, with more than 1 million placed annually.⁵⁴ Mechanical complications including bleeding are rare, occurring in 0.2% of small-bore drains (< 16 F) and 1.4% of large-bore drains (> 20 F).⁵⁵ Risk factors and strategies to reduce complications are similar to those described for thoracentesis, including the use of ultrasound guidance for tube placement. There are minimal data regarding chest tube insertion in patients with abnormal hemostasis. Some guidelines recommend delaying chest drain insertion until the INR is < 1.5 if clinical circumstances allow, although there have not been high-quality trials to support this recommendation.⁵⁵ In a randomized trial of prophylactic FFP prior to chest tube insertion, no difference was found in bleeding rates in patients with mild coagulopathy receiving prophylactic FFP and those who were not.⁵⁶ Two studies examined chest tube placement in patients receiving clopidogrel and showed no increase in the incidence of bleeding for those patients when chest tubes were inserted in the midaxillary line with ultrasound guidance.^{57,58} To minimize the bleeding risk for both chest tube insertion and thoracentesis, we recommend that providers performing the procedure have sufficient experience, use ultrasound guidance, and be familiar with the chest wall anatomy, particularly the variation in the path of the intercostal artery.

Paracentesis

At least 150,000 paracenteses are performed annually in the United States.⁵⁹ Paracentesis is regarded as a safe procedure, with an overall serious complication

rate of approximately 1% to 2% and a severe hemorrhage rate of 0% to 0.97%.^{11-14,43,60,61} However, bleeding complications, when they occur, can cause substantial morbidity.^{12,60}

Hemorrhagic complications from paracentesis typically occur as a result of needle puncture of a superficial abdominal wall vein, mesenteric varices, or the inferior epigastric artery. A systematic review identified three types of hemorrhagic complications associated with paracentesis: abdominal wall hematomas (52%), hemoperitoneum (41%), and pseudoaneurysm (7%).¹² In this review, renal disease (creatinine level > 1.2 mg/dL or glomerular filtration rate < 60) was present in 70% of patients with bleeding complications. Other studies have also found a correlation with renal disease and increased bleeding risk, with the definition of renal disease varying widely by study.^{43,61} Its presence is a marker for a higher risk procedure that should be performed by an experienced operator.

In a prospective study of 515 paracenteses, therapeutic paracentesis was associated with a slightly higher risk of complication than was diagnostic paracentesis. There was a trend toward an increased complication rate in patients with platelet count < 50,000/ μ L, alcoholic cirrhosis, and advanced liver disease.¹³ The midline approach is traditionally considered the least likely to cause hemorrhagic complications because it is a relatively avascular region; however, there have been rare reports of hemorrhage with midline procedures.¹² As with the other procedures described, operator experience and ultrasound guidance are additional ways to decrease complication rates. A retrospective review of 69,859 paracenteses showed a 0.8% rate of any bleeding complications. This risk was decreased by 68% when ultrasound guidance was used.¹ The use of ultrasonography with Doppler to evaluate for abdominal wall vessels has not been studied, but it is an additional tool that may further reduce bleeding risk. The authors of a prospective study found no bleeding complications when the operators had adequate training, which they recommended to be 10 supervised procedures.⁶⁰

Paracentesis is reported to be safe in the setting of coagulopathy and thrombocytopenia. In a review of 608 procedures, McVay and Toy⁴³ showed no increase in hemorrhagic complications of paracentesis in the setting of mild to moderate coagulopathy. Another retrospective study of 4,729 paracenteses had a 0.19% rate of severe hemorrhage. The authors found no increase in risk related to operator experience,

elevated INR, or thrombocytopenia.⁶¹ A prospective study of 1,100 large-volume paracenteses had no hemorrhagic complications in patients with a mean INR of 1.7 (as high as 8.5) and a mean platelet count of 50,400/ μ L (as low as 19,000/ μ L).⁶⁰ Because of the low rate of bleeding complications, the American Association for the Study of Liver Diseases recommends against the prophylactic use of FFP or platelets prior to paracentesis.⁶² On the basis of the available evidence, the presence of an experienced operator and use of ultrasonography are the best practices to decrease the hemorrhagic risk of paracentesis.

