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## The Use of Anticoagulants and Antiplatelet Medications in Cirrhosis

### Dr. Buch:

This is *GI Insights* on ReachMD, and I'm your host, Dr. Peter Buch. Joining us today to talk about the use of anticoagulants and antiplatelet medications in patients with cirrhosis is Dr. Naga Chalasani. He's a co-author of the article, titled "The Safety of Anticoagulants and Antiplatelet Agents in Patients with Cirrhosis," which was published in *Alimentary Pharmacology and Therapeutics* in November 2022. Dr. Chalasani is also the David W. Crabb Professor of Gastroenterology and Hepatology at Indiana University School of Medicine in Indianapolis.

Welcome to the program, Dr. Chalasani.

### Dr. Chalasani:

Happy to be here, Dr. Buch.

### Dr. Buch:

Thank you so much. To start us off, Dr. Chalasani, can you give us some background on your article? Why is this so important?

### Dr. Chalasani:

Yeah. Patients with cirrhosis, like general population, also need anticoagulation, for example, venous thromboembolism or pulmonary embolism or for atrial fibrillation, and also they get heart disease. They have stents put in, and they need antiplatelet agents, and thus, understanding how best we can safely administer these type of medications to patients with cirrhosis is really important. I might add, though, the incidence and the prevalence of cirrhosis is growing because of diabetes, obesity, alcohol, MASH, etc. Therefore, primary care physicians and cardiologists, gastroenterologists, routinely encounter this scenario where they have to consider giving these agents to patients with cirrhosis.

### Dr. Buch:

Thank you for that. And how does cirrhosis affect coagulation?

### Dr. Chalasani:

In multiple ways, most of the coagulation factors, as you know, are synthesized in the liver, so as the liver disease gets worse, majority of the coagulation factors are deficits. There is deficiency of the coagulation factors, except for Factor VIII. Also, patients with cirrhosis have thrombocytopenia because of hypersplenism and some rather hypofunctioning bone marrow, so in combination, there are very deranged coagulation and hemostasis. For a length of time, it was only believed that the patients with cirrhosis are at risk for bleeding, but in the course of the last 15 years or so, it's become clear that not only they have excessive risk for bleeding, they also can have excessive risk for thrombosis, whether it is DVT, portal vein thrombosis, so it's both sides of the equation that can happen in patients with cirrhosis and advanced chronic liver disease.

### Dr. Buch:

And moving on to testing, do viscoelastic tests have any role to play to considering anticoagulation therapy in cirrhotic patients?

### Dr. Chalasani:

:There are tests, for example, transient elastography. I think it's TEG testing. That is done in the ICUs, as well as in the operating rooms, but it is done more acutely when patients are bleeding, but not routine clinical outpatient practice. At our place, for inpatients, we do TEG testing. It is a bit hard to interpret, but your points that the current way to measure coagulation abnormalities with platelet count PT/INR is fraught with problems, but at the moment at bedside, that's really what we have.

**Dr. Buch:**

So tell us a little bit more about the testing that you do at your institution.

**Dr. Chalasani:**

It's called TEG testing. It's a comprehensive way you assess for clotting and how clot is dissolved, and there are multiple parameters that the machine spits out, and based on the characteristics of a TEG test result, you can say whether somebody is in a prothrombotic state or a more bleeding diathesis state that helps you to tailor your anticoagulation in a sick patient.

**Dr. Buch:**

That's great, and that's very useful for us to know about. So please compare the use of unfractionated heparin with low molecular weight heparin in cirrhosis.

**Dr. Chalasani:**

There are some head-to-head studies comparing unfractionated versus low molecular weight heparins, and the jury is that the low molecular weight heparins are effective and also safer in patients with cirrhosis. Keep in mind that the heparins as a side effect can cause thrombocytopenia. So if you are encountering a patient requiring heparin in your practice, either outpatient or inpatient, I suggest choosing the low molecular weight heparin rather than unfractionated, the traditional heparin infusion.

**Dr. Buch:**

Thank you for that very important bit of information.

For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Naga Chalasani about his recent article on the safety of anticoagulants and antiplatelet medications in cirrhotic patients.

Now from your vantage point, Dr. Chalasani, how would you approach a patient with cirrhosis who had a previous variceal bleed and who now needs anticoagulation?

