Complex Cases in VTE: Applications to Clinical Practice

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Jori May: Hi everybody, thanks for tuning in. We are here for our last podcast in our series on venous thromboembolism in primary care. And today we're going to be talking about complex cases. My name is Jori May. I am an Assistant Professor at the University of Alabama at Birmingham, an adult hematologist that specializes in thrombosis. And I am fortunate to be joined by two experts today in hematology and primary care. Before I have them introduce themselves, I'll clarify that none of us have any conflicts of interest relevant to the discussion today and that we have discussed and we're going to use our first names when speaking to each other throughout the podcast. So, with that, Paul, if you would introduce yourself to our audience.

Paul Lewis: Yeah, thank you, Jori. Hi, I'm Paul Lewis. I'm a family physician. I've been in practice now for 20 years with BayCare Medical Group. And I'm also clinical faculty for University of South Florida College of Medicine in the Department of Family Medicine.

Jori May: Great. Thanks for being here, Paul. And Stephan.

Stephan Moll: Yeah, thank you, Jori. I'm Stephan Moll. I'm an adult hematologist at the University of North Carolina in Chapel Hill. I'm a coagulationist, and I'm specifically seeing a lot of patients and do clinical research on patients with thrombosis, anti-coagulation issues.

Learning Objectives

- Analyze complex VTE cases that are likely to be seen in the primary care setting and develop appropriate treatment plans
- Engage in case discussions and collaborative problem-solving to address challenging scenarios in VTE management, integrating the latest evidence and expert insights

Jori May: Great. Well, we're going to dive right into the discussion because we have lots of interesting cases that we can go through today. So, our objectives are going to be to analyze complex VTE cases that are likely to be seen in the primary care setting and to develop appropriate treatment plans. And we're going to engage in case discussions and collaborative problem solving to address challenging scenarios in VTE management, integrating the latest evidence and expert insights. I'll say the past podcasts have really hopefully built a foundation on which some of the concepts we're going to discuss today might rely. We'll try to, this to exist separate from those other podcasts. So, we'll try to re-address certain key concepts, try to bring some things forward that we have previously discussed. But if you want more detail, I encourage you to check those out, as well.

Jori May: So, with that, let's dive in. And with each of these kind of case scenarios, I'm going to pose to our panelists what they do with this certain type clot or a certain type of patient.

And so, let's start by talking about superficial venous thrombosis. So, oftentimes when we're thinking about treating thrombosis with anticoagulation, we're often thinking about deep vein thrombosis. But superficial thrombosis is something that often may pop up in the primary care clinic. And I think it's important to address how we might manage that. And so, Paul, if you can start off, what do you do when you get an ultrasound and you find a superficial clot? What's your first thought in approaching that?

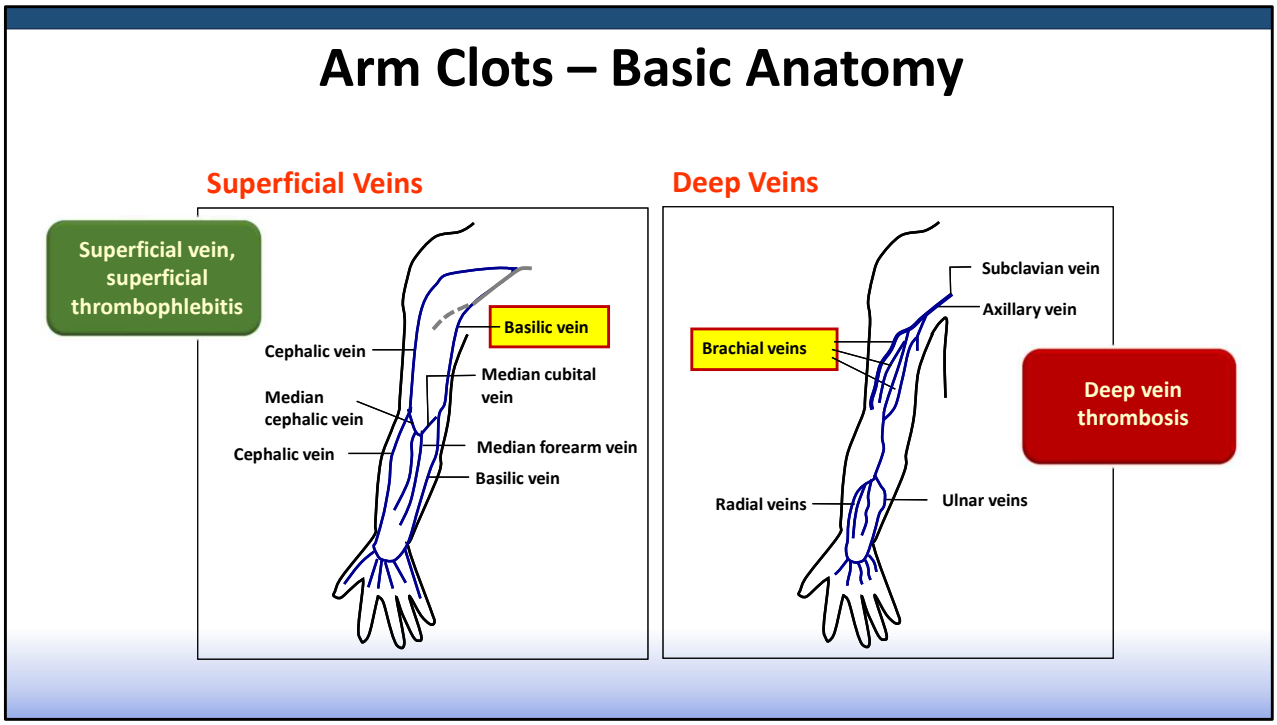
Paul Lewis: Yeah, and it's interesting because some of this too, is what is the patient's perspective on this, especially if you're having that discussion, or even if you clinically suspect maybe this is superficial, from that standpoint. But again, I think one of the things is to clarify, again, is there a deep venous thrombosis and that the vernacular is just so important. And I know there's been some efforts from a radiology perspective to really identify the veins that make up deep versus superficial, but I've seen a lot of variability in that, as I read ultrasounds from various groups. So again, as a primary care physician, I certainly will try to get to the bottom of it. I don't want to cause confusion or panic for the patients. That's probably the first thing.

And so again, as I tell the residents too, it's like, if you need to and you get on the phone and clarify, you can get ahold of these folks, that's something that maybe is sometimes helpful. But that's again, one of the first things I'll do is just to clarify that before I'm making any phone calls to the patients or any actions, so to speak. But I don't know other perspectives on that?

Stephan Moll: Well, when you say you see some discrepancies between the different radiology groups, what are you referring to? Where are the discrepancies?

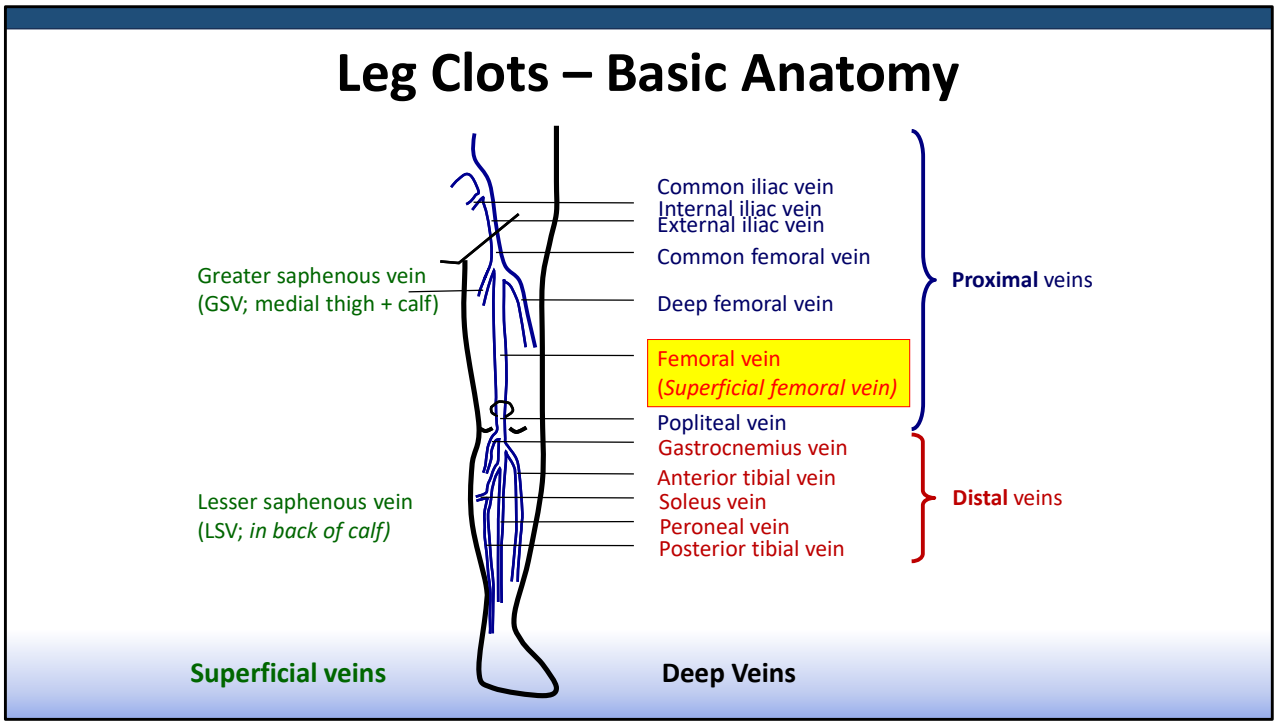
Paul Lewis: Yeah, well again, the vernacular of deep versus superficial venous based on the anatomy and which anatomy are they using, in terms of the ultrasound. So, that's where I've seen variability in the ultrasounds themselves. It's always very nice when it says superficial venous thrombosis period, nice and simple, right? And that is the case sometimes, but oftentimes there is not a nice succinct final reading and it's a lot of body of text in there. And so again, just to be cautious that I'm not missing something. I'll often give feedback to that radiology group that, you need to be more clear, but especially if I'm getting this in the middle of the night or after hours.

