Things We Do for No Reason™: Routine Correction of Elevated INR and Thrombocytopenia Prior to Paracentesis in Patients with Cirrhosis

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Inspired by the ABIM Foundation's Choosing Wisely® campaign, the "Things We Do for No Reason™" (TWDFNR) series reviews practices that have become common parts of hospital care but may provide little value to our patients. Practices reviewed in the TWDFNR series do not represent "black and white" conclusions or clinical practice standards but are meant as a starting place for research and active discussions among hospitalists and patients. We invite you to be part of that discussion.

CLINICAL SCENARIO

The hospitalist admits a 52-year-old man with alcoholic cirrhosis for tense ascites and altered mentation. Home medications include furosemide, spironolactone, lactulose, and rifaximin, but his family notes he ran out last week. Although afebrile and hemodynamically stable, the patient's coagulopathy, with an international normalized ratio (INR) of 2.3, and thrombocytopenia, with a platelet count of 37,000/μL, worries the hospitalist. The hospitalist wonders whether to transfuse fresh frozen plasma (FFP) and platelets prior to diagnostic paracentesis to reduce the risk of procedural bleeding.

WHY ROUTINELY DOING THIS MIGHT SEEM HELPFUL

Many patients undergoing paracentesis have severe liver disease and present with both thrombocytopenia and elevated INRs. While platelet count and INR serve as surrogate markers for bleeding risk in many settings, clinicians often extrapolate this concept to patients with cirrhosis. Many hospitalists routinely check INR and platelet count and administer FFP and platelets prior to diagnostic or therapeutic paracentesis to mitigate procedure-related bleeding risk. Some medical resources recommend this practice,[1] while case reports and personal experiences with bleeding in these patients create availability bias that influences perception of bleeding risk.[2] One recent study of patients with decompensated cirrhosis presenting to a US tertiary care center found that, of those receiving large-volume paracentesis, 22.2% received prophylactic FFP and 17.3% received prophylactic platelets before paracentesis.[3]

WHY ROUTINELY DOING THIS IS NOT HELPFUL

Advances in our understanding of coagulation in cirrhosis demonstrate neither INR nor platelet count accurately predict bleeding risk in this population. Additionally, evidence demonstrates the overall safety of paracentesis in cirrhosis—even in the presence of high INR and thrombocytopenia—and the lack of benefit from prophylactic transfusions with FFP or platelets.

Substantial evidence in patients with cirrhosis demonstrates that changes in coagulation and platelet function confer a "balanced coagulopathy" in which patients oscillate between hyper- and hypocoagulable states. In a cirrhotic liver, hepatic synthetic dysfunction results in a complex milieu through reduced production and plasma concentrations of both pro- and anticoagulant factors that can lead to either bleeding or clotting.[4] This "rebalancing" makes prothrombin time (PT) and INR unreliable indicators of bleeding or clotting risk. Similarly, in patients with cirrhosis, thrombocytopenia does not necessarily reflect impaired clotting ability. These patients experience an increase in production of von Willebrand Factor, which may compensate for low platelet counts by producing stronger platelet adhesion to collagen.[4] Unfortunately, we currently lack a reliable test or risk score to assess true bleeding risk in patients with cirrhosis.

Observational studies support these laboratory findings. Large case series consistently demonstrate no association between INR or platelet counts and bleeding risk in either diagnostic or therapeutic paracentesis, including large-volume paracentesis (See Appendix for a list of recent representative studies).[5-10] Moreover, prophylactic transfusion of FFP or platelets does not significantly reduce bleeding risk.

In a 1991 study by McVay et al, the researchers examined bleeding outcomes of 441 paracenteses performed on hospitalized patients.[11] Among patients who did not receive FFP prior to paracentesis, only one required a transfusion for procedure-related bleeding, an event rate of 0.25%. This single patient had a normal platelet count and an elevated PT to the same extent as 261 others who underwent paracentesis without complication. In a pooled analysis that included 391 paracenteses and 207 thoracenteses, the authors concluded

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neither PT nor platelet level predicted bleeding risk. Similarly, the largest published case series on this topic examined 4,729 paracenteses over a decade on a liver unit and found low rates of major bleeding (0.19%).[9] Furthermore, preprocedure INR or platelet count did not correlate with bleeding risk. The authors did not report preprocedure transfusion rates, but they noted transfusions occurred only "occasionally."

Subsequent observational studies have consistently revealed low bleeding risks even in settings of high coagulopathy prevalence. Grabau et al reviewed all large-volume paracenteses performed in a gastroenterology clinic over 7 years.[10] In over 1,100 procedures, no major bleeding events occurred despite 27% of patients having INR greater than 2.0 and 54% having platelet counts less than 50,000/μL. Kurup et al examined bleeding risk among 304 procedures performed on patients with platelet counts less than 50,000/μL referred to radiology for ultrasound-guided paracentesis.[7] Three bleeding events occurred, an overall event rate of 0.99%. They also found no association between preprocedure platelet count and bleeding risk.

