

Lisa Baumann Kreuziger:

Welcome to this podcast on guideline directed treatment of venous thromboembolism called VTE, including special populations. This is the third in a series supported by an educational grant from the BMS Pfizer Alliance. It's important to note that the content was developed independent of the funder. In this episode, you'll learn to identify and apply current evidence-based guideline on management of VTE, including VTE in special populations such as patients with cancer. The views and opinions on this podcast are those of the speakers and reflect the synthesis of science. Content should not be considered as the official policy of the American Heart Associations. I'd like to introduce myself. This is Lisa Baumann Kreuziger. I am a hematologist in Milwaukee Varsity and the Medical College of Wisconsin. One disclosure I have is I am a member of the chest guideline panel and we will be discussing those guidelines today. I'm honored to be joined by one of my other guideline panel members, Scott Woller, and I'll have him introduce himself.

Scott Woller:

Well, hi Lisa. Thank you and thanks so much for the kind invitation to join today. This is Scott Woller. I am chair of medicine at the Intermountain Medical Center here in Murray, Utah and professor of medicine at the University of Utah. As Lisa alluded to, I co-chaired the most recent chest guideline update on the treatment of venous thromboembolism and just delighted to be here serving this AHHA panel today.

Lisa Baumann Kreuziger:

Thanks so much, Scott. We're also honored to be joined by Dr. Ann Leonhardt-Caprio, please introduce yourself.

Ann Leonhardt-Caprio:

Thank you, Lisa and Scott. It is really an honor to join both of you here today. Such experts in this field. I am a nurse practitioner and the program coordinator of the Comprehensive Stroke Center at UR Medicine in Rochester, New York. I'm also assistant professor of clinical nursing at the University of Rochester School of Nursing, where I teach in the doctor of nursing practice program nurse practitioners and clinical leaders. And I'm thrilled to be here today to share a little bit with you of the VTE treatment guidelines.

Lisa Baumann Kreuziger:

Thank you so much. So, for our listeners out there after this podcast today, we hope you'll better be able to understand and apply the current evidence-based guidelines on managing VTE and recognize certain circumstances when certain anticoagulant classes are preferred in select situations such as VTE in patients with cancer and other conditions. So, just as a matter of background, venous thromboembolism is a clot in the vein of the legs, which is called deep vein thrombosis or a clot involving the lungs, which is called a pulmonary embolism. VTE is common and represents the third leading preventable cause of cardiovascular death. And the incidence of VTE varies with age and we think that the baseline risk is about one to two per 1000. But underlying illness that especially cancer, which we're going to discuss today, leads to an incidence that's much higher than that.

In VTE as in many other conditions, evidence surrounding best practice and novel therapies is always emerging, and guidelines have historically assumed the responsibility of reviewing that evidence and synthesizing it for clinicians to use. So, some brief background on guideline development when

guidelines are made, the most common method methodology being used is a process called the grading of recommendations. Assessment, development and evaluation are called the grade approach. The certainty of evidence is defined as the extent to which our confidence in the estimate effect is adequate to support the recommendation the certainty of the evidence is categorized as high, moderate, low or very low. And the experts today will discuss multiple different guidelines and discuss those levels of recommendations with them.

Oftentimes, the guidelines also attempt to take into consideration additional aspects of pragmatic nature in providing care for patients, including the resources that are required, cost-effectiveness of the treatments, equitably acceptability and feasibility of implementation of that recommendation. Oftentimes it's helpful to think of a case in order to understand the implication of guidelines. So, to kick things off, let me start with this case. So, a 62-year-old man presents to your clinic following, returning home from a vacation in New Zealand and he has a swollen right leg. You obtain an ultrasound and diagnose the patient with a deep vein thrombosis of the femoral popliteal and posterior tibial veins. So, what clinical guidelines do they advise surrounding the treatment for this patient? And I'll ask Scott to give us some advice.

Scott Woller:

Well, thank you Lisa. It's always helpful to think about this decision making in the setting of a clinical case in a clinical scenario. And I guess I'd begin simply by saying that in maintaining thrombosis top of mind in circumstances such as these and considering the pretest probability, that is to say the likelihood of the disease being present will guide decision making. In a former podcast, we discussed using that pretest probability, including the simple blood test, the D-dimer, to increase that pretest probability assessment certainty. And so in this circumstance where the diagnosis has already been obtained, the question really becomes one of therapy. And to take perhaps one step back just a smidge in considering this patient's presentation, the patient arguably could have presented with isolated distal DVT, that is to say blood clots involving only the lower portion of the leg below the popliteal vein.

