ADVANCES IN ENDOSCOPY

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Endoscopic Interventions in Patients with Thrombocytopenia



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G&H What is the minimum platelet count traditionally required before patients can undergo endoscopic procedures?

WR This question comes up often in cancer centers, where thrombocytopenia is a common problem, even for simple interventions such as biopsy. Unfortunately, there is not much guidance on this issue in the literature, and what guidance there is consists of doctors picking different numbers without much evidence to support them one way or the other. Many doctors frequently cite the University of Washington's work in graft-vs-host disease, in which 50,000/µL was chosen as the platelet cutoff; however, there was not much evidence supporting this number. Reviewing the literature shows that there is frequently a reluctance to perform diagnostic endoscopy, much less therapeutic endoscopy, in patients with less than 50,000 platelets/µL because it is thought that biopsies or other interventions are too risky. In addition, when a physician is asked to perform endoscopy for bleeding in a thrombocytopenic patient, there is frequently a presumption that the bleeding will be diffuse and will not be amenable to endoscopic intervention.

Being at a cancer center, my colleagues and I are frequently asked to perform endoscopic procedures in patients who have less than 50,000 platelets/µL even after transfusion(s), and we do not seem to have a high incidence of adverse outcomes. Therefore, to assess the risk of endoscopy in thrombocytopenic patients, my colleagues and I recently conducted a study on this issue. We thought that it would be useful not only for us, but also for the overall gastroenterology community, to examine experiences in thrombocytopenic patients and the

types of complications, if any, that resulted in order to determine the minimum platelet count required to perform endoscopic interventions safely.

G&H How did you select the threshold platelet count for entry into the study?

WR We looked at the common terminology criteria for adverse events (CTCAE) and used the associated platelet counts. If a patient was referred for endoscopy and his or her initial platelet count was $50,000/\mu L$ or less (CTCAE grade 3), then that patient was included. If the platelet count was above $50,000/\mu L$, we did not consider the patient to have thrombocytopenia. If the patient received a platelet transfusion and his or her platelet count was under $75,000/\mu L$, then we included the patient.

G&H How were bleeding events identified and managed?

WR The study was a retrospective review, so we looked at patients who had thrombocytopenia as a diagnosis and/or received platelet transfusions and then also underwent an endoscopic procedure. We were able to identify these patients through billing information and then reviewed every endoscopic report to see whether any intervention, even as simple as a biopsy or a hemostatic intervention, was performed. We looked for the indication if the intervention was primarily for bleeding, to rule out conditions such as graft-vs-host disease, or to evaluate symptoms such as vomiting. We were interested in interventions, if any, for gastrointestinal bleeding in the setting of thrombocytopenia as a subgroup. Therefore, we

looked specifically for any measures that were employed to control bleeding and then the type of outcomes resulting from those interventions.

G&H Based on your results, how should endoscopists approach biopsy and polypectomy in thrombocytopenic patients?

WR We found not only that endoscopy could be performed in patients with less than 50,000 platelets/ μL but that therapeutic maneuvers could be performed to control bleeding and that such interventions would have a beneficial impact on the patient's transfusion requirement. Thus, we feel that the traditional threshold of 50,000 platelets/ μL that many doctors adhere to or aim for should be put aside, and a lower platelet threshold of perhaps 25,000/ μL or 30,000/ μL should be employed for endoscopic procedures, including biopsies. This change would require fewer platelet transfusions to prepare a patient for endoscopy.

There was not a lot of experience specifically with polypectomy in our study, but if it appeared to be clinically indicated, polypectomy could probably be performed with a platelet count under 50,000/μL, likely in the 30,000/μL or 40,000/μL range, particularly if the polyp was small (<10 mm). Most of the polyps were removed with the cold snare technique to avoid leaving behind an ulceration. A larger polyp that would require snare cautery probably should not be dealt with in a thrombocytopenic patient because the treatment would leave behind an ulcer that would need time to heal and that could bleed if the platelet count drifted lower. Therefore, we tended to remove all lesions with the cold snare technique so that any bleeding would be immediate and the endoscopist could deal with the bleeding during the procedure if it became an issue.

The study findings show that endoscopy can be performed safely and that useful information can be obtained that could alter management decisions, particularly in a bleeding patient. If a patient is bleeding and has a platelet count of $35,000/\mu L$ and the doctor cannot increase the platelet count with platelet transfusions, endoscopy should probably still be performed because the doctor could intervene successfully and help in the management of the patient. Our study of bleeding patients included primarily those undergoing upper endoscopy, but some of the findings can apply to lower gastrointestinal bleeding as well. The bleeding site is likely to be focal, rather than diffuse, and interventions such as clipping may be beneficial.

G&H Are there any preventive measures that should be taken when endoscopic procedures are done in patients with thrombocytopenia?