Stephan Moll: So, Paul, can I add to that? I, in somewhat similar manner, see some confusion. I've seen this over the years, where people confuse a basilic vein with a brachial vein.



Stephan Moll: And just to clarify, the basilic vein is a superficial vein. The brachial vein is the main deep vein proximally in the arm.

So, one is a superficial vein and superficial thrombophlebitis and the other one is a deep vein thrombosis, and that changes how we approach the management.



Stephan Moll: And then the other confusion I've seen over the years every so often is, and it almost sounds too simple, but it does happen. What's called the superficial femoral vein is occasionally taken as a superficial vein, even though it's a main deep leg proximal vein, also called femoral vein. So yes, one needs to be clear what one is dealing with.

Stephan Moll: I would like to add to that a second aspect that comes up, I see patients in clinic every so often, or not infrequently, they have recurrent clots in the past and need to be on long-term blood thinners because of recurrent clots. And I always do this myself and encourage the trainees, take a history of each single clot, because what was called a clot in the past, let's say 15 years ago, may well have been just a superficial thrombophlebitis.

So, take a history and make sure that, is it a localized symptom, localized redness, pain, swelling, which is more suggestive of a superficial clot, or was it really a diffuse ankle and calf swelling and pain and redness, which is more suggestive of a DVT? So, clinically, make some assessment like a pre-test probability assessment. This sounds much more like a superficial clot versus a deep clot. Otherwise, when a physician gets too easily into the “oh, the patient has had recurrent clots”. Thinking about DVT needs long term anticoagulation. Then the third thing to mention is it can be very helpful when the patient talks about the clot, they may just use their, with a past history of clots, they may use their hands and point towards the inner thigh, for example, the inner calf, I had pain and redness.

And you immediately think, oh, that's the location of the greater saphenous vein, the inner thigh, or they point towards the back of the calf in a very localized manner, that's the lesser saphenous vein. So, your mindset is already, maybe this is just a superficial clot in the past, realizing also that the superficial clots can extend into the deep venous system and both may be present at the same time.

Superficial Vein Thrombosis: Diagnosis

- Confirm that the clot is superficial
  - Reconfirm: is the vein cited in the ultrasound report a deep vein or a superficial vein?
- Review clot symptoms
  - Superficial
    - Localized at surface
    - Palpable
    - Patient can point to it
  - Deep: more diffuse

Jori May: I think those are some very helpful points. If I might emphasize that the first and foremost, making sure that you're actually dealing with a superficial clot. Sometimes that's a matter of, if the ultrasound report only gives you the name of the vein, looking it up and double checking is this a deep vein or is this a superficial vein.

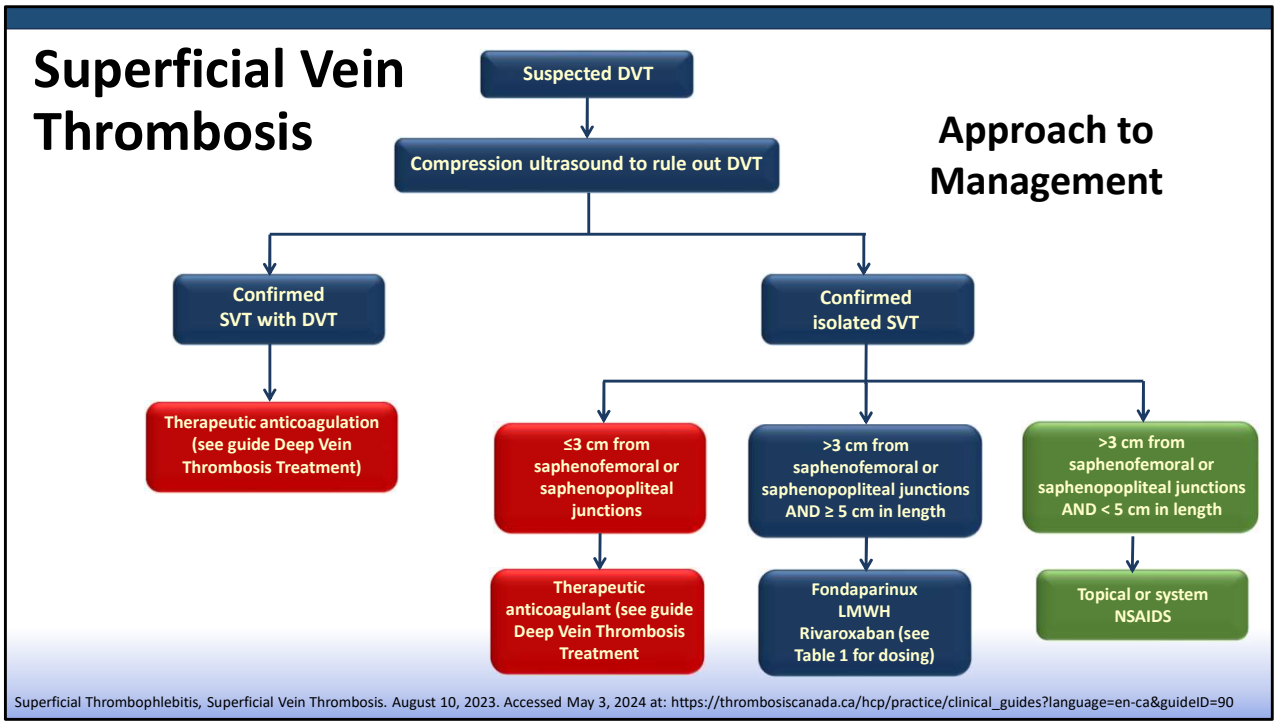
And then the second point of the difference that we see in the symptoms of DVT versus a superficial clot is that superficial does tend to be localized at the surface, can be palpable. You know, an area that usually the patient can point to rather than a deep clot, which tends to be more diffuse in the symptoms that the patient describes. So, I think, you know, really important again to highlight making sure that we know what we're dealing with first and foremost.

Stephan Moll: Jori, you bring up a point, and you've said that twice, when the ultrasound shows a superficial clot or has a clot in a vein. Now, I wouldn't think that we would always do an ultrasound. You have a localized redness, a pain, or palpable cord where you had a prophyll IV line. It's maybe three centimeters long, not very symptomatic. That sounds very much like a superficial clot. I personally would not do a Doppler ultrasound in every single case where you think there is a superficial clot. Paul, what do you think about that comment?

Paul Lewis: Yeah, again, upper extremity in the hospital or recent IV, I think you have a lot more of a causality there. Makes sense. I'd be more comfortable with not doing an ultrasound in that case. You've got that almost a cause-and-effect in that scenario. So, it's a good point. Save some resources, save some time. And if you can just go ahead and make that diagnosis and then give somebody some treatment pearls off the bat, that's always very helpful.

Jori May: Absolutely. That's a great point. And so, then brings us to, so, what do you do in that situation? So, whether it's on ultrasound or based on symptoms, you've diagnosed a superficial clot. Stephan, what's your treatment approach for a patient like that?

Stephan Moll: Well, I have to tell you, as a hematologist, I often don't see these patients in the acute setting. I get more consulted afterwards. Maybe they had a DVT plus a superficial clot with the question long-term blood thinners, yes, no, or they had a superficial clot. Should we discontinue at a certain time? However, we've created this DVT walk-in clinic here at UNC where patients with acute clots come in that are seen by our physician assistant.



Stephan Moll: So, increasingly over the last two years, we have had these cases, typically not the ones that Paul, you mentioned, the hospitalized patient with a catheter-associated small clot, but if the superficial clot is not very extensive, that means less than five centimeters, two inches, not very symptomatic, then classically observed and we don't treat with anticoagulants. If it's a more extensive clot, more than five centimeters or fairly symptomatic. or there's a persistent risk factor for the clot, or it's close to the deep inner system, then we think about treatment. And if it's really the smallish superficial clot associated with a phlebotomy stick or IV line and the IV line is now out, then I mean, some people use ice, some people use hot compresses, whatever makes a patient more comfortable. There's been a Cochrane database publication review of the literature. And really, barely any of these methods have been systemically investigated. People use nonsteroidals for pain relief, and that makes sense for the anti-inflammatory effect. In fact, that makes sense. But with these small clots, there's really symptomatic management and no anticoagulation.