Lumbar Puncture

Approximately 400,000 lumbar punctures (LPs) are performed in the United States annually.¹⁵ The risk of bleeding complications due to LP is small but can carry devastating neurologic consequences. Accordingly, LP is considered a higher risk procedure than are CVC placement, thoracentesis, tube thoracostomy, or paracentesis regarding bleeding complications. Much of the literature surrounding this issue pertains to the risks associated with central neuraxial anesthesia, although there are some retrospective series that focus on LP.

The risk of hematoma following epidural anesthesia is 1 in 150,000 and following spinal anesthesia is 1 in 220,000.¹⁶ The risk with LPs is probably similar, though there are no reliable published estimates. Three mechanisms of epidural hematomas have been described: rupture of epidural veins, rupture of epidural arteries, and hemorrhage from vascular abnormalities.¹⁷

Potential risk factors for hemorrhagic complications include CNS disease; rapidly decreasing platelet counts; disseminated intravascular coagulation; multiple attempts or a traumatic LP; and difficult anatomy such as ankylosing spondylitis, spinal stenosis, or obesity.^{16,17,63} In cases that are anticipated to be more difficult, an experienced operator or image guidance (eg, real-time fluoroscopy or ultrasound guidance) can be used to decrease risk.

A review of a series of studies involving both adult and pediatric populations showed that 39 LPs were performed at a platelet count < 10,000/ μ L, 204 at counts between 11,000 and 20,000/ μ L, 817 between 21,000 and 50,000/ μ L, and 858 between 51 and 100,000/ μ L. There were no bleeding complications in any of the studies.¹⁶ A separate review showed a correlation between an abnormal coagulation status and hemorrhagic complications of LP, but it is

unclear whether other risk factors were present and what constituted an abnormal coagulation status.⁶³ Given the paucity of data regarding optimal platelet levels for LP and the potential risks of hematoma, consensus guidelines recommend platelet count of 50,000/ μ L or greater, with clinical judgment guiding practice when platelet counts are between 20,000 and 49,000/ μ L.¹⁶

In a review of 613 patients with spinal hematomas, the majority of which were spontaneous, 16.9% of patients were receiving anticoagulation. A bleeding diathesis, including pharmaceutical anticoagulation, in combination with LP was seen in 6% of circumstances. LP or neuraxial anesthesia without a hemorrhagic diathesis accounted for 4.2% of the cases.¹⁷ A retrospective review showed a correlation between starting anticoagulation within 1 hour of the procedure and the risk of major complication.⁶⁴ Based on expert opinion and observational data, the recommendations suggest that therapeutic systemic anticoagulation be held prior to spinal anesthesia or LP.⁶⁵ In 2013, the United States Food and Drug Administration issued a safety communication recommending that neuraxial procedures be delayed 12 hours after prophylactic low-molecular-weight heparin is administered and 24 hours after therapeutic administration.⁶⁶

Given the serious consequence of bleeding after LP, a more conservative approach to patients with hemostasis disorders must be taken. Vigilance on the part of the provider for postprocedural signs of bleeding, such as back pain or new neurologic symptoms, is necessary for immediate recognition and treatment of bleeding if it does occur.

Periprocedural Use of Antithrombotic Medications

Periprocedural management of antithrombotic medications is a challenge often faced by physicians performing invasive procedures. The potential for increased risk of bleeding while using these medications must be weighed against the risk of thrombotic events and delayed diagnostic tests and treatment when they are temporarily discontinued. These risks vary by procedure type and individual patient comorbidities. To help determine the risk of stopping antithrombotic medications, expert consensus guidelines provide risk stratification based on the indications for anticoagulant or antiplatelet therapy.⁶⁷⁻⁶⁹ As discussed, most invasive procedures performed in the ICU are considered to have

a low risk of hemorrhage.^{65,68} In addition to the risk of hemorrhage associated with a given procedure, one must consider the potential consequences associated with a procedure-related hemorrhage. For example, though the risk of hemorrhage associated with LP is low, the consequences of bleeding around the spinal cord may be clinically devastating.

