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Venous Thromboembolism: A Chronic Disease

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Commentary

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DESCRIPTION

Venous Thromboembolism (VTE), encompassing Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE), is frequently a chronic condition. Anticoagulant therapy is critical during the first three months of treatment. The decision to continue therapy must weigh the likelihood of a recurrent episode against the risk of bleeding. In this delicate balance, clinicians must evaluate the relative risks of recurrence and bleeding. The emphasis placed on each of these risks will vary over time, necessitating periodic reassessment. Patients can be categorized based on whether the initial event is provoked or unprovoked. Among provoked events, those linked to major or minor transient risk factors and those associated with major or minor persistent risk factors are differentiated [1]. This classification is based on the recurrence risk at one and five years, which varies across different categories. Patients with major transient risk factors have a low recurrence risk. Conversely, those with major persistent risk factors or unprovoked VTE face a high risk of recurrence. For patients with high transient risk, anticoagulation is typically discontinued after three to six months, given the low recurrence rates (1% at one year and 3% at five

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years). However, other factors must be considered in PE cases. A systematic review and meta-analysis of individual participant data assessed the link between Residual Pulmonary Vascular Obstruction (RPVO) and planar lung scans. Patients had to have received anticoagulant therapy for at least three months for acute PE and were evaluated for the risk of recurrent VTE or death from PE one year after stopping treatment. The study found that the risk of recurrent VTE at one year was 5.8% in participants with RPVO<5%, compared to 11.7% in those with RPVO ≥5% (with no significant difference in recurrence rates between provoked and unprovoked cases in this group) [2].

The situation is different for unprovoked VTE. A systematic review and meta-analysis of the marvelous trial concluded that in patients experiencing a first episode of unprovoked VTE who had completed at least three months of anticoagulant treatment, the risk of recurrent VTE was 10%, 16%, 25%, and 36% at one, two, five, and ten years, respectively. The recurrence rate of VTE was higher in males than females. Furthermore, patients with proximal DVT had a higher recurrence rate of VTE than those with distal DVT [3]. In the marvelous 2 study, another systematic review and meta-analysis, the event rate of recurrent VTE per 100 person-years was 1.08 and 1.55 in patients on direct oral anticoagulants and vitamin K antagonists, respectively, with a case fatality rate of 4.9%. These data indicate that even patients with a first unprovoked VTE have a small but ongoing long-term risk of recurrent VTE, even with extended anticoagulation [4]. Several studies have highlighted the importance of Residual Venous Thrombosis (RVT) as a predictor of recurrent VTE. A meta-analysis found that RVT was associated with a slightly increased risk of recurrent VTE in previous unprovoked or provoked deep vein thrombosis cases [5]. In between are patients with low persistent risk factors, but their risk of recurrence after stopping anticoagulation remains high (a 1-year recurrence rate of 11%) and could be comparable to that of unprovoked VTE [1]. Further complicating matters, Inflammatory Bowel Disease (IBD) is linked to an increased risk of thromboembolism, with IBD patients having a threefold higher risk compared to controls. However, the relative risk of complications during flare-ups is significantly higher, with an incidence exceeding 15% [6]. This is also true for other inflammatory diseases. Regarding thrombophilia, the risk increases in severe thrombophilia (deficiency of natural anticoagulants or combined abnormalities). For patients with minor transient risks, the recurrence risk