If it gets to the bigger ones, then the more proximal, closer to the deep system, anticoagulation comes in. And if it's more of the extensive one, then the two drugs that have been studied and the one that has been best studied is one that we don't really use much, fondaparinux as a subcutaneous drug at a prophylactic dose. And that's really important to keep in mind. It's a prophylactic dose that was studied against no anticoagulation, New England Journal of Medicine. And the fondaparinux was beneficial in decreasing progression of clot.

Superficial Vein Thrombosis: Treatment

- SURPRISE trial: 45-day treatment of superficial vein thrombosis, rivaroxaban 10 mg versus fondaparinux[1]
  - Rivaroxaban 10 mg non-inferior to fondaparinux
- Apixaban at prophylactic dose
- Low molecular weight heparin at prophylactic dose

1. Werth S, et al. Superficial vein thrombosis treated for 45 days with rivaroxaban versus fondaparinux: rationale and design of the SURPRISE trial. *J Thromb Thrombolysis.* 2016 Aug;42(2):197-204.

Stephan Moll: The recurrent clot, they treated for 45 days, pulmonary embolism development, even though those side effects all were pretty uncommon, even in the placebo-treated group. Then there has been a second trial that was more recent, probably now six or seven years ago, the SURPRISE trial, where people then looked at rivaroxaban, again, a prophylactic dose, the 10 milligram. And they compared it to the, at least the scientific gold standard, which was the fondaparinux at prophylactic dose, and the rivaroxaban was non-inferior to the fondaparinux. So, really by data set, if one treats a superficial clot with anticoagulation, then a prophylactic dose of rivaroxaban is very reasonable. In my practice, in our practice here, we often say, well, if rivaroxaban is effective, we can equally use apixaban, and we use apixaban at a prophylactic dose. Some people then also say, well, if fondaparinux is effective at prophylactic dose, we can also use low molecular weight heparin at a prophylactic dose. And we can do that empirically and non-evidence-based and it makes sense to me. And then the length is a little more poorly defined. The two studies that I mentioned treated for 45 days, which is fairly long period of time. And some shorter periods of time may well be sufficient for some people.

Superficial Vein Thrombosis: Treatment

- At indication for treatment:
  - Prophylactic dose of DOAC
  - Evaluate after 2 – 6 weeks
  - Anticoagulation may be stopped when patient is asymptomatic
- For clots close to the deep venous system (e.g., 3 cm of deep junction with femoral vein):
  - Full-dose anticoagulation
  - Consider treatment for 3 months

Stephan Moll: So, my clinical approach is that if there is an indication of treatment, I say, let's use a prophylactic, typically a DOAC. And I tell the patient, maybe for two or four weeks, let's see how you do. It may be up to six weeks. But once it becomes fairly asymptomatic, the swelling is down. It may well be appropriate to stop the anticoagulation after two or four weeks, depending on how big the clot was.

If the clot was close to the deep venous system then it may make sense to use full-dose anticoagulation because that is almost a DVT. It's a little moving, not really written in stone, but if it's, let's say, within three centimeters or so of the deep junction with a femoral vein, I probably would use full-dose anticoagulation, then I probably would go for three months as I would treat a DVT that was triggered by something.

Jori May: I think that's helpful. And another thing to maybe emphasize is you're describing in all of these people a limited duration of anticoagulation. Maybe to highlight, is there anyone with a superficial clot that you would consider anticoagulating for a longer period of time? Or is that kind of clearly superficial clot, only a limited duration?

Stephan Moll: It's typically a limited duration, but I also mentioned if there's a persistent risk factor, such as malignancy, we do know that people who have a superficial clot have a higher risk of future DVT and PE, and they have some risk of recurrence. So, if there's a strong persistent risk factor, it may be appropriate to think about longer-term anticoagulation. We're talking about prophylactic anticoagulation anyway. So, I might consider that.

Jori May: Well in my practice, I'm very similar. I think that ideally, a patient doesn't require anticoagulation conservative management upfront for small clots. For larger clots, as you mentioned, anticoagulation and really encouraging limited duration. I see people in my practice, again, kind of you mentioned before, some confusion. And they are under the impression that because they've had a superficial clot that was maybe without clear risk factors, that requires indefinite anticoagulation as you would for a deep clot. But I think we know that the risk of developing a deep clot is there, but kind of generally accepted that for a superficial clot, longer term is not necessary. That being said, if someone had a superficial clot without a clear reason, we have to be aware of that they may be at risk for that happening again. So of course, things like modifying any behavior to prevent VTE, physical activity, other things that we know can help prevent thrombosis are important to consider. But in general, I think limited duration is what I lean on.

Stephan Moll: Jori, the situation that I also see is that a patient had a superficial thrombophlebitis in a varicose vein and one treats the superficial clot, for let's say, four weeks and the symptoms resolve but the patient's at higher risk for recurrence because they continue to have a varicose vein typically and then the question comes up, should one remove the varicose vein and involve vascular surgery? And I typically say, not after the first clot. They may have had varicose veins for the last eight years. This is the first clot in a varicose vein. I typically say these are not dangerous per se. The risk for PE is really low. The risk for progression is low. One clot in a varicose vein, treat until you say, it's in the vein and then observe. But if there's a second episode of a clot in a varicose vein, then I argue, look, you've shown that you clot in this varicose vein. Let's send you to vascular surgery and they can discuss the endovascular laser ablation.

Paul Lewis: And, Jori, if I could just comment again, as we started to say, the majority of these cases, I'm taking care of at the primary care. I can only think of a handful I've sent to hematology because they're so complex, but a large preponderance of them, we're doing NSAIDs and, you know, heating pads and trying to determine just what caused it. So, it's really helpful to have this background information from you both.

Jori May: Absolutely.

Jori May: Okay, so now we're going to dive into venous thromboembolism in travel, long distance travel. So, we know that long distance travel can increase the venous thrombotic risk. But there's a lot of nuance to how we manage patients in these scenarios. So, let's first think about a question that I'm sure Paul, you get in your practice is, someone who's never had a blood clot before, but they're getting ready to go on some sort of long distance travel, whether they're flying by plane or they're going on a long car trip. I wonder if you could take us through any sort of counseling that you give to those patients, as well as things that you might consider, other risk factors that might put them at higher risk during their period of travel.

Paul Lewis: Yeah, absolutely. And surprisingly, you get this question a lot. And I guess that's a good thing because people are aware. If we think back maybe even 10 or 20 years ago, people were perhaps less aware of blood clots in general. So, to me, it's great that people are aware. But then of course, then there's always a lot of fallacies that they may have on this. But yeah, I definitely get this quite a bit. And so, in terms of what I do is, determining where they're going, how far it is, what's their mode of travel, are they able to get up and stretch intermittently or at least move their legs from that standpoint? And then, what are their, as we've discussed a few other times, what are their other major or minor risk factors that might put them at risk for getting a thrombosis overall and looking at that? So, I've generally used in terms of my definition, if somewhere between four to six hours as that threshold where they may have an increased risk of thrombosis. And then again, much like we would do with a preoperative patient, what other risk factors do they have? Do they have obesity? Are they on birth control pills? Is this any sort of family history? If we get into that degree of depth, oftentimes it's not, but they do want to know what to do and how else they can prevent it. So that's at least my kind of my initial approach in having that discussion with these patients.

Stephan Moll: And during my length conception is more like longer or intermediate travel is six to eight hours. And I don't see the primary patient so much, but I see patients who never had a clot, but their family member had a clot. So, they wonder, should I be on blood thinners? And I often say, most patients don't need anything. But, if it's more than six, eight hours to a different continent or from the East Coast to the West Coast without any interruption, then maybe some patients that were at higher risk with a family history or the very obese or recent surgery might benefit from anticoagulation.

VTE and Long-distance Travel

Recommendation 17

In long-distance (>4 hours) travelers without risk factors for VTE, the ASH guideline panel *suggests* not using graduated compression stockings, LMWH, or aspirin for VTE prophylaxis (conditional recommendation, very low certainty in the evidence of effects ⨁◯◯◯).

Recommendation 18

In people who are at substantially increased VTE risk (eg, recent surgery, prior history of VTE, postpartum women, active malignancy, or ≥2 risk factors, including combinations of the above with hormone replacement therapy, obesity, or pregnancy), the ASH guideline panel *suggests* using graduated compression stockings or prophylactic LMWH for long-distance (>4 hours) travel (conditional recommendation, very low certainty in the evidence of effects ⨁◯◯◯).

Schünemann HJ, et al. ASH 2018 guidelines for management of VTE: prophylaxis for hospitalized and nonhospitalized medical patients. *Blood Adv.* 2018;2(22):3198–3225.

Stephan Moll: The American Society of Hematology came out with a guidance document in 2018, and they state that in patients without any significant VT risk factors who just travel long distance, even if it's really long distance to New Zealand from here they suggest not to use any compression stockings or low molecular weight heparin or even aspirin. Aspirin, one wouldn't think is very effective in venous clots anyway. So, if there are no significant risk factors, no prophylaxis is really needed.