In addition to observational data, one randomized, controlled trial evaluated the effects of FFP and platelet administration on bleeding risk among 60 patients with cirrhosis undergoing invasive procedures, including 19 paracenteses.[6] Enrollment criteria included INR greater than 1.8 and/or platelet count less than 50,000/μL. One hundred percent of patients randomized to the usual care control arm received platelets or FFP as compared to 17% in the thromboelastography (TEG)–guided transfusion strategy arm. TEG assesses the viscoelastic properties of evolving clot formation in whole blood. Only one patient, a patient in the control arm who received FFP, developed procedure-related bleeding. Although receiving many fewer transfusions, the TEG-guided group experienced no bleeding.

In the presence of multiple studies demonstrating lack of benefit from FFP and platelet transfusion, guidelines published by the American Association for the Study of Liver Disease (AASLD), the American Gastroenterological Association (AGA), and the Society of Interventional Radiology (SIR) acknowledge the inaccuracy of platelet count and INR in predicting bleeding risk.[12-14] Both AASLD and AGA recommend against routine transfusion of platelets and FFP prior to paracentesis.[12,13] SIR guidelines from 2019 recommend against using an INR threshold for low-risk procedures like paracentesis and lowered their recommended platelet transfusion threshold from less than 50,000/μL to less than 20,000/μL.[14] While we have limited safety data for paracentesis in patients with very low platelet counts, Kurup et al observed no bleeding events in the 19 patients in their cohort with platelets less than 20,000/μL undergoing ultrasound-guided paracentesis.[7]

In addition to lack of proven benefit, preprocedure transfusion exposes patients to objective risk. Transfusion-related acute lung injury and transfusion-associated circulatory overload develop at a rate of 0.48 and 3.8 per 100,000 components transfused, respectively.[15] FFP transfusions also risk anaphylactic reactions with incidence ranging from 1:18,000 to 1:172,000.[16] Platelets carry additional risk of bacterial contamination and resultant sepsis estimated at 1:5,000 to 1:8,000 per unit.[17] Volume expansion from transfusions may contribute to portal hypertension and increase risk of variceal bleeding in decompensated liver disease.

Finally, FFP and platelet transfusions carry a significant cost. Rowley et al estimated eliminating preprocedure transfusions over 2 years and 3,116 paracenteses saved their institution $816,000.[5] Furthermore, checking and correcting INR and thrombocytopenia can lead to procedural delay. Studies have demonstrated increased mortality from delaying paracentesis.[18]

WHEN IT IS HELPFUL

While most patients undergoing paracentesis have cirrhosis, patients without cirrhosis also undergo this procedure. Although several cited studies examined paracentesis among all-comers with ascites, our recommendations specifically apply to patients with ascites from cirrhosis.

Furthermore, although no paracentesis data in patients with severe coagulopathy (INR >2.5 or platelet count <20,000/μL) suggest periprocedural transfusion helps, we also lack data to prove it does not help.

Current recommendations from the AASLD suggest correcting coagulopathy in patients with clinically evident disseminated intravascular coagulation or hyperfibrinolysis prior to procedures.[12] While no clear guidance related to paracentesis exists on when to assess for these entities, we recommend evaluating for them only when the clinical situation otherwise merits doing so and not solely for the purpose of screening prior to paracentesis. Measuring fibrinogen before paracentesis to predict bleeding risk is an emerging concept, but it cannot be routinely recommended at this time.[13] Other factors that may play an important role in bleeding risk—ultrasound guidance, operator experience, and ability to avoid epigastric vessels and collateral veins—are beyond the scope of this article.

WHAT SHOULD BE DONE INSTEAD

Given that laboratory evaluations like INR and platelet count cannot predict which patients with cirrhosis will experience major bleeding complications after paracentesis and given that routinely transfusing FFP or platelets does not confer benefit and may cause serious harm, providers should avoid measuring INR or platelet count to prepare for paracentesis. Likewise, providers should avoid routinely transfusing FFP and platelets prior to paracentesis even in the presence of abnormal laboratory values because such values do not accurately reflect bleeding risk in patients with cirrhosis. Perform clinically indicated paracentesis without the delays that accompany unnecessary laboratory evaluations or transfusions.

RECOMMENDATIONS

Keep the following in mind with patients presenting with ascites from cirrhosis:

- Do not routinely use platelet count or INR when preparing for paracentesis, whether diagnostic or therapeutic, be-

cause no evidence-based "cutoff" for safe performance of paracentesis exists.
- Do not routinely transfuse FFP or platelets for prophylaxis prior to paracentesis in patients with cirrhosis.
- Reserve preprocedure transfusion of FFP or platelets for patients with disseminated intravascular coagulation, hyperfibrinolysis, or other indications for transfusion unrelated to procedural prophylaxis.

CONCLUSION

Case series representing diverse institutional experiences with thousands of patients consistently demonstrate that bleeding after paracentesis is rare (<1%), mortality from bleeding occurs very infrequently, and neither INR nor platelet counts predict bleeding risk during paracentesis in cirrhosis. These studies demonstrate that abandoning routine correction of coagulopathy does not lead to worse outcomes, can avoid potentially significant transfusion-related adverse events, and can save scarce resources.