As this patient presented, why with a deep vein thrombosis in the proximal circulation, that is to say popliteal or more proximal as is the case here or pulmonary embolism, where astutely, a first step would be to consider that patient's risk. So, I'm going to speak to this patient's presentation in the setting of deep vein thrombosis and where current guidelines advise we go in the treatment of patients such as these. So, in this case, this is a patient who presents with proximal DVT of the leg, and the most recent chest guidelines align with guidance from other societies such as the American Society of Hematology to recommend firstly anticoagulation in patients with proximal DVT. Historically, if we look at treatment modalities that are available, why these were patients that initially required a parenteral anticoagulant such as enoxaparin or heparin for that matter, and then that important overlap period of a minimum duration of five days.

And until upon initiating warfarin, of course that INR was greater than two on two consecutive days, emerging evidence has shown that in fact the direct oral anticoagulants including apixaban, the trade name is Eliquis, rivaroxaban, the trade name being Xarelto, and then edoxaban, the trade name Savaysa, represent alternatives to the vitamin K antagonist warfarin that was formerly used. And in fact, in the most recent chest guidelines, we actually recommended electing a direct oral anticoagulant over a venomancan antagonist for the initial treatment phase of venous thromboembolism. Invariably, these medications all differ slightly, and I'll highlight a principle, a difference between edoxaban and the ladder to rivaroxaban and apixaban. And that principle difference is that edoxaban was studied with parenteral anticoagulation for a lead-in period of five to 10 days, whereas rivaroxaban and apixaban in

that initiation phase when anticoagulation was first started, why they are initiated with a increased dosing.

Rivaroxaban increased dose is 15 milligrams twice a day for 21 days, and then that treatment phase dosing is 20 milligrams daily. Thereafter, that compares with the apixaban where the dosing is 10 milligrams twice daily for the first seven days and then five milligrams twice daily thereafter. The key takeaway, if you will, is that the initiation phase differs from the treatment phase for the treatment of venous thromboembolism and that apixaban and rivaroxaban do not require parental anticoagulation to kick things off from a patient satisfaction perspective, why avoiding parental anticoagulation in that initiation phase is often favorable. I'll also highlight that the direct oral anticoagulants when compared to the old tried and true warfarin are as safe and arguably perhaps safer, that there's some evidence to demonstrate superiority as far as effectiveness goes, and we have a good degree of certainty that they are just as effective.

Other real meaningful benefits include that there's no routine monitoring that's necessary when the direct oral anticoagulants are elected for the treatment of venous thromboembolism and really no meaningful direct oral anticoagulant food interactions. Although I'll always highlight that the way to optimally take rivaroxaban in that treatment phase is with food best preferred the largest meal of the day. And again, comparatively when you think about the direct oral anticoagulants in relationship to warfarin and haltingly few drug drug interactions or the DOAC when compared to warfarin. So, for all of those reasons, when I think about this case presentation that you laid out here in this gentleman who presents after long haul travel with a clinical symptoms compelling for deep vein thrombosis, radiology, supportive of that diagnosis, current guidelines would advise firstly anticoagulation, and then secondly that a direct oral anticoagulant would be preferentially selected in a patient such as this.

Lisa Baumann Kreuziger:

Fantastic, thank you. So, let's move from typical VTE to our special populations. So, what do our guidelines recommend for the treatment of cerebral vein or cerebral venous sinus thrombosis? Anne, will you take this one?

Ann Leonhardt-Caprio:

I would love to. Thanks Lisa. This is a very special population. It's not something that occurs commonly. And if you don't mind, I'll actually introduce the topic here with a case as well. A case actually of a patient that I saw last week, which was a 42-year-old woman who had a recent severe sinus infection, history of migraines and was on oral contraceptives. She was on no other medications and came to the emergency department with a headache, nausea and vomiting, which were progressively worsening for two days and new onset of brief episodes of twitching on the left side. So, as Scott talked earlier about that pretest probability, these are all some significant neurologic symptoms in someone who's younger has had a severe sinus infection that can put you at increased risk of cerebral venous sinus thrombosis also is on oral contraceptives and ultimately her imaging CT of the head, a CT angiogram and an MRI were all consistent with cerebral venous sinus thrombosis of the left transverse sinus and sagittal sinus.

