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Managing Anticoagulants During Acute GI Bleeds: Guideline-Based Best Practices

Dr. Buch:

This is *GI Insights* on ReachMD. I'm Dr. Peter Buch, and today I'm joined by Dr. Neena Abraham to discuss how we should manage anticoagulation and antithrombotics during and after acute GI bleeding. Dr. Abraham is a Professor of Medicine and the Medical Director of the Cardiogastroenterology Clinic at the Mayo Clinic in Phoenix, and she's, of course, a leader in the field.

Dr. Abraham, welcome back to the program.

Dr. Abraham:

Thank you, Dr. Buch. Nice to be here with you.

Dr. Buch:

To start us off, Dr. Abraham, why are there different practices for anticoagulants and antithrombotics across different medical organizations?

Dr. Abraham:

Since 2008, I've had the privilege of writing many of the guidelines and consensus statements for many medical organizations—not just the GI societies in the United States, but also with the Canadian GI societies, the American College of Emergency Physicians, and of course, the American Heart Association and the American College of Cardiology. And why the recommendations slightly vary—they don't vary a great deal among those organizations because I had a big hand in creating them and they do have a lot of similarities, if not completely similar across all of them—where they do differ is in the methodology.

For example, the 2022 American College of Gastroenterology-Canadian Association of Gastroenterology was conducted using the most rigorous grade methodology I have ever participated in. We teamed up with methodologists at McMaster University as well as the Cochrane Collaboration, and when you elevate the level of your literature review and survey to that degree, you're going to find smaller elements and important details that often will get missed in other types of practice statements.

And that's the key thing to remember—not every organization, and in fact, I'd say most organizations, do not put out guidelines. They call them guidelines, but there's actually a methodology involved that's very rigorous to create guidelines. So as a user, you need to understand where you're getting recommendations and what level of rigor was involved in creating them, because that's where they differ.

Dr. Buch:

Thank you for that. So if we zero in on acute reversal of warfarin, why is 4-factor prothrombin complex concentrate preferred over fresh frozen plasma?

Dr. Abraham:

This goes back to data that showed that the use of FFP was associated with a high instance of adverse events, especially pulmonary edema and congestive heart failure associated with a transfusion of FFP, and that's because it takes large volumes of FFP to be transfused very slowly for you to even modestly decrease an INR if the patient's having a super therapeutic INR GI bleed related to warfarin. And so at first, the transfusion medicine society, the American Society of Hematology, came out saying FFP should not be used for the reversal of warfarin in the setting of bleeding, GI or otherwise. And then when we examined the data, we agreed with their recommendations based on the data which they cited and used for that recommendation that it was not the right way to go.

The other thing that's particularly important for gastroenterologists is we have more than sufficient good quality data showing that we

should not be delaying addressing endoscopically the acute GI bleed. So if you are delivering FFP appropriately, you're transfusing large volumes over very long periods of time because they must be transfused slowly so that you don't get the adverse effects. So you're actually delaying getting in there and doing your endoscopic hemostasis beyond that 24-hour window. So for that reason, it just doesn't work fast enough. The same is true with vitamin K, which used to be recommended. It just doesn't work fast enough, so that's why we've all agreed—the GI societies as well as the hematology societies—that four-factor prothrombin complex concentrate is the right way to go. That will normalize an INR in less than two hours—in most cases 60 to 90 minutes—and has none of the undesirable side effects.

Dr. Buch:

What should we know about acute reversal of novel anticoagulants? Does four-factor prothrombin complex concentrate also have a role here?

Dr. Abraham:

Yes. That is also an area that has evolved a lot since the first reversal agents for direct oral anticoagulants were made available. Initially, the drug-specific reversal agents were required to reverse, and people were giving them regardless of need. We now know that that's not necessary to reverse every patient on a direct oral anticoagulant. And in fact, in our 2022 guideline, we encourage and require an additional step in that decision-making process. First, you need to triage the patient who's having an anticoagulation GI bleed, whether it's warfarin or direct oral anticoagulant, and only those with life-threatening hemorrhages should even be considered for reversal. And that's because reversal comes with a high risk of thromboembolism.

To give you a sense of comparison, if you were to reverse someone with FFP—which we do not want you to do, but that's been the gold standard in these studies—the thromboembolism rate in endoscopic bleeding cases is seven to eight percent, so consider that your baseline for risk of thromboembolism. Now, if you use an agent such as idarucizumab, which reverses dabigatran, that risk of thromboembolism at 30 days is about five to six percent. But if you use a drug such as andexanet alfa, that rate can go up to 12 to 30 percent depending on the dosages used.

So you can see they're very effective in reversing the anticoagulant effect, but the downside is real, and so that's why triage is really important. Patients who are experiencing life-threatening hemorrhages are the only ones in whom a reversal agent should at all be considered, and those are patients who fulfill what I call the rule of five. They've had more than five units of blood transfused and/or they have dropped more than five grams in hemoglobin. Usually, these are the patients who are in ICUs on pressors, and their bleeds are considered life threatening. So those are those life-threatening hemorrhages in which a reversal agent should be considered.

Now for DOACs, we were once limited to only those DOAC-specific reversal agents, but we now have enough studies—mostly cohort studies and small single-arm clinical trials—that when we pooled the data for our 2022 guidelines, it showed that PCC could also be very effective for reversing direct oral anticoagulants.