But if the patient's at substantially increased risk such as recent surgery, major surgery, a fairly big surgery, or they have a history of previous VTE, are not on long-term anticoagulation, or they recently had a delivery, or they have an active malignancy, maybe if they have birth control pills and have a body mass index above something 35 or so, then it would be appropriate to think about some DVT prophylaxis. And the ASH Guidelines, based on a lack of data says, well, anything really is possible. You can wear graduated compression stockings. You can give low molecular weight heparin. And they say for anything, maybe more than four hours. Now, while they speak out for low molecular weight heparin, and this was 2018, six years later, we often use the direct oral anticoagulants.

Stephan Moll: And that's what I often do in the patients who've had a clot before, who are not on anticoagulation anymore. But we know they're at higher risk because of a previous clot. Now they fly long distances. That's when I say anything more than six hours, take one pill of a direct oral anticoagulant, one to two hours before you fly. It has a main effect at three hours to four hours after intake. And then the apixaban lasts for 12 hours or a little more. Rivaroxaban for 24 hours. So, just take one pill before you fly. And then before you return, you do the same thing.

That's fairly easy to do. And the patients I see who've had a clot before, who are at higher risk with future travel, they've been on a DOAC before, you know they're tolerated well. A risk for bleeding with one pill is low. However, if I recommend this to a family member who's never been on a DOAC, but is at higher risk because of the family history, I say take one pill at a time when you don't fly to make sure that you tolerate it well, that you don't have an allergy or something and suddenly on the plane you break out because this is the first time you've taken an apixaban or a rivaroxaban pill.

Paul Lewis: So, Stephan, again, this is an interesting concept for me. So, in a patient, if they had a very high risk, then it is reasonable to go ahead and give a dose of, or a few doses, of the apixaban to take with them. We do this with a lot of other things when people travel, antibiotics, et cetera. So, it's interesting from a thrombotic standpoint to give them some, apixaban or rivaroxaban to take with them prophylactically. And again, in internal medicine, we do a lot of drugs. It's pretty exciting to think now we can do this with thrombotic medication too.

Stephan Moll: Yeah. And my practice is that I just recommend one pill before you fly and one pill before you come back. I have seen colleagues who then say, well, take the pill for another two or three days after you arrive. I don't buy into that, but it wouldn't be wrong. There's just a lack of data. Jori, what do you do? What do you recommend?

Jori May: I similarly, I do often go for a day or two after travel. I don't necessarily have reason for that, but just out of concern that if, you know, there is still a prothrombotic period that continues, or if some amount of thrombus starts in the setting of travel, a day or two gives me more peace of mind. But to your point, I don't have any rationale for that. The one thing I'll add to the conversation is that sometimes it's difficult to get insurance approval for this indication.

I've run into issues where people initially, I'd say I have a patient who's had a VTE in the past, they have some leftover apixaban that they can take and we've set up this expectation that they take it with travel. But then they have trouble filling a new prescription without necessarily a new VTE diagnosis. So, we ultimately are able to navigate that, but I do want to put that out there, as sometimes that can be a barrier for patients, particularly in someone who maybe hasn't had a clear blood clot in the past.

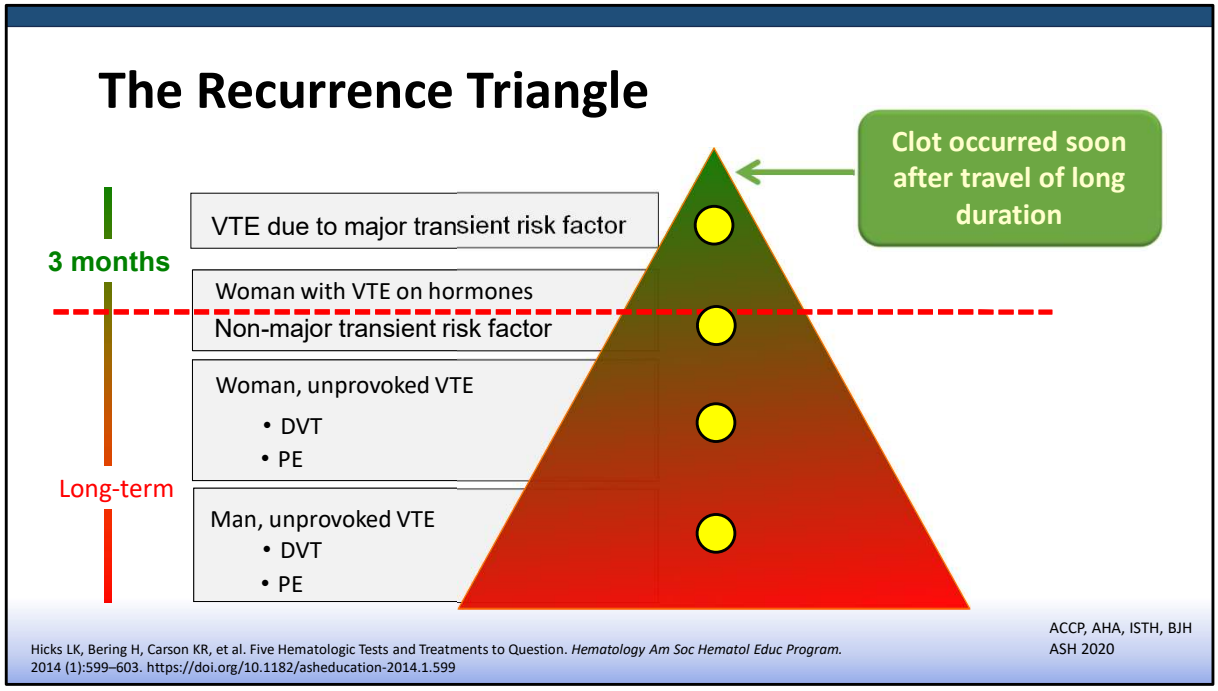
Jori May: Yeah, so great discussion. I think, you know, a lot of nuance here. Another area with travel-related clotting that I think is complicated is, how can we say that a clot is related to travel or not? So, we have a patient who traveled and now has a blood clot. And so, in our discussion earlier in the podcast series, we talked about things being major transient risk factors.

So, a major risk factor that happens and improves, that's the patient that can be on anticoagulation for a limited period of time versus a blood clot that's what we would call unprovoked or there's no major transient risk factor. The concern being that patient has ongoing risk and therefore that patient would require longer term or even indefinite anticoagulation. So, I find traveling really difficult because how much travel is enough travel to say that the clot is related?

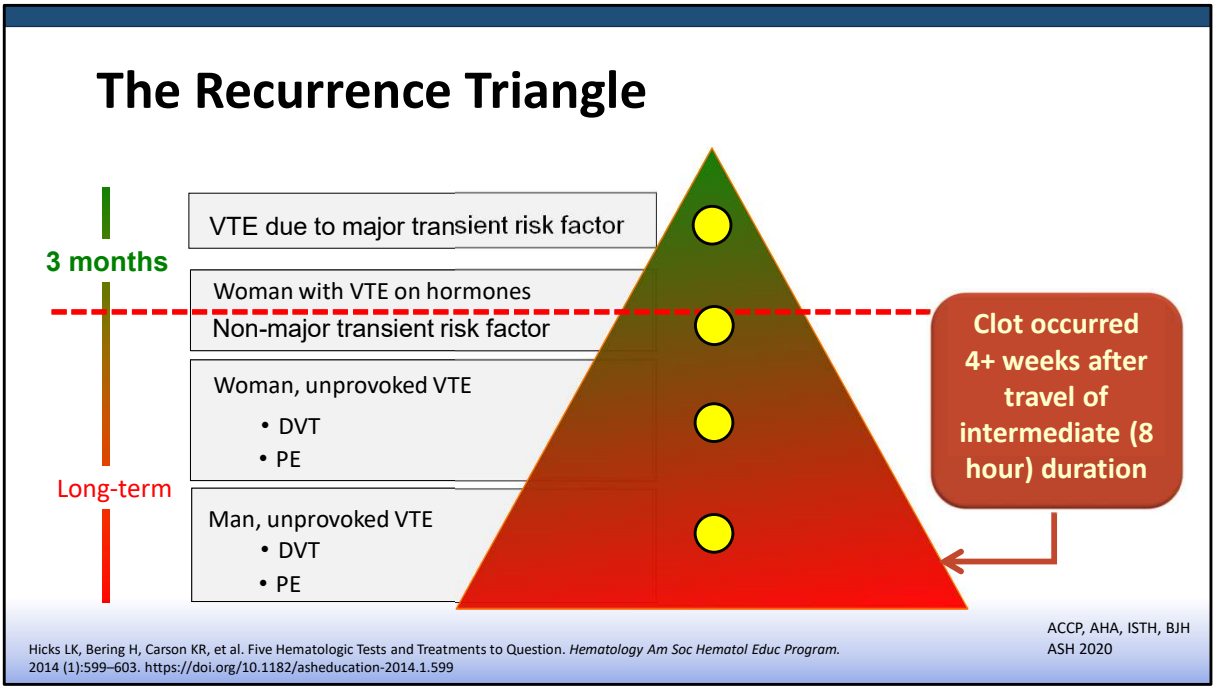
And so, I wonder, Stephan, if you could give us a little bit of a framework of how you think about that, certainly considering other risk factors that the patient might have, but in a patient that doesn't have any other risk factors, what's a travel situation that you feel comfortable saying it was significant enough to cause a VTE?