And this essentially, to put it simplistically, is a VTE of the brain. We think about this in the same terms that we do of a clot in the leg, a clot in the lungs. It's a venous thrombosis in a different spot, but it's rare and it can be kind of frightening because these can cause intracranial hemorrhage, which we'll address in just a minute. But to directly answer the question what the guidelines recommend for treatment, the chest guidelines recommend anticoagulation therapy for patients with cerebral vein or venous sinus thrombosis. And their formal review of the evidence warranted a weak recommendation for anticoagulation. But the panelists on this guideline upgraded the guidance to a strong recommendation

because there's a high value on the uncertain but potentially life preserving benefit of anticoagulation. And I practice with these patients frequently, and this really is our standard of care is to anticoagulate. The American Heart Association American Stroke Association released a scientific statement in 2011, which made class two A, level B recommendation for immediate anticoagulation with adjusted dose unfractionated heparin or weight-based low molecular weight heparin in a full anticoagulant dose followed by a vitamin K antagonist regardless of the presence of ICH. So, this is something important to know that cerebral venous sinus thrombosis, one of the presenting issues can be intracranial hemorrhage, and that puts a lot of pause on anticoagulating. However, unfortunately the treatment really to prevent further hemorrhage is anticoagulation to treat that clot. This is one of the reasons though why we usually recommend starting with that IV unfractionated heparin or low molecular weight heparin to watch someone and make sure that they don't have neurologic decline suggesting progressive hemorrhage and then switching over to vitamin K antagonists. So warfarin, one of the reasons for this is because DOACs haven't, or the direct oral anticoagulants haven't really been studied specifically in patients with cerebral venous thrombosis.

So, while warfarin is the most studied, it may be reasonable to consider the underlying etiology of the thrombosis. So there might be additional considerations if the patient has had cancer, which I think that Dr. Woller will talk to us about shortly. The other thing is that despite vitamin K antagonist or warfarin being probably the primary recommendation for treatment, there may be instances in which you have folks that are very difficult to manage on warfarin that are not therapeutic. And so if they're not getting therapeutic in that early period, then you actually run the risk of the thrombosis worsening. So, there may be case by case basis where you might want to consider a direct oral anticoagulant. And there's one other consideration whenever you're thinking about cerebral vein thrombosis, and that is in patients who have vaccine induced thrombosis and thrombocytopenia. So, we've seen with adenovirus vaccination for Covid and an associated thrombocytopenia, some risk of cerebral venous sinus thrombosis.

And while it is rare it has been seen, it is studied and it usually develops around five to 30 days after vaccination with that adenovirus vaccine, you want to make sure that if you have someone with a venous sinus thrombosis, that what you are assessing for is have they had one of these vaccines recently? Because the treatment for this with the vaccination history, it needs additional treatment with IVIG. And so this is one of those circumstances where you just don't want to automatically anticoagulate without getting that further history. So, to kind of wrap up with the patient that I saw when she was in the hospital, she was started on a heparin drip at our hospital, we use what's called a neuro protocol heparin drip, and that's a heparin drip that doesn't have a bolus and it has a slightly lower APTT goal of 54 to 72. Head CT at 24 hours after she was therapeutic was stable. And so warfarin was initiated and she did very well.

Lisa Baumann Kreuziger:

Fantastic to hear, and I appreciate you highlighting some of the limitations that we sometimes have with the evidence in the literature that leads to guideline recommendations, but we then need to pull in other aspects of clinical care to properly care for these patients. So, thank you for that. We're going to move from the deep vein system to superficial vein thrombosis. So Scott, how should patients with an isolated superficial vein thrombosis of the leg be treated?

Scott Woller:

Yeah, thanks Lisa. Well, you know, let out remarking on comparative limitations of evidence, and when we look at the body of evidence that exists for the treatment of superficial vein thrombosis of the lower

extremities, it's comparatively less than the treatment of DVT. Now that being said, there's been some real impactful advances in the management of patients with superficial vein thrombosis over the last few years. Historically, these were patients that we would initially treat with conservative therapy including non-steroidals, warm compresses, elevation, and the like. But increasingly it was acknowledged that a subsidy these patients would progress on to having a deep vein thrombosis and or pulmonary embolism, albeit at a lower rate than what we see when DVT is present. Likewise, it's important to highlight that physical exam is inadequate to be able to discern superficial vein thrombosis as an isolated entity versus SVT and concomitant DVT.