**Dr. Chalasani:**

Generally speaking, variceal bleeding is not thought to be a function of coagulation abnormalities. It is thought to be a function of portal hypertension, the pressure in varices. So if you have a patient with previous variceal bleeding or varices, just the fact that you placed them on anticoagulation should not increase their risk of variceal bleeding. Having said that, when I'm treating a patient with either previous variceal bleeding or somebody with cirrhosis and known varices, I first, if possible, like to eradicate the varices. We at our center do variceal ligation banding, but you can also use beta blockers to reduce the portal pressure. Once you feel that you're on optimal doses of beta blockers, that's when you start anticoagulation. This is when you're considering elective anticoagulation. However, though, there are going to be circumstances where somebody comes in with PE and you don't really have time to do all that. I would once again reiterate if a patient requires lifesaving anticoagulation even in the face of previous variceal bleeding or large varices, I would cautiously start anticoagulation the best way you can, whether it is some of the newer direct-acting anti coagulants or low molecular weight heparins.

**Dr. Buch:**

Thank you. That's a wonderful segue into our next question. How safe are direct oral anticoagulants in cirrhosis?

**Dr. Chalasani:**

They are safer than warfarin. They are safer than long-term, for example, low molecular weight heparin. So today, if you have to use an anticoagulant in patient with cirrhosis, the first choice should be considering a direct acting oral anticoagulants, and the current generation of DOACs are safe from a liver standpoint. Some of you may recall the very first generation direct-acting oral anticoagulant, called ximelagatran, had better toxicity. However, the currently marketed DOACs are very safe from a liver toxicity standpoint. And there are a number of head-to-head studies that have been done with warfarin and for different indications. They all consistently show that the DOACs are more effective, and also, safer.

I would say one thing though. The package inserts for these medications say that they are contraindicated in patients with Child C cirrhosis, which means that you have things like refractory ascites, profound hepatic encephalopathy, or hepatorenal syndrome. Those are the kinds of patients where you should be quite cautious regardless whether you give DOACs or any other form of anticoagulation because these patients are touch and go. So other than that, I think in my practice and my colleagues here, we are very geared towards using these direct-acting oral anticoagulants as the first line.

**Dr. Buch:**

Thank you. So, Dr. Chalasani, is it safe to give aspirin and or P2Y12 antagonists to cirrhotic patients?

**Dr. Chalasani:**

Some patients with cirrhosis, especially NASH cirrhosis, they have heightened risk for cardiac disease. They require aspirin. And in medicine, it is all risk versus benefits, so if the indication is compelling, I would use aspirin. I would suggest that you use enteric-coded 81 milligrams of aspirin, but I sometimes co-administer with H2 receptor antagonist, such as ranitidine or famotidine, occasionally low-dose things, like omeprazole, to reduce the risk of GI bleeding. But if you're using 81 milligrams of aspirin, risk of precipitating renal failure, for example, one could see with NSAIDs it's significantly lower. So depending on the indication that you're considering aspirin, enteric-coated baby aspirin is reasonable.

And in terms of right to some of the newer antiplatelet agents, I think they also are safer in patients with cirrhosis. For example, you have a coronary stenting done, and they need things like clopidogrel, I would use them, but I would look at the package inserts to see if they require dosage adjustment. For example, some of these medications are metabolized by cytochrome P450 enzymes, and there are profound changes in what happens to these enzymes in people with advanced cirrhosis, so I would once again balance risk versus benefit, and I would look at in a particular patient with cirrhosis based on ideology their Child's class. I would choose one that is safer than others because not all are created equal. For example, some P2Y12 inhibitors have reversible binding as opposed to others are irreversible. Some of that may be important as well.

**Dr. Buch:**

Now in the last few minutes of our discussion today, are there any additional thoughts you'd like to share with our audience?

**Dr. Chalasani:**

I would just reiterate that cirrhosis now in some patients is thought to be a prothrombotic state. When we were in medical school studying, we thought they're only at risk for bleeding. That is no longer the case. I think patients can bleed, patients with cirrhosis, but they also can have DVTs, portal vein thrombosis. They also can have pulmonary embolism. So when you're seeing a patient with cirrhosis with one leg swollen, don't attribute that to just the pedal edema. It could be a DVT. That's one point. Number two is that I think a comfort in using anticoagulants and antiplatelet agents is expanding rapidly. It is safe and much safer than warfarin. So I think if your practice has a fair number of patients with cirrhosis, I think getting familiar with this area with the literature is going to be helpful for you and your colleagues.

**Dr. Buch:**

What an excellent review on the use of anticoagulants and antiplatelet medications in cirrhosis. I want to thank my guest, Dr. Naga Chalasani, for sharing his insights.

Dr. Chalasani, thanks so very much for joining us today.

**Dr. Chalasani:**

You're welcome, and you have a good rest of the day.

**Dr. Buch:**

For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit [ReachMD.com/GIInsights](https://ReachMD.com/GIInsights) where you can Be Part of the Knowledge. Thanks for listening.