Stephan Moll: Good question. So, in general, in clinical trials, one considers any risk factor within the preceding three months of the diagnosis that may have contributed to the clot, be it a surgery within the last three months or be it major trauma within the last three months. So, you could say that to you if there was any significant travel in the last three months, maybe it contributed.

But as you get more removed from the airline travel or from the long-distance travel, the contribution is much less and gets much more questionable. So, I want to know how soon after the travel did you develop the leg symptoms? Often that's been present for a week or two before they finally seek medical attention. So, I try to nail it down. But if the symptoms occurred four or six weeks after a 12-hour car ride, I'm really not very impressed by that. But if it's within one or two days of the travel, then I'm much more impressed, and it probably contributed more. Often the airline travel is not a strong contributing factor. It's the multiple other risk factors, the body mass index at onset and the birth control pill, etc.



Stephan Moll: So, I put these people, because of the lack of real data, in our recurrence triangle that you addressed a little bit the broad base of the triangle, the high risk for recurrence, that's a patient with a truly unprovoked clot, long-term blood thinners, and the tip of the triangle, low risk for recurrence if you stop and we treat only for three months. It's kind of where somewhere in this intermediate, I don't quite know how much that it contributed but if it was very close to the airline travel, and it was really a travel of 12 hours or 16 hours, then that's really much more of a significant transient risk factor and I may think about short-term blood thinners.



Stephan Moll: Whereas if the clot happened four weeks after an eight-hour travel, I would think that's probably not significant contributing. That's more in the lower part of the triangle, more like an unprovoked clot, more long-term anticoagulation.

Paul Lewis: So again, just to clarify, it's really a good point to drive home or Jori, your expertise. So, less than two days that airline travel, especially if it was a longer duration, may have a higher degree of causality as opposed to one week, two weeks or greater. And so, I'm just trying to say in terms of a threshold, so a few days is maybe a week, possibly greater than a week or two, probably not. Is that fair?

Stephan Moll: Maybe that's fair. I'm thinking more in the kind of four weeks or more. I'm unimpressed, probably unprovoked. If it's someone that lasts four weeks and it was a long-distance travel, maybe it's more related because you can postulate it was a small distal DVT initially, then over the next few days, over the next two weeks, progress to form a more proximal DVT. Unfortunately, that's such a vague concept.

But if you really want to make it black and white, I would say anything more than four weeks, I'm unimpressed. If it's within four weeks of a travel, I'm more impressed. And then clearly the length of travel and did the patient sleep while flying to New Zealand, pop in a pill and then didn't get up for eight hours or a car ride of 12 hours. And they just stopped very briefly once or twice versus they had crying children in the back and they had to stop and interrupt multiple times. That all factors into it, but it feels, I wish I could give more guidance here on this podcast, but it's such a gestalt kind of thing. And I may be wrong with this, but that's how I approach it.

Jori May: Yeah, I take the same approach. I do think that I have a, I have to have a high threshold, right? Because I, you know, we know so, so many people travel and for these durations, and we know that the risk is there, but it's relatively low risk. So, it really has to be, you know, in close proximity for really long travel and someone who really didn't move around in order for me to feel comfortable that it is truly related to travel and therefore anticoagulation can be safely stopped.

Primary, Secondary Prevention/Risk Assessment in Patients at Highest Risk for VTE

- 32-year-old woman
  - Smoker
  - Takes oral contraceptives
  - Planning a trip to Europe

Jori May: Great. Okay, so let's do, you know, we're kind of venturing into this idea of VTE prevention because I think that's something that, you know, Paul, you can speak to, maybe that primary care doctors get asked about a lot. You know, I think what I'm going to do is pose some specific scenarios and kind of get your input on what you would do for this patient for prevention of VTE. So, we already talked about travel, but let's kind of make you put your mark down of what you would do for this patient, a 32-year-old female who is an active smoker. She's on oral contraceptives and she is planning an eight-hour trip to Europe. Is that a patient that you would talk to about anticoagulation or compression stockings? What would you do in that patient? Maybe I'll go to Paul first and then to Stephan.

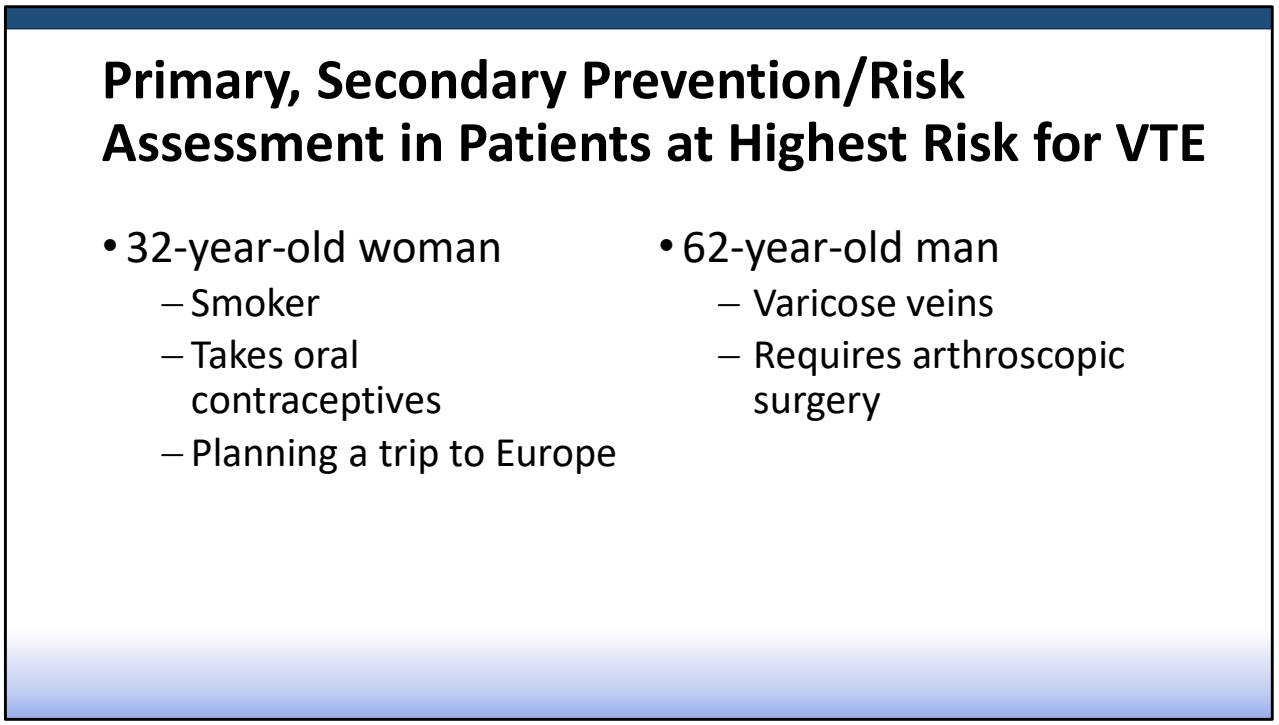
Paul Lewis: Yeah, I guess the first thing I would do is find out who put her on the oral contraceptives and hopefully they did some counseling on the smoking and hopefully it wasn't one of my residents, hopefully it wasn't a resident physician. But yeah, I mean clearly, the individual has some risk factors there and at a minimum I'd be counseling to be very active. Perhaps again, if you have any success in the smoking and decreasing or stopping it at least we can't smoke in the plane anymore. But those would be a few things I would do initially. But I'd be concerned this person, especially if they're going to sit there in the row for 12 hours and not move, that they may develop a thrombosis.

Jori May: Stephan, what do you think?

Stephan Moll: I would not give this patient, would not recommend anticoagulation. Yes, she has some risk for this. Smoking is a very minimal risk factor for venous clot. It is active smoking, but it increases risk 1.2, 1.4 fold. The absolute risk is really low. And yes, birth control pills are a risk. And then the smoking on top of that multiplies it some. But the absolute risk overall would be low. Unless there's something else, her body mass index is 32 or 35, unless there's a family history on top of that. So, in general, I would just say routine, move around every so often, but I would not give chemical drug prophylaxis. Stockings, I'm not a big friend of them because they often don't fit right, they cut into the flesh and they may actually, in my mind, may make things worse. They may prevent some of the swelling that people just develop because of the hypobaric pressure up there. But, if they don't really fit well and they're cut into the tissues, I'm not sure they're really beneficial in patients. So, this patient, I would not give anything. The other thing, and this is also a recurrent theme throughout our podcasts. You also want to know in general, how pro-thrombotic is this person? If this is a 32-year-old woman, she's been pregnant three times before while she was smoking and she never had a clot. She had two C-sections and she didn't clot. You know she's not a clotting nightmare. On the other hand, if she had never had any predisposing situations where she could have had a clot, then it's much more unclear how prothrombotic she is. Still, the absolute risk of this patient would be low.