And it's a nice opportunity to highlight that if SVT, especially in the upper part of the leg is suspected, then a definitive diagnosis with duplex ultrasound is indicated because up to 30% of patients with SVT will have concomitant deep vein thrombosis. So, that's really an important clinical pearl. There have been a couple of very nice studies now that have looked at how to optimally treat these patients and the inclusion criteria I think are important. The very nice CALLISTO study was really the cornerstone of studies looking at the treatment of a superficial vein thrombosis of the lower extremities enrolling over 3000 patients with at least five centimeters of thrombosis in the greater saphenous vein to be eligible.

And what CALLISTO told us was that the frontal anticoagulant fondaparinux, which is given in a dose of 2.5 milligrams subcutaneously once daily for the duration of 45 days was favorable in protecting against progressive thrombosis when compared with placebo. And in fact, it was those data that led to the chest guidelines statement to suggest fondaparinux anticoagulation over other therapy or low dose low molecular weight heparin for the treatment of superficial venous sinus thrombosis of the lower extremities. Subsequent study assessed fondaparinux in relationship to the oral activated factor 10 inhibitor rivaroxaban 10 milligrams daily for that similar duration of time. And in fact, rivaroxaban was thought to be a reasonable alternative to the parenteral form of therapy for superficial vein thrombosis fondaparinux.

So, when we think about the treatment of superficial venous sinus thrombosis of the lower extremity, taking into account the patient's symptoms and the severity of their disease, it's very reasonable to elect anticoagulation over not fondaparinux 2.5 milligrams daily for a duration of 45 days or rivaroxaban 10 milligrams orally daily for a duration of 45 days are both reasonable. A closing thought is that firstly it's important to consider the clinical presentation of these patients.

SVT, superficial vein thrombosis can be an initial presentation of an occult malignancy, albeit rarely. And it's a nice opportunity to highlight the importance of assuring that all age appropriate cancer screening is up-to-date. And secondly, we don't tend to generally advise anticoagulation therapy among patients who have SVT in the setting of a venous catheter or a venous access. So that's a circumstance where limited evidence exists for the use of anticoagulation. Broadly speaking, we however would advise that in patients who are symptomatic and are similar to those that were enrolled in those prospective randomized control trials, that anticoagulation can be selected over conservative therapy alone for the treatment of superficial venous thrombosis of the lower extremities.

Lisa Baumann Kreuziger:

So Scott, you just mentioned that cancer is a risk factor for thrombosis and we also and anybody with thrombosis need to ensure that their cancer screening is completed. So, how about a patient with cancer who also has a venous thrombosis, what is the optimal treatment for those patients?

Scott Woller:

Yeah, thanks Lisa. Well, this is a really exciting domain and there's been a lot of advance in the literature surrounding the treatment of cancer associated thrombosis. So, the term you'll hear me use is CAT, C-A-T, and that refers to thromboembolism in the deep veins or in the pulmonary artery circulation associated with cancer. So, cancer associated thrombosis. Now historically from studies that were done in the early 2000, we had a good body of evidence to demonstrate that firstly, patients with cancer were at a significant increase risk for thromboembolism. And secondly, that when compared to the only other anticoagulant readily available at that time, warfarin, why low molecular weight heparin was superior for the treatment of cancer associated thrombosis. So, those studies were principally done with dalteparin. Although in other countries, tinzaparin is available and in the United States it's primarily adjacent evidence that leads to the use of enoxaparin.

Historically in patients with cancer associated thrombosis. Fast-forward ahead to the age of the direct oral anticoagulants and of course, and because of their comparative effectiveness seen in the original studies among patients with VTE in the absence of cancer and taking into account patient quality of life, there was a real interest in understanding whether perhaps the direct oral anticoagulants might be an alternative to be considered to anticoagulation with low molecular weight heparin among patients with CAT. Those studies have been completed and when we look at the aggregate body of evidence comparing the direct oral anticoagulants with low molecular weight heparin among patients with cancer associated thrombosis, there's a good signal that they are as effective as the parenteral anticoagulants and likely should be considered a first line therapy among patients with cancer. The most recent update from the American College of Chest Physicians recommended preferentially selecting a DOAC over low molecular weight heparin on a case by case basis among patients with cancer associated thrombosis.