For low-risk procedures, it is often possible to continue anticoagulant and antiplatelet medications without increased bleeding risk. The use of aspirin or nonsteroidal antiinflammatory drugs is not associated with increased bleeding risk, even in the case of LP.⁷⁰ Several small studies have shown that thoracentesis or small-bore chest tube placement is safe in patients receiving clopidogrel.^{57,58,71} Direct oral anticoagulants, such as inhibitors of thrombin or factor Xa, are increasingly being used in place of vitamin K antagonists. At this time, recommendations for periprocedural management of these medications are based on expert opinion. These recommendations include holding direct oral anticoagulants for a 24-hour window before and after low-risk procedures and 5 days prior to high-risk procedures.⁷² More research is needed to validate these recommendations.

Use of FFP and Platelet Transfusions Prior to Procedures

Physicians have increasingly turned to prophylactic FFP and platelet transfusion to help mitigate the risk of procedural hemorrhage, but there is little evidence to support this practice. In 2006, approximately 4 million units of FFP and 9 million units of platelets were transfused in the United States.⁵³ A prospective study of 1,923 ICU admissions showed that 15% of plasma transfusions were administered as preprocedural prophylaxis and 36% as prophylaxis without a planned procedure. In this study, more than 10% of patients in the ICU received a plasma transfusion during their hospital stay.⁷³ A prospective study of the factors associated with prophylactic FFP transfusion showed considerable variation in the practice of physicians regarding the decision to transfuse.⁷⁴

The laboratory tests that many physicians use to determine bleeding risk, such as PT, INR, and PTT, were not developed to assess this risk and have not been validated as accurate tools in this setting. PT and PTT were developed to assess for an inherited coagulopathy in bleeding patients, and INR was developed to monitor clotting in the setting of vitamin K

antagonists. They have not been validated to assess bleeding risk in patients who are not bleeding.⁷⁵ A systematic review of 24 observational studies and one randomized control trial examining the correlation of preprocedural coagulation tests and risk of bleeding showed insufficient data to support PT and INR as predictors of bleeding risk.⁷⁶

In addition, several studies have shown that in the case of mild to moderate coagulopathy, the laboratory measures of coagulation fail to improve significantly following transfusion. This was examined in a prospective study of the effect of FFP transfusions in patients with an INR of 1.1 to 1.85. In this study, only 0.8% of patients had normalization of the INR, and only 15% had improvement of at least halfway to normal.⁷⁷ A separate study showed that at an INR of 1.8, there is only a 50% chance that there will be any significant change after FFP transfusion.⁷⁸ An analysis of the effect of FFP transfusions administered in the emergency department also demonstrated the limited efficacy of FFP when the INR is in the mildly abnormal range. The authors found there was a change in the INR of 0.03 when the pretransfusion INR was < 2, 0.77 when the INR was 2 to 5, 2.14 when the INR was 9 to 12, and 4.63 when the INR was > 12.⁷⁹

Furthermore, transfusions of blood products are known to carry significant risks that must be considered (Table 2).⁸⁰⁻⁸³ Frozen plasma transfusions carry a risk of transfusion-related acute lung injury (TRALI) estimated

TABLE 2] Risks of Blood Product Transfusions

Risk	Approximate Incidence per Unit
Acute hemolysis	1:50,000 to 1:100,000
Anaphylaxis	1:30,000
Mismatch due to human error	1:6,000 to 1:20,000
Transfusion-associated lung injury ^a	1:12,000
Transfusion-associated circulatory overload	1:356
Infectious risks	
HIV	1:2.4 million
Hepatitis C	1:2 million
Hepatitis B	1:200,000
Bacterial	1:1 million leads to sepsis fatality