Returning to our clinical scenario, the hospitalist should not transfuse FFP or platelets and should not delay the diagnostic paracentesis.

Do you think this is a low-value practice? Is this truly a "Thing We Do for No Reason™"? Share what you do in your practice and join in the conversation online by retweeting it on Twitter (#TWDFNR) and liking it on Facebook. We invite you to propose ideas for other "Things We Do for No Reason™" topics by emailing TWDFNR@hospitalmedicine.org.

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References

1. Shlamovitz G. Paracentesis. *Medscape*. 2018. Accessed April 16, 2019. https://emedicine.medscape.com/article/80944-overview
2. Tversky A, Kahneman D. Judgment under uncertainty: heuristics and biases. *Science*. 1974;185(4157):1124-1131. https://doi.org/10.1126/science.185.4157.1124
3. Barnhill M, Lee A, Montero A. Adherence rates to recommended guidelines for paracentesis in cirrhotic patients at a tertiary care center and associated complications. *Am J Gastroenterol*. 2017;112:S504.
4. Tripodi A, Primignani M, Mannucci PM, Caldwell SH. Changing concepts of cirrhotic coagulopathy. *Am J Gastroenterol*. 2017;112(2):274-281. https://doi.org/10.1038/ajg.2016.498
5. Rowley MW, Agarwal S, Seetharam AB, Hirsch KS. Real-time ultrasound-guided paracentesis by radiologists: near zero risk of hemorrhage without correction of coagulopathy. *J Vasc Interv Radiol*. 2019;30(2):259-264. https://doi.org/10.1016/j.jvir.2018.11.001
6. De Pietri L, Bianchini M, Montalti R, et al. Thrombelastography-guided blood product use before invasive procedures in cirrhosis with severe coagulopathy: a randomized, controlled trial. *Hepatology*. 2016;63(2):566-573. https://doi.org/10.1002/hep.28148
7. Kurup AN, Lekah A, Reardon ST, et al. Bleeding rate for ultrasound-guided paracentesis in thrombocytopenic patients. *J Ultrasound Med*. 2015;34(10):1833-1838. https://doi.org/10.7863/ultra.14.10034
8. De Gottardi A, Thévenot T, Spahr L, et al. Risk of complications after abdominal paracentesis in cirrhotic patients: a prospective study. *Clin Gastroenterol Hepatol*. 2009;7(8):906-909. https://doi.org/10.1016/j.cgh.2009.05.004
9. Pache I, Bilodeau M. Severe haemorrhage following abdominal paracentesis for ascites in patients with liver disease. *Aliment Pharmacol Ther*. 2005;21(5):525-529. https://doi.org/10.1111/j.1365-2036.2005.02387.x
10. Grabau CM, Crago SF, Hoff LK, et al. Performance standards for therapeutic abdominal paracentesis. *Hepatology*. 2004;40(2):484-488. https://doi.org/10.1002/hep.20317
11. McVay PA, Toy PT. Lack of increased bleeding after paracentesis and thoracentesis in patients with mild coagulation abnormalities. *Transfusion*. 1991;31(2):164-171. https://doi.org/10.1046/j.1537-2995.1991.31291142949.x
12. Runyon BA. AASLD Practice Guideline: Management of Adult Patients with Ascites Due to Cirrhosis: Update 2012. *The American Association for the Study of Liver Diseases;* 2012. Accessed April 16, 2019. https://www.aasld.org/sites/default/files/2019-06/141020_Guideline_Ascites_4UFb_2015.pdf
13. O'Leary JG, Greenberg CS, Patton HM, Caldwell SH. AGA clinical practice update: coagulation in cirrhosis. *Gastroenterology*. 2019;157(1):34-43.e1. https://doi.org/10.1053/j.gastro.2019.03.070
14. Patel IJ, Rahim S, Davidson JC, et al. 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. *J Vasc Interv Radiol*. 2019;30(8):1168-1184.e1. https://doi.org/10.1016/j.jvir.2019.04.017
15. Blumberg N, Heal JM, Gettins K, et al. An association between decreased cardiopulmonary complications (transfusion-related acute lung injury and transfusion-associated circulatory overload) and implementation of universal leukoreduction of blood transfusions. *Transfusion*. 2010;50(12):2738-2744. https://doi.org/10.1111/j.1537-2995.2010.02748.x
16. Pandey S, Vyas GN. Adverse effects of plasma transfusion. *Transfusion*. 2012;52(Suppl 1):65S-79S. https://doi.org/10.1111/j.1537-2995.2012.03663.x
17. Kleinman S, Reed W, Stassinopoulos A. A patient-oriented risk-benefit analysis of pathogen-inactivated blood components: application to apheresis platelets in the United States. *Transfusion*. 2013;53(7):1603-1618. https://doi.org/10.1111/j.1537-2995.2012.03928.x
18. Kim JJ, Tsukamoto MM, Mathur AK, et al. Delayed paracentesis is associated with increased in-hospital mortality in patients with spontaneous bacterial peritonitis. *Am J Gastroenterol*. 2014;109(9):1436-1442. https://doi.org/10.1038/ajg.2014.212