And the American Society of Hematology guidelines suggested that a DOAC or low molecular weight heparin could be preferentially selected among patients with CAT. So when we look at the comparative evidence and the treatment of cancer associated thrombosis in the individual studies, there appeared to be a signal of bleeding risk that existed among patients with luminal GI malignancies randomized to either rivaroxaban or edoxaban when individually compared to low molecular weight heparin, whereas that comparative signal of an increased risk for bleeding was not seen in the apixaban studies. So, the way the guideline panelists elect to address this was to firstly provide the guidance that in the treatment of CAT, it was recommended to elect an oral 10A inhibitor, a apixaban, edoxaban or rivaroxaban over low molecular weight heparin for the initiation and treatment phases. And that was a strong recommendation. However, out of deference to that observation of bleeding risk, we elected to insert a remark that highlighted that observation that perhaps edoxaban and rivaroxaban appeared to be associated with the higher risk of GI bleeding than low molecular weight heparin.

And that uniquely among patients with cancer associated thrombosis and luminal GI malignancy, either low molecular weight heparin or apixaban may be preferred. Lisa, just a few closing pearls when I think about cancer associated thrombosis. The first is that in those patients who have a perturbation of their GI tract, either because of nausea or mucositis, while electing low molecular weight heparin over a oral therapy may be preferred. Likewise, we know that chemotherapeutics are always evolving and as such, the interactions that may exist, especially involving the CYP3A4 and the P-glycoprotein pathways with the relative metabolism of the direct oral anticoagulants are important to consider. Finally, in patients with cancer associated thrombosis, sometimes thrombocytopenia exists. There does exist some guidance surrounding downward dose adjustment of low molecular weight heparins in patients with CAT that have thrombocytopenia. So, in those cases why perhaps low molecular weight heparin has a more robust body of evidence that would lead to individual case by case dosing, that to date does not exist for the selection of the direct oral anticoagulants.

Lisa Baumann Kreuziger:

Thanks so much, Scott. So, it really seems that direct oral anticoagulants are the first line therapy for patients with VTE and you told us about cerebral vein thrombosis and the use of low molecular heparin and warfarin. Are there other circumstances when VTE should preferentially be treated with those two agents?

Ann Leonhardt-Caprio:

There are, and thank you for asking that question, Lisa, because I think that there are many patients and providers that are thrilled that direct oral anticoagulants are on the market and can be a first line medication for so many things, including atrial fibrillation and VTE right now. And Scott went over some of the advantages to the direct oral anticoagulants, including the lack of routine monitoring. There aren't meaningful drug food interactions, which is a great thing when you're trying to teach somebody to live healthy and tell them that they actually can eat vegetables. And there are few drug-drug interactions. And also when considering VTE, you can have initiation phase dosing without parenteral lead-in. There's a comparatively short half-life whenever you're comparing with warfarin, which simplifies procedural interruptions and you don't really need bridging for most procedures either. So, that can limit the amount of time that folks with VTE are off of anticoagulation.

But there are circumstances and populations where direct oral anticoagulants should probably be avoided. They should be avoided in pregnancy and in breastfeeding. Patients with coexisting mechanical heart valves or rheumatic heart disease plus atrial fibrillation are recommended to be treated with warfarin. And for thrombotic antiphospholipid syndrome, there have been four open-label randomized controlled trials, three with rivaroxaban and one with an apixaban among patients with a diagnosis of antiphospholipid syndrome or triple positive APS overall in that population, the use of DOACs compared with VCAs was associated with an over fivefold increased odds of subsequent arterial thrombotic events, especially stroke, which is something that we really want to be concerned about. The odds of subsequent VTE or major bleeding we're not significantly different between the two groups. So we are talking about arterial clotting and specifically stroke here. But in those with antiphospholipid syndrome, warfarin may be the better choice.

And the target INR for that would be 2.5 according to the CHEST 2021 guidelines. Now there is the CHEST 2021. Guidelines do give a weak recommendation with low certainty of evidence for the direct oral anticoagulants during the treatment phase. However, you want to think about the fact that APS is a heterogeneous condition and there might be some groups of patients that considering a direct oral anticoagulant would be reasonable. This has to happen on a case by case basis and really considering the risks and benefits. And I may actually use a similar example to what I discussed whenever we were talking about the cerebral venous sinus thrombosis. While the best evidence may be to use warfarin in those patients who you really have challenges managing the warfarin, getting them to a therapeutic dose, having concerns about getting their blood drawn, there may be some individuals with antiphospholipid syndrome who are considered for direct oral anticoagulant.