Jori May: Yeah, I think those are important points. And a couple of things to highlight there, right, is behavioral counseling is so important here. Even if we can educate a patient on getting up frequently during the flight rather than sitting for 12 hours, I think that's a really important piece. And that there are so many, as much as I can try to make a case simple and straightforward, there's so many more questions to be asked. I think just highlighting that really understanding the patient, their individual risk is so important because risk is not one set of factors, it's a combination of so many things together.

Stephan Moll: And then the education part, and we've addressed that also, and we've talked about the bookmark that at least we in our hematology clinic use. I make a point to tell the patients the four symptoms of DVT, the swelling, pain, redness, warmth, typically diffuse, and the four symptoms of PE, shortness of breath, chest pain, unexplained cough, and a fast heart rate when you're not doing anything. And the bookmark allows us to give it to them before their flight or whatever they do before the surgery and they may remember it or may not remember it, but at least there has been some initial education.



Jori May: So, let's move to some specific scenarios in surgery. And you know, I think we know when we're thinking about joint surgeries, major knee replacements, hip replacements, those are things that are recommended to have anticoagulation prophylaxis for thrombosis prevention. But what arthroscopic surgeries in general, we don't recommend anticoagulation prophylaxis, but there is a thrombotic risk with any procedure and with anything that might require some immobilization.

So, let's go again to a specific scenario. A 62-year-old gentleman who's going to have arthroscopic surgery, but we know he has significant varicose veins. And how that might change our calculus and if we would think about doing anything differently in that patient. And Paul, I'll go to you again first and get your thoughts on this gentleman.

Paul Lewis: Sure. Yeah. Yep. So, significant varicose veins. It would give me some pause, right? As you mentioned, we don't typically think of arthroscopic surgery as being a major prothrombotic event. Of course, we always want to take a good history and see what other risk factors they may have, if any, because again, the nature of thrombosis being multifactorial. But there was concern then, again, I mean, one thing is making sure that, during the surgery itself, that they have appropriate compression during the surgery. If there was a big concern, again, I may at least give a phone call to my friendly neighborhood hematologist to have a discussion, but I think they would have to have some other risk factors before I would do anything, other than being active and try to counsel them.

Jori May: Stephan, any other thoughts on that case?

Stephan Moll: I like the term that Paul uses, it gives me pause. One doesn't necessarily immediately need to know what to do, but just to pause and think, okay, what about the body mass index? What about the family? Is it just get, what are the risk factors? Arthroscopic surgery, yes, does not need prophylaxis in all comers. But when you say the 62-year-old with significant varicose veins, the patient probably has had significant varicose veins for the last 10, 15 or 20 years and never had a clot, right? So, this patient has already told you, I'm not very clottable. So, that is the pause where I say, okay, well, he's not at huge risk, even with the arthroscopic knee surgery. But as a hematologist, I see patients who've had a DVT, so I'm biased towards giving DVT prophylaxis if there is some even not huge risk, but somewhere, pause and say, there is some risk to it. So, with significant varicose veins in the 62-year-old man with arthroscopic surgery, I probably would say, prophylactic anticoagulation is fairly safe. Yeah, I would do this for how long? A week or two, apixaban 2.5 BID or rivaroxaban 10 QD or enoxaparin 40 once daily. I probably would do that if then also the finances and the patient is agreeable to that. And the surgeon's agreeable to that too.

VTE and Major Orthopedic Surgery

- Patients having total knee or total hip replacement are at increased venous thrombotic risk
- What is appropriate postoperative prophylaxis?
  - Aspirin BID
  - Enoxaparin
  - DOACs

Jori May: So, we mentioned arthroscopic surgery, but let's actually circle back to more major orthopedic surgery, like total knee and total hip replacement. I think we know that those patients are at increased venous thrombotic risk. And there's a lot of debate about what appropriate postoperative prophylaxis looks like, whether that's aspirin twice daily, whether that is enoxaparin. And I'm curious, Paul, if you've run into issues with this in your practice, or if you get looped in into any of those discussions on making decisions on what to use in the post-operative period for major orthopedic surgery.

Paul Lewis: Yeah, I would say, I sure do. Because this is, oftentimes you've seen these patients for preoperative clearance and for heart and vascular causes or respiratory causes. But again, to be complete as you're thinking about, what are the other risk factors with any surgery, we have to think of thrombosis. And something that I've seen in the orthopedic literature and I've also seen in the hospitals, they, many of these post-op hip and knee patients are placed on aspirin twice a day. And many do fine on that aspirin twice a day, but then I struggle with the patient that has maybe a few more risk factors than none. And how would we approach that? So again, I would love your opinion, perhaps Jori, of how you would approach somebody who has maybe some major or minor risk factors and they're about to go for an orthopedic surgery and you fear that they're going to end up in that camp where they're going to get the 81 aspirin BID and you'll see them in a week with their blood clot or worse, their PE. Love some guidance on that.

Jori May: Right. Yeah, you know, I think this is a challenge I see, you know, that our health system deals with frequently and there's conflicting literature and even professional society guidance on what to do here. I do think a lot of times, in the orthopedic surgery literature, the default has become aspirin twice daily, based on some clinical trials that suggested that there was not an increased risk with that regimen of kind of more significant venous thromboembolism, although the data does suggest potentially a higher risk of deep vein thrombosis, maybe more distal than proximal. Ultimately, the challenge is that a lot of times the patients that we're seeing are not that clinical trial population. As you mentioned, those patients that have multiple other risk factors, which is a theme that we keep coming back to in this podcast. So, what else is going on with that patient? Are they obese? How mobile are they? Do they have other risk factors related to their surgery? So, I see sometimes that we use the aspirin regimen that was based in studies that was kind of a routine total hip, total knee. But what about those patients where this is a repeat surgery? What if they have an infected joint? That patient, in my mind, is not necessarily appropriate for aspirin. And someone where I do try to advocate in those people who do have additional risk factors who would not have been included in those clinical trials that supported some use of aspirin to really use true anticoagulation for venous thrombosis prevention.

Paul Lewis: That's really helpful and it is interesting because more and more patients are being done with these surgeries as in outpatient surgery centers. And so, I'm wondering in my head, as you gave that guidance, that perhaps we still do the more complicated ones in the hospital, perhaps that's a defining line, almost by itself. If you're more complicated or either medically or because it's a revision or something, that's going to be done in the hospital. Perhaps those folks do need more than the usual, whereas the other, more healthier population, outpatient surgery could probably do just fine with the aspirin twice a day. That's really helpful.

Jori May: That's a great point. Yeah, absolutely. So yes.

Stephan Moll: Jori, I'm not much involved in DVT prevention after orthopedic surgery here, with guidance document at my institution, but question to you, if you're involved in that, what about a patient who needs a hip replacement, let's say a 62-year-old, who has a body mass index of 36? Would you and the orthopedic colleagues want to use aspirin? No other risk factors, just the BMI and the hip replacement, what would you use?

Jori May: You know, I think my default and preference is always going to be anticoagulation. I mean, as I've personally reviewed the literature, my concern is that aspirin is really may not be sufficient and particularly in people who have additional risk factors. And I think we know obesity is a risk factor for initial venous thrombosis. We know that can affect post-surgical recovery as well. It might be harder for that person to, you may, a person who is not as fit, maybe will not ambulate as much in the post-operative period.

So, certainly something to think about. I certainly understand the concern about bleeding risk. That's always maybe the reason for some hesitation about using anticoagulation over antiplatelet therapy and that the health of the joint is so important and we don't want bleeding into that joint. But I don't think that the literature consistently suggests that enoxaparin has a higher bleeding risk necessarily than aspirin twice daily.

I think access is a big issue too that I hear from our surgeons, making sure that the patient can get enoxaparin where aspirin is cheap and easy. But obesity does raise a light bulb for me that I might be more concerned that patient should be on enoxaparin.

Stephan Moll: So, you mentioned enoxaparin, what about the use of the direct oral anticoagulants after the chart replacements?

Jori May: Yes, so I, it's a great point. I mentioned enoxaparin because that's come up in some of the newer clinical trials. The direct oral anticoagulants have been studied, as well. I do think in working with surgical colleagues, some do still have more hesitation about those medications, more comfortable with the idea of enoxaparin, although we know that the half-life of those medications are not hugely different. So, just from a bleeding risk perspective, that's sometimes their concern. It's a great point and that is certainly in the repertoire of what you can use in the post-operative period.

Stephan Moll: And it addresses, thank you, Jori, it addresses an issue that's an overarching topic throughout the podcast. Aspirin is not very effective on the venous side, in general. Aspirin is effective in the high flow arterial side. It has a little bit effect on the venous side. It has a little bit effect in unprovoked clots for prevention of, but it's not very effective compared to anticoagulants.