^aEstimated to occur in 5% to 8% of critically ill patients who undergo transfusion.^{80,81}

Sources: Baron,⁸² Toy et al,⁸³ and Rana et al.⁸⁶

at 1 per 12,000 units, anaphylaxis in 1 per 30,000 transfusions, and hemolysis in 1 per 50,000 units.⁵³ The incidence of TRALI in a review of 5,208 patients who were critically ill was 5.1%, which is higher than the incidence seen in other patient populations.⁸⁰ Plasma transfusions are associated with an increased risk of acute lung injury (OR, 2.32; 95% CI, 1.46-3.71).⁸⁴ Two studies showed an increased mortality (OR, 2.00; 95% CI, 1.11-3.59) when FFP was administered prophylactically in the absence of coagulopathy.⁸⁴ The incidence of transfusion-associated circulatory overload in patients in the ICU is reported at 1 in 356 units transfused, but some believe this to be underreported.^{85,86} A prospective study of transfusion-associated circulatory overload in patients in the ICU described a rate of 6%, with the volume of plasma transfused and rate of transfusions cited as significant risk factors.⁸⁷ Platelet transfusions also carry significant risk per platelet transfusion: 1 in 14 risk of febrile reaction, 1 in 50 risk of an allergic reaction, and 1 in 138,000 risk of TRALI.⁸⁸ The rate of alloimmunization to platelets is approximately 8%, making it important to avoid unnecessary transfusions, particularly in those likely to require platelet transfusions later (eg, patients with hematologic malignancies receiving chemotherapy with or without bone marrow transplantation).

At least 30% of patients in the ICU will have abnormal coagulation study results during their hospitalization, the majority of which will be mild to moderate.⁷⁵ Because many patients who are critically ill will undergo invasive procedures, their care providers will frequently face the question of the utility of prophylactic plasma or platelet transfusions. A randomized control trial in 81 patients who were critically ill and undergoing invasive procedures (central venous catheterizations, thoracenteses, percutaneous tracheostomies, and abscess or fluid drainage) with an INR of 1.5 to 2.2 (mean INR, 1.8) showed no difference in bleeding complications in those who underwent transfusion prophylactically and those who did not.⁵⁶ There is a growing body of evidence suggesting transfusions are administered too frequently.^{75,88-92} A caveat to this is that the majority of the evidence we have tends to be in patients with mild to moderate hemostasis disorders (INR < 3 or platelet count > 50,000/ μ L). We do not have sufficient evidence to guide practice when the abnormalities are more severe, but we know that risk of spontaneous hemorrhage significantly increases when the INR is > 4.5.⁹³ Therefore, providers must take into account the severity of coagulopathy when weighing the risk

of bleeding vs the risk of correcting that risk in patients undergoing invasive procedures.

Use of Prothrombin Complex Concentrates

Prothrombin complex concentrates (PCCs) are indicated for the reversal of life-threatening bleeding in patients receiving warfarin and are increasingly taking the place of FFP transfusion in these situations. The use of PCCs to reverse coagulopathy prior to invasive procedures has not been examined. Although PCCs can rapidly and effectively reduce INR, their use increases the risk of thromboembolic events twofold.⁹⁴ The increased risk of thromboembolic events is significant when compared with the rarity of bleeding complications associated with the procedures common to critical care; therefore, we do not recommend the use of PCCs as prophylaxis in patients who are not bleeding.

Conclusion

Bleeding complications secondary to commonly performed critical care procedures are rare but can be associated with significant morbidity and mortality. Operator experience, minimization of procedure attempts, and use of ultrasonography have all been shown to decrease the rate of complications. There is limited evidence to support the routine use of prophylactic FFP or platelet transfusions prior to procedures in patients who are not bleeding and have mild to moderate hemostasis disorders. At this time, many patients are likely exposed to blood products that provide them no benefit and carry potential risks.

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