But again, that's one of those areas where it has to be patient specific because the guidelines don't give us really clear direction on those individual cases. There was an editorial that accompanied this study that advised strong consideration for switching basically all antiphospholipid syndrome patients that were currently receiving DOACs to VKAs is given that shared decision making can be considered in rare circumstances with respect to the use of other agents. But that shared decision making is really best used when there's clinical equipoise, which now doesn't seem to apply to many patients with antiphospholipid syndrome and prior thrombosis. There are some additional references that you can check out. The 2018 ASH guidelines gave no specific guidance statement on the management of

antiphospholipid syndrome patients in 2020. The ISTH scientific subcommittee guidance statement recommended a VKA over DOAC for most patients with APS.

And in 2020, the 16th International Congress on antiphospholipid antibodies task force report on antiphospholipid syndrome guidance is similar to the CHEST statement. There are some populations where you may want to use DOACs with caution, and the first is those with gastric bypass. So, whenever you are initiating or continuing direct oral anticoagulant treatment after gastric bypass surgery in patients with VTE or atrial fibrillation, being vigilant regarding the possibility of reduced drug absorption is important. So, apixaban seems to be adequately absorbed after for gut resection or bypass. It may be better to avoid rivaroxaban in patients that are undergoing stomach resection or exclusion of the duodenum and the proximal jejunum. Ileostomy or distal ileal resection had no effect on rivaroxaban or apixaban absorption. And an injectable anticoagulant or VKA might be a better option for anticoagulation if DOAC concentrations can't be measured after the surgery.

I already mentioned that mechanical valve and rheumatic heart disease patients with atrial fibrillation probably should be considered for warfarin. There's randomized controlled trial evidence that shows that DOACs are as effective as warfarin for stroke prevention and have a lower risk of intracranial hemorrhage among patients with AFib. But those studies did not include patients with atrial fibrillation due to rheumatic heart disease. And in a trial of over 4,500 patients randomized to either warfarin or rivaroxaban, there was a 25% greater outcome of the composite of stroke, systemic embolism, myocardial infarction, or death from vascular or unknown causes among those receiving rivaroxaban compared with a VKA and a reduction in survival days.

And that was published by Connolly in the New England Journal of Medicine in 2022. This was an unexpected observation given that there were former randomized controlled trials comparing rivaroxaban with VKA therapy in patients with atrial fibrillation and bioprosthetic mitral valves that showed a lower risk with rivaroxaban of stroke at one year of follow up and no significant difference in mortality. So, it's not really clear why this unexpected observation occurred, but the lower rates of sudden cardiac death and death from mechanical or pump failure with vitamin K antagonist therapy than with rivaroxaban therapy aren't readily explained by the effects on stroke, bleeding or valve deterioration. And finally, cirrhosis with child C. There are areas of uncertainty including end stage renal disease and in those patients direct oral anticoagulants haven't been trialed for VTE treatment.

Lisa Baumann Kreuziger:

Thank you so much for that fantastic summary. So, just overall, we know that the guidelines that are available to us aggregate the best evidence that we have and provide really the roadmap to evidence-based care for our patients with VTE. So, just to give a bullet point summary of the talking points that we discussed here today. So, for the treatment of VTE, DOACs are the first line for most patients. Anticoagulation can also and should also be used for treatment of cerebral vein thrombosis. And in that situation, low molecular heparin and warfarin are the most studied treatments. For superficial vein thrombosis, anticoagulation is suggested if somebody is at high risk for extension, and in that situation we use prophylactic dose fondaparinux or rivaroxaban. For patients with cancer associated thrombosis, direct oral anticoagulants are advised, but those with GI malignancy, apixaban, or low molecular heparin may be preferred.

Other certain populations in which direct oral anticoagulants should be used with caution include those with a gastric bypass or a GI resection surgery. Then there's other patient populations that low molecular weight heparin and warfarin are preferred, including that low molecular heparin should be used in pregnancy, whereas low molecular heparin or warfarin may be used in breastfeeding. And then warfarin is preferred in patients with mechanical heart valves, atrial fibrillation with and rheumatic heart



This transcript was exported on May 25, 2023 - view latest version [here](#).

disease, or in those with thrombotic APS. So, special thank you to Dr. Scott Waller and Dr. Ann Leonhardt-Caprio for their expert guidance today. And thank you to the audience for listening.