VTE and Major Orthopedic Surgery

- Patients having total knee or total hip replacement are at increased venous thrombotic risk
- What is appropriate postoperative prophylaxis?
  - Aspirin BID
  - Enoxaparin
  - DOACs

Assess each patient's multifactorial risk for VTE and use most effective anticoagulant for each individual patient, generally enoxaparin or a DOAC

Jori May: We're in agreement. This is always a challenging topic. So, I think, you know, encouraging folks to really assess that multifactorial risk and to have conversations about, you know, what's really most appropriate for an individual patient is key there.

Upper Extremity DVT

- Patient receiving home antibiotics with a PICC who then gets a swollen arm
- Diagnosed with upper extremity catheter-associated VTE
- What is the next step?
  - Removal of the catheter?
  - Anticoagulation?

Jori May: So, another unique situation that we might run into is upper extremity deep vein thrombosis.

And so, if we can maybe talk initially about that situation where we have a patient who has a central line for home antibiotics, they come into your office, they have a swollen arm, they're found to have an upper extremity deep vein thrombosis. What are the considerations for line-associated VTE in the upper extremity? I think the question I always get is, does the line need to come out? What do we need to do? Do we put the patient on the blood thinner?

And maybe I'll go to Stephan first. You know, what do we know about upper extremity catheter-associated VTE?

Stephan Moll: I think that's fairly straightforward, at least in my mind. The DVT is likely going to be a proximal arm DVT. A proximal DVT should always be treated with three months of anticoagulation if the patient tolerates it well. So, in this case here, a DVT, and let's say it's in the brachial vein, three months of anticoagulation. Longer if the PICC line is still in place. Because what caused the clot? In this case, it was occlusion or the partial occlusion with the central venous line. So, at least three months and as long as the line is in.

The second question that you ask is, does the PICC line need to be removed? No, it does not, unless the patient is severely symptomatic and you want some flow channel to open up again. But this patient needs anticoagulation and then the clot will start to dissolve, collaterals will open up and the PICC line is needed. So, there is no need to remove it unless there's severe symptoms. This also comes up not infrequently with patients on dialysis who have central venous lines and they have a central venous line-associated clot. It's really the typical concept is, you need to be treated as long as the obstruction is still in place, at least three months and as long as the obstruction is in place.

Now there's certainly some modifying risk factors. You mentioned that this patient also has an infection. So, the infection is a risk factor for clots. So, here, I would go through my typical, why did the patient have a clot, my ABC risk factor identification: a PICC line, an infection, inflammatory disorders. And then we would go through the usual, what about hormonal therapy, or maybe this patient has chemo, maybe the PICC. I'm getting, the point I want to make is, not to forget about potential other risk factors that may modify the treatment somewhat.

Jori May: Yeah, that's helpful. I think the other situation that sometimes comes up is, unfortunately, patients who are sick enough to require central venous access may require it again in the future. And so, I wonder what you think about, well, I have a patient who's had a PICC-associated DVT in the past, and unfortunately, they have a new infection and they need a new PICC line. So, what do you think about in that situation and how might you handle that patient?

Stephan Moll: Good question. I'll use Paul's term from earlier. It gives me pause. This patient has shown me in the past that they like to clot. Now they have a similar situation as they did before. So, then I think, maybe this patient should have DVT prophylaxis. However, I also wonder, with the first PICC line or central venous catheter insertion, was a very traumatic process? There was a lot of trauma, swelling, and that's why they developed the clot. Or was it a completely smooth, easy one that it's really just the central venous line that caused the clot? So, I would want to think about that too, but in general, I would think, hmm, similar situation, maybe we should give DVT prophylaxis. For how long? As long as the line is in place.

Jori May: Absolutely, that's helpful to think about.

VTE and Cancer

- Cancer increases the risk of VTE
  - Primary prevention and use of prophylaxis (Khorana Score)
  - Selection of anticoagulant in a patient with VTE and active cancer
  - Limitations with intraluminal malignancies
  - When to stop in patients who are “cured”

Jori May: And so, I think we have time to run through one additional case and one scenario that I think shows up frequently in clinical practice, particularly within primary care and elsewhere, is the question of cancer and venous thromboembolism. We know that cancer increases the risk of VTE, but what are kind of some nuances of considering VTE prevention and treatment in people with cancer? So, I guess if we can first talk about primary prevention, I think this is an area that comes up, is sometimes addressed by the patient’s oncologist, but sometimes not. I wonder, Paul, if you have patients in your practice, patients with cancer, do you think about or talk to them about VTE and VTE prevention? Or is that really, kind of in the oncologist's wheelhouse more than yours.

Paul Lewis: I would say that most of the time, and my colleagues would probably agree with me based on surveys, they would say, well, that's the oncologist's job, right? I mean, but again, my counter to that, and when I tell when I work with residents is, well, we're all on the same team and where it's a team sport, taking care of patients. So, you need to think about that patient in front of you. So, when I see a patient with cancer, an active cancer, I do think about that fact very often. I like to think, well, the oncologist has this, so I need to trust the oncologist. But again, our poor hematology oncology colleagues are so busy and sometimes there's extenders and lots of different handoffs. So, I just assume it has not been addressed and I will say, okay, what is this patient's cancer and are they actively being treated for that or not? If I'm concerned, I'm getting on the phone, I'm calling whoever is treating them at that point. That's at least how I try to approach that visit. Again, it's usually for a physical, it's something totally unrelated for their cancer, med refill, but you got to think about it as a team sport.

Jori May: Yeah, I think it's a great point, you know, and there is emerging literature and guidelines support the use of primary prophylaxis in people who are considered to be high risk for VTE that have cancer. There is a risk score that helps us make that distinction called the Khorana score. But the data does suggest that there has not been a lot of uptake of that, just because using anticoagulation in people with cancer is really complicated, and how to do that safely and effectively is really challenging. So, not necessarily saying that that's right or even the job of the primary care doctor, but I think it's great that you're thinking about it. And even again, as we keep coming back to patient education as being key here, making sure that a patient with cancer understands that they are potentially at risk for increased clots and giving them Stephan's bookmark of what are the symptoms that they need to watch for so that they can be proactive about it.

I guess the other questions that come up is so, sometimes we have people who develop VTE while they have cancer. There are kind of historical preference for certain anticoagulants. And I wonder, Stephan, if you could talk about your calculus for what's the correct anticoagulant or how do you select an anticoagulant for a patient with VTE that has an active cancer?

Stephan Moll: So what we've known for 20 years is that warfarin is not as effective as low molecular weight heparin. So, then low molecular weight heparin became the gold standard for 15 years or so until the direct oral anticoagulants came along. And now we have the choices, either low molecular weight heparin or the direct oral anticoagulants, in general, equally effective and safe. And the guideline from the American Society of Clinical Oncology, ASCO, gives you the choice to use either one of those. And easy are the direct oral anticoagulants, so they are most widely used. And low molecular weight heparin is much less used these days. Warfarin is not a choice. So, it's either typically apixaban or rivaroxaban. Dabigatran could be used as well, but it's here in the US, apixaban and rivaroxaban.

Jori May: And I think there was, and there still is some conversation about this question of people with intraluminal malignancy. So, anything, you know, a mass that's growing in the GI tract or in the GU tract that perhaps those direct oral anticoagulants may be associated with a higher bleeding risk than an enoxaparin.

Stephan Moll: Yeah, that's correct. That's what the studies showed. And one can interpret that in two different ways. And neither one of us is an oncologist. So, it's up to the oncologist to then discuss it with, well, they may ask us. But yes, it's that situation where sometimes people say, oh, you should be treated with a low molecular weight heparin. However, the majority of patients with intraluminal malignancies who have a clot, who get treated with a DOAC, don't have GI bleeding. So, one can certainly use a direct oral anticoagulant, much easier to use for many people than low molecular weight heparin. So, it's not that because you have an intraluminal malignancy, you need to be on the low molecular weight heparin, or you cannot be on a direct oral anticoagulant. You still have both choices. If a patient, however, has a GI bleed on a DOAC, then it's very reasonable to say, well, yes, that is somewhat higher risk than low molecular weight heparin. Let's switch you over to low molecular weight heparin. Some people use these data from the studies and not inappropriately to say, a priori, intraluminal malignancy, gastric, colonic, you should be on low molecular weight heparin. And as they're as effective as a DOAC, that's perfectly fine as a choice, if the patient does not mind and cost is not an issue. Do you see that similarly, Jori?

Jori May: And I do, yes. I mean, I think, you know, at least initially when with that data became available, there was kind of like you mentioned this across the board, anything intraluminal, there was hesitation and low molecular weight heparin was used. But I think more and more it's recognizing that, well, maybe the risk isn't as high. Low molecular weight heparin is a lot more difficult for patients.

If it's maybe for a short period of time, until we feel like we have disease control and then we can switch to the direct oral anticoagulants, I think the biggest concern is just really some sort of mass that is really friable, more prone to bleeding before intervention that low molecular weight heparin might be preferred. But ultimately, with the goal of getting them on a medication that's easier and better for quality of life.

And Paul, I guess to conclude the question of patients with cancer, I think sometimes when patients are hopefully cured and doing better, that they fall out of their oncologist's care. And so, I think just to the primary care doctor who may be seeing that patient long-term, speaking to, if a patient does have a VTE associated with cancer, when do you think about or are you ever tasked with being the one to stop anticoagulation? Or do you feel like the oncologist kind of manages that as well?

