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## The Prevalence and Severity of Recurrent VTE in Children

### Announcer:

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### Dr. Jaffray:

Hello, my name is Julie Jaffray. I'm from Children's Hospital Los Angeles. And this presentation is on the Prevalence and Severity of Recurrent VTE in Children. So what is recurrent VTE, just so we're all on the same page. So it's a venous thrombosis of a site that was either previously uninvolved with the initial VTE, or there was interval documentation of DVT or PE resolution, and then there was another clot. This can occur during anticoagulation therapy. These patients may be symptomatic or it's an incidental finding. Typically, the highest risk time is within the first six to 12 months after the initial event.

So what are the consequences of recurrent VTE in children? So they can develop post thrombotic syndrome, especially if there's recurrent DVT in that same limb. These kids can have chronic pain and swelling, and they can have venous insufficiency. And this is a really big deal when you're talking about a teenager who may not be able to participate in sports any longer or walk as much as they used to be able to with their friends. Patients can have loss of venous access. So if they've had a CVC-related VTE and they have another one in a different vein or in the same vein, they can lose access in that vein, which could be really important if they need lifesaving treatment such as having TPN all the time or chemotherapy, and they can no longer access that area. In addition, when children have two or three or more VTEs, we end up putting them on lifelong anticoagulation. And again, a really big deal when you're talking about a child versus maybe a 60 or 70 year old person. Patients who have repetitive and recurrent pulmonary embolism can end up having really severe pulmonary hypertension. And the most severe form of that is chronic thromboembolic pulmonary hypertension or CTEPH.

So the incidence of recurrent VTE, well, a study that was done looking at a Canadian registry of pediatric VTE events estimated that the incidence is about 10%. Now, this study didn't go into exactly if the patients had anticoagulation or not, or what their underlying risk factors were, but they did find it to be about 10%. They also noted that the mean time from their first thrombotic event to the recurrence was about six months, and that ranged from three months to five years. They also looked at post thrombotic syndrome and recurrence in the figure below in this same study of the Canadian registry. And what I want you to look at is that the recurrence rate is in the gray boxes. And you'll notice that the older that the children get, especially in the older teenagers of 16 to 18 years, is the highest incidence of end up getting a recurrent VTE.

So what about patients who are on anticoagulation? Does that affect the recurrence incidents? Well, a group of investigators from the Rivaroxaban pediatric trial, this is a direct oral anticoagulant, they got together and described a cohort of their patients at their hospital from 2011 to 2016 who had a VTE. They had 346 children in this study, and they found that those who received anticoagulation, 5.5% had a recurrence versus those who did not receive anticoagulation, 10.5% had recurrence. In the table at the bottom, they broke it up between patients who had a CVC-related VTE and those who had a non-CVC-related VTE. They broke it up even further to look at those who had recurrence during anticoagulation and those who had recurrence following discontinuation of anticoagulation.

So some high-risk groups where the incidence is even larger are children with thrombophilia. One study looked at 301 children who had a history of a VTE and either had factor V Leiden, an elevated lipoprotein a, prothrombin gene mutation, protein C or S or antithrombin deficiency, or more than one of those at the same time. They found that in these patients who had a thrombophilia, incidents went up to 21% that had a recurrent VTE after stopping anticoagulation. And if they had combined defects, that went up to 48%. In the figure on the side where they did a Kaplan-Meier curve in terms of survival, and you can see the difference of survival by the patients who had no thrombophilia defects, those who had a single defect and those who had a combined defect. Children who've had a CVC-related VTE and then have a new CVC placed are also at a really high rate of getting another VTE. One study found that they looked at 432 children at their hospital that had a history of a CVC-associated VTE, then went on to have another CBC placed. 50% had recurrence. Another study looked at the TriNetX database, and they found that 119 children with sickle cell disease and had VTE, they found that 8% had recurrence in one year, which is fairly similar to the Canadian data, but that 21% by the time they looked at five years from the index case ended up getting another VTE.

So in summary, and how can you relate this to your current clinical practice is that recurrent VTE can occur frequently in children, especially in those who do not receive anticoagulation. But the patients I really want you to pay special attention to are those with a thrombophilia, history of a CVC-related VTE and getting a new CVC placed and those with sickle cell disease. Thank you very much for your attention.

**Announcer:**

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