What I like about PCC is it's got so many of the necessary factors from the clotting cascade in it, including protein C5, that it hits all the anticoagulations very effectively. If you're going to only bring in one reversal agent for your local hospital and you're on the Pharmacy and Therapeutics Committee, this is the one I'd recommend. It's cheap and cheerful. It works really effectively, very predictably, and more importantly, it's incredibly inexpensive compared to the DOAC-specific reversal agents on the magnitude of thousands of dollars, which is a cost usually borne by the patient, especially if they're on Medicare.

Dr. Buch:

For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Abraham about anticoagulant and antithrombotic management.

So, Dr. Abraham, I'd like to shift over to best practices for restarting anticoagulation. When a patient on warfarin experiences a GI bleed, what factors guide your decision on when to resume the warfarin?

Dr. Abraham:

So, remember, when it comes to the management of a GI bleed, the objective is to get in there very rapidly—within 24 hours—and shut down that bleed, which means using endoscopic hemostasis, whether it's mechanical, thermal or a combination of the two to eliminate the risk of rebleed. So at the end of your endoscopy, you need to have a sense of how confident you are that the person's not going to be rebleeding, and that has a lot to do with your technical skill in delivering endoscopic hemostasis. But in general, we want you to restart the warfarin as soon as possible—usually within 24 hours of achieving immediate hemostasis. And I'm emphasizing immediate because if endoscopic hemostasis is delivered appropriately, the risk of rebleed is actually very low.

But I do appreciate that different gastroenterologists have different skill sets, and some may not deal with as many GI bleeds as large or

in large volume centers, and I also appreciate that in some smaller centers, endoscopy is not performed by gastroenterologists who have more experience with this but also by surgeons and others who may not have to deal with this at all. So there will be variation in the success of endoscopic hemostasis based on experience and skills.

But in general, you want to restart the warfarin the next day at the absolute latest. Immediate hemostasis is what you're looking for because we can always deal with a rebleed, which should occur rarely if the procedure is being done by someone who's well qualified to do it in the first place. Where we see a lot of rebleeds is usually from patients who have been addressed by physicians who just don't have the experience and the facility with endoscopic hemostasis that we would hope.

Dr. Buch:

Now, since the last publication of the ACG and the Canadian Association of Gastroenterology joint guidelines in 2022, what new evidence or practice shifts have we learned?

Dr. Abraham:

Our recommendations still hold, and they have been replicated by organizations across the world. Where we have seen practice shifts, which is really interesting, is when people deviate from our recommendations, bad things happen.

The second thing where we've seen a lot of practice shifts is in the data supporting different endoscopic methods for hemostasis in this patient population. Previously, we did not have a section on preferred endoscopic hemostatic methods in the 2022 guideline because there was no data or insufficient data.

Starting in 2024, we started seeing the emergence of single-site studies exploring hemostatic clips versus no clips, thermal therapy versus injection therapy, the combined approaches, and all the things that we would ordinarily know what to do with in a patient who is not on these drugs because we know what the best practices are and what the best data is.

What's really moved forward, which I think is an important thing to have happened, is we have more and more data emerging on this subset of patients in particular and what works in the endoscopy suite for them. And I think that's really important data and a big practice shift because people will be now wondering, "Okay, well, I've held the drugs correctly. I know when to restart the drugs. But what do I do while I'm sitting here facing this GI bleeding lesion?" Clarifying what to do during the procedure is a big step forward.

Dr. Buch:

Can you share with us some of the alternative approaches?

Dr. Abraham:

One of the most popular approaches that now we have some nice data around is the use of mechanical clipping. For endoscopists out there, you'll know that there's something called a through-the-scope clip, which has two prongs versus an over-the-scope clip that looks more like a trap that you try and suck your lesion into. And there's been some nice studies out of Germany in patients in whom 70 percent of them have been on antiplatelets and anticoagulants showing that the initial hemostatic rate for the use of a hemostatic clip as solo therapy is actually very high—it's 100 percent. But there is a rebleed rate of about 35 percent, which is similar between through-the-scope clips and over-the-scope clips, so one's not better than the other, and that has everything to do with technical failure.

And there's some very common reasons that predict whether or not that clip is going to fail. Something as simple as you have not actually put the tines of the mechanical clip around the lesion to actually oppose the edges—that's a real problem for some people. Other people don't bother washing off the clot, so they don't actually know where the edges are to approximate. And other things such as they just misfire the clip and they don't grab the whole lesion. These are predictable technical failures that will lead to that 35 percent rebleed rate, and again, it has nothing to do with the choice of the clip—over-the-scope versus through-the-scope—but has everything to do with the skill set of the endoscopist, and we now have good data from Europe showing that.

Dr. Buch:

Thank you so much. That's a great way to round out our conversation, and I want to thank my guest, Dr. Abraham, for joining me today to discuss how we can best manage anticoagulants and antithrombotics in patients experiencing acute GI bleeding.

Dr. Abraham, thanks for this incredibly informative discussion.

Dr. Abraham:

Thank you so much for having me again.

Dr. Buch:

For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in our series, visit *GI Insights* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening, and see you next time.