Paul Lewis: Yeah, occasionally I will, but I'll often try to partner with the oncologist in that case to make that decision. Again, unless it's fairly obvious and they're out a long way. But again, it goes back to our theme of individually risk assessing that patient. What else do they have going on? Maybe now they're less mobile. Maybe they have other things. So, I think that's all the other factors that are important to take into account.

Stephan Moll: And that's a very appropriate and good point, Paul. In addition to that, the point I want to make is, a cancer-associated DVT or PE does not equal a cancer-associated DVT-PE. One patient can be different. What do I mean? One patient with cancer who may undergo colon resection surgery and then develops a DVT within two days. Are the risk factors where the cancer and the colon surgery, which one is really the major risk factor can be difficult to decide. That patient is different to the patient who has colon cancer and no surgery and develops a clot due to the colon cancer, does not have a removal risk factor. So, that also needs to be taken into consideration with these individual risk factor assessments.

Conclusions

- Take the time to define the clot:
  - New or old?
  - Proximal or distal?
  - Superficial or deep?
- Define the risk factors: A…., B…, C…
  - Multifactorial nature of VTE

Jori May: Well, I think that's a nice place for us to conclude that we've touched on some really important themes and complex cases in this podcast. And so, if I might just take a moment and really try to summarize the really key points from what we've covered in this full series.

You know, what I've learned from both of you is, step one is really taking the time to define the clot. Is this a new clot? Is this old? Is this a proximal DVT? Is this a distal DVT? Is this in a superficial vein or a deep vein? Not taking the radiology report or the patient history at face value, but really diving deeper to fully understand what the clot is, what you're dealing with, because that has such an influence on how we manage these folks.

The second thing that we keep coming back to is that risk of VTE is not clear in one thing. Understanding the individual patient's risk factors, as Stephan always says, in an A, B, C, and D fashion. There are multiple things that likely contributed to the patient's risk. So, making sure that we're thinking about all the potential contributors, not just focusing on one surgery, but also thinking about family history, thinking about thrombotic challenges in the past, thinking about all the things that might contribute to a patient's long-term risk of VTE and their risk in that moment is really essential.

Conclusions

- Take the time to define the clot:
  - New or old?
  - Proximal or distal?
  - Superficial or deep?
- Define the risk factors: A…., B…, C…
  - Multifactorial nature of VTE
- Anticoagulation duration as a spectrum:
  - Major transient risk factor: limited duration
  - Unprovoked (no major transient risk factors): Default → Indefinite duration
  - Everything else in between: recurrence triangle, multidisciplinary collaboration

When making those decisions about anticoagulation duration, I, from this discussion, think of it as a spectrum. So, we know that certain risk factors are what we call major transient risk factors, a big surgery, a big hospitalization. Those are people where limited duration anticoagulation is appropriate. That's one side of the spectrum. The other side of the spectrum is that patient that has no risk factors. We can't find anything reversible in that patient. They had what we would call an unprovoked clot that requires indefinite anticoagulation because we are concerned that patient has ongoing risk for VTE.

So, everything else though is in the middle of that spectrum. Everything else in between is where I turn to Stephan's recurrence triangle, to have conversations and assessment of where does my patient fit within this recurrence triangle? Where do I think their risk is? And how do I have that risk-benefit conversation with them about whether they need continued anticoagulation or not? And for the primary care provider, those are the patients I think that often working together with someone who specializes in thrombosis care, if that's available to you, can be really helpful.

Conclusions

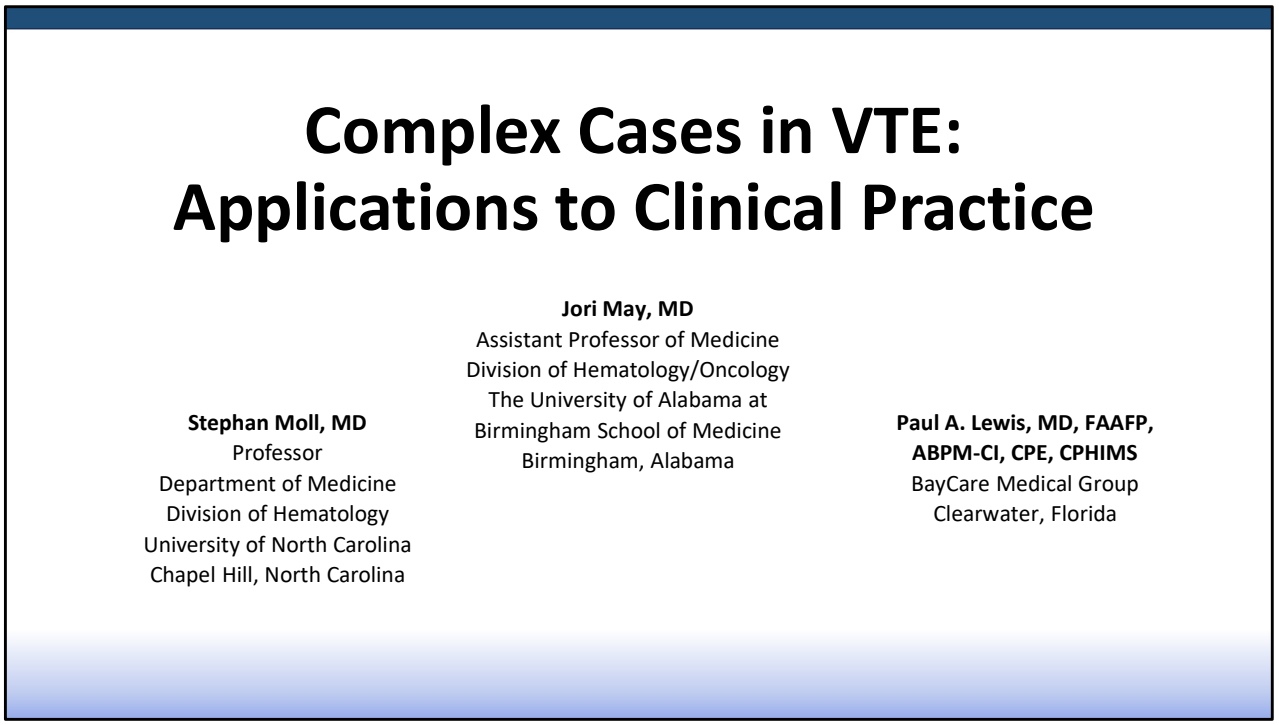
- DOAC “failure” is uncommon
  - Think twice before labeling it/switching to another agent
- Don’t bridge DOACs!
  - Generally hold for 2 days for procedures is sufficient
  - PAUSE algorithm is a helpful guide
- Address menstrual bleeding and iron deficiency whenever starting anticoagulation in a patient that menstruates

Jori May: The next point to think about is our anticoagulants tend to work. We didn't really talk about this in this podcast, but a frequent question that we get and something we touched on in the last podcast is this concept of, are anticoagulants failing, or a patient developing a blood clot while they're taking a blood thinner. We want to emphasize that with the oral 10A inhibitors, the direct oral anticoagulants, this is uncommon. So, these medications tend to work well. So, really pushing ourselves to, rather than saying the anticoagulant didn't work, we've got to switch to something else, to think twice and dig deeper to figure out, is this really a new clot or is this just scar tissue that we see in the vein? Or is there some sort of underlying disorder that's contributing to the risk for this “failure” that we need to pay attention to and manage? So, really thinking twice before we just simply switch to another agent.

Another take-home point that I have from this podcast is reminding ourselves that, with the direct oral anticoagulants, if we are having a procedure in those patients, patients do not need to be “bridged”. So, we're used to bridging this concept of using enoxaparin for a period of time around an operation, or around a hold of anticoagulation. But we learned in this podcast, in general, a short hold of the direct oral anticoagulants prior to a procedure is safe and effective. So, we do not need to bridge those patients.

And lastly, something that came up frequently in the podcast is the importance of remembering bleeding complications associated with anticoagulants, making sure that we're evaluating for bleeding risk and in particular thinking about any patient who menstruates that, before we start an anticoagulant, that we're thinking about how we're going to manage their menstrual bleeding, which is likely going to get worse, as well as proactively managing any iron deficiency that exists and ensuring that we have a plan for managing it, if that menstrual bleeding continues.

So, it's a lot of take-home points, but hopefully a summary of some really robust discussions that we've had.



Jori May: I want to conclude by saying thank you to our panelists. We've talked today about challenging cases of VTE that are often seen in the primary care setting, but we've had some really wonderful conversations about a range of topics. So, thank you to Stephan and thank you to Paul for talking with me, this has been fantastic.

So, this concludes our podcast series where we focus on the diagnosis, the treatment and management of VTE. And we hope that you found this discussion helpful just as I think we have. If you've missed any of the preceding podcasts, please be sure to check those out to get a complete picture of our discussion and what we hope illustrates the best practices for managing patients with DVT or PE.

And of course, don't forget to complete your CE evaluations and claim your CE credit. And again, thank you to Stephan and Paul and thank you to our audience for your attention.