WR Doctors usually focus on the platelet count, but there are also other preventive measures, such as stopping aspirin use. Patients with thrombocytopenia have a limited number of platelets, so using aspirin, which increases the risk of bleeding, should be avoided. Platelet transfusions may raise the platelet counts, but patients can grow refractory to platelet transfusions; in fact, 23% of the patients in our study fit the criteria for being refractory to transfusions. Other preventive measures include limiting the number and size of biopsies and using nonthermal means to help stop bleeding, such as clips or injections.

G&H Should any endoscopic procedures be completely avoided in patients with thrombocytopenia?

WR As mentioned earlier, I think that cautery should be used for removal of a polyp only for very compelling clinical reasons. When collecting our data, we did find several cases of percutaneous endoscopic gastrostomy tube insertion, but there were so few that we decided not to include these cases in the report. In the future, we may examine the use of endoscopic retrograde cholangiopancreatography in patients with thrombocytopenia, but again the clinical situation should dictate the need for endoscopy.

G&H Should there be changes to the way platelet transfusions are used in thrombocytopenic patients?

WR There has been a trend to conserve platelets because of shortages, and oncologists have reduced their thresholds for automatic prophylactic transfusions. The platelet threshold used to be $20,000/\mu L$; currently, it is $10,000/\mu L$. Some centers do not transfuse unless the patient manifests bleeding or is scheduled for a procedure. The question is, what is the goal? Is it a particular value? Our study found that 50,000 platelets/ μL is, in a large number of patients, an unreasonable goal because it cannot be reached and patients become refractory with more and more platelet transfusions; if the procedure is just a simple biopsy, a platelet count of $25,000/\mu L$ to $30,000/\mu L$ should suffice.

G&H Are thrombocytopenic patients who take clopidogrel at higher risk for bleeding?

WR Doctors frequently do not want to perform a number of endoscopic interventions, particularly those involving colon polyps, on patients taking clopidogrel. This is similar to the clinical situation approximately 10 years ago, when doctors would cancel endoscopic pro-

cedures in patients using aspirin. Now, however, endoscopists routinely perform procedures on patients using aspirin because the cardiovascular risk of stopping aspirin outweighs the endoscopy-related risk. Clopidogrel has thrown doctors into a quandary. I think that the type of clinical situation is important. If a patient has an emergency bleed and is on clopidogrel, the endoscopy should be performed. It would be preferable for a thrombocytopenic patient to have additional platelets before undergoing an endoscopic intervention, but if a transfusion is not readily available, the procedure should probably still be considered if the patient's platelet count is above 25,000/µL.

G&H How are patients with extremely low platelet counts usually managed?

WR Typically, if a patient has a platelet count under 10,000/μL, supportive measures such as blood, proton pump inhibitors, and platelets are given, and endoscopy is deferred until the platelet count rises, probably to over 25,000/μL. Performing an endoscopic procedure in a patient with an extremely low platelet count, such as 5000/μL, is associated with a high risk of bleeding. Such patients are very sick. In our study, 30-day mortality in the group that was scoped, which consisted of patients considered stable enough for sedation, was high (18.7%), indicating a fairly ill population, often people with underlying cancer who are on therapy. Patients with even lower platelet counts would have an even higher 30-day mortality rate, and the likelihood of successful intervention would be very low.

G&H What are the next steps in research in this area?

WR Prospective study of this issue is needed in which, to be complete, all consultations for gastrointestinal bleeding are examined, to see which patients go on to endoscopy and which can be helped by such intervention. There is some selection bias as to which patients we are asked to see and those in whom we perform endoscopy. In addition, because the current platelet transfusion practices are not standardized, future studies would require a protocol with a uniform approach to these patients upon which oncologists and gastroenterologists can agree.

Dr Ross has no relevant conflicts of interest to disclose.

Suggested Reading

ASGE Standards of Practice Committee; Levy MJ, Anderson MA, Baron TH, et al. Position statement on routine laboratory testing before endoscopic procedures. *Gastrointest Endosc.* 2008;68(5):827-832.

Krishna SG, Rao BB, Thirumurthi S, et al. Safety of endoscopic interventions in patients with thrombocytopenia. *Gastrointest Endosc.* 2014;80(3):425-434.

Ohmoto K, Yamamoto S. Prevention of variceal recurrence, bleeding, and death in cirrhosis patients with hypersplenism, especially those with severe thrombocytopenia. *Hepatogastroenterology*. 2003;50(54):1766-1769.

Ponec RJ, Hackman RC, McDonald GB. Endoscopic and histologic diagnosis of intestinal graft-versus-host disease after marrow transplantation. *Gastrointest Endosc.* 1999;49(5):612-621.

Schiffer CA, Anderson KC, Bennett CL, et al; American Society of Clinical Oncology. Platelet transfusion for patients with cancer: clinical practice guidelines of the American Society of Clinical Oncology. *J Clin Oncol.* 2001;19(5):1519-1538.

Van Os EC, Kamath PS, Gostout CJ, Heit JA. Gastroenterological procedures among patients with disorders of hemostasis: evaluation and management recommendations. *Gastrointest Endosc.* 1999;50(4):536-543.