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How Do We Effectively Integrate the Latest VTE Treatment and Secondary Prevention Guidelines Into Clinical Practice?

Announcer:
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Dr. Siegal:
Hello, everyone. I'm Dr. Deborah Siegal. I'm a hematologist and thrombosis physician at the Ottawa Hospital in Ottawa, Canada, and I'm going to be discussing the treatment of venous thromboembolism and how guidelines affect clinical practice review.

So we'll start off by setting the stage and of course reminding folks that venous thromboembolism includes deep vein thrombosis and pulmonary embolism, DVT and PE, and also superficial vein thrombosis. But we're going to focus our discussion on DVT and PE today. And actually, these are common cardiovascular diseases, the third most common cardiovascular disease after acute coronary syndrome and stroke, and they have an annual incidence of 1 to 2 per thousand persons, which is really helpful to tell patients when they've been diagnosed with this condition. 90% of VTE starts in the deep veins of the calf, and of those, 25% extend to involve the proximal veins. And if those are left untreated, 40% to 50% of those embolize to become a pulmonary embolism.

And so it's important to recognize that the diagnosis of VTE is increasing over time and actually increases with age.

So this is a slide that summarizes just why we think VTE is so important to identify and treat early. 5% to 10% of individuals with symptomatic pulmonary embolism present with shock, and up to 30% of folks die at 30 days without treatment. So it is really important to, you know, make this diagnosis early and get people on treatment as soon as possible. The true mortality of undiagnosed PE is likely less than 5%, because mortality after PE is often related to comorbidities, things like cancer, perhaps recent surgery, which are common in this setting. It's also important to remember that without treatment, about 50% of people will recur and that there are long-term complications for our patients who are living with this condition.

So, again, the ASH guidelines have suggested this time frame for the treatment of anticoagulation after VTE diagnosis. And you can see initially, there's this early 5 to 21 days, followed by the primary treatment of 3 to 6 months, and then secondary prevention treatment, based on an assessment of the risk of recurrence.

This slide summarizes the recent ASH 2021 guidelines for the initial treatment of deep vein thrombosis and pulmonary embolism. You can see on the top, for folks with uncomplicated deep vein thrombosis or PE with a low risk of complications, they're actually suggesting home treatment over hospital treatment, which is important for physicians and hospitals. For deep vein thrombosis or pulmonary embolism, the suggestion is to use DOACs over vitamin K antagonists, like warfarin. Finally, with pulmonary embolism in individuals who have hemodynamic instability, this is a recommendation to use thrombolytic therapy followed by anticoagulation over anticoagulation alone, and again, one of the strong recommendations of this guideline.

And then finally, for intermediate risk, or so-called sub-massive pulmonary embolism, the guidelines suggest anticoagulation alone over

the routine use of thrombolysis in addition to anticoagulation. And this is, again, an evolving space with lots of new therapeutic interventions that are under evaluation.

So for high-risk PE, this slide summarizes the guidelines from CHEST and from ASH. Essentially, both of these guidelines make recommendations that individuals who have hemodynamic compromise, for example, systolic blood pressure of less than 90 mm Hg who do not have a high bleeding risk, that systemically administered thrombolytic therapy is recommended over no such therapy. So, again, this recommendation to use thrombolysis for people who are hemodynamically unstable or who have hemodynamic compromise from their pulmonary embolism.

So what type of thrombolysis is being recommended for high-risk pulmonary embolism? So, essentially, the CHEST guidelines and the ASH guidelines suggest systemic thrombolysis over catheter-directed approaches at this point based on the evidence that's currently available. However, there was some nuance to that as you can see on the left-hand side with the CHEST guidelines showing that, you know, people who have failed systemic lysis or have shock likely to cause death before the effects can take place, that catheter-directed approaches be used. And the ASH guidelines show, again here, as systemic thrombolysis over catheter-directed approaches. Both of these are weak or conditional recommendations based on low certainty of evidence, which is important to keep in mind.

What about intermediate risk? Pulmonary embolism, again, lots of activity in this space with new therapeutic approaches. The guidelines suggest that in patients who have pulmonary embolism without hypotension, that systemic-administered thrombolytic therapies not be provided. So we're not going to be thrombolysing people who have intermediate-risk PE routinely. Okay, and again, strong recommendation, low certainty of evidence.

In the middle, you can see that thrombolysis is reasonable if the person has a low bleed risk or if they're younger or you think that they're at high risk for decompensation, for example, due to concomitant cardiopulmonary disease. And then, finally, on the right you can see that the ASH guidelines suggest anticoagulation alone over the routine use of thrombolysis, a conditional recommendation based on low certainty evidence. And again, this is a challenge in clinical practice and as we're gathering data from randomized trials to understand just how best to treat patients with intermediate risk PE, particularly those who have intermediate high risk with evidence of right ventricular strain and myocardial necrosis.

So there are lots of options for anticoagulation of patients who have acute venous thromboembolism. This is a slide that shows different DOACs and their dosing strategies. It's important to keep in mind that the dosing for acute venous thromboembolism may be different than the dosing for atrial fibrillation, and so it's just good to keep in mind and check the dosing is appropriate for the indication that it's being given for. Of course, there's also vitamin K antagonists like warfarin for individuals, for example, with antiphospholipid antibody syndrome. And low-molecular-weight heparin may be appropriate for some patients, particularly those with cancer who have GI tumors at risk of bleeding or those who require procedural interventions, just because of the periprocedural management component.

So I'll just pause here to reflect on the fact that the issue of assessing provoking factors in the setting of VTE is really important at the outset and then at the end of that 3 to 6 months of primary treatment.

And that's because risk factors confer variable risk. They're not all the same, and you can see here from this slide, there's quite a variable risk in terms of low-, kind of moderate-, and high-risk cancer. For example, here in the middle has a relative risk of 2 to 4 for recurrence. Recurrent VTE also associated with a high risk for recurrence, and then unprovoked as we've talked about. So those are some of the highest risk factors that we see among individuals. Other things like male sex, obesity, inflammatory bowel disease also increase the risk, not as high, but certainly can contribute to risk and then decisions for ongoing treatment after the primary therapy is over.

So I'll just encourage you to keep track of patient comorbidities and risk factors at the outset, during the treatment, and then after primary treatment in order to better assess the patient's risk of recurrence in the future, and candidacy for ongoing anticoagulation.

And I'll end there and hope that this was interesting and a good learning experience for you, and we'll see you again. Thanks so much.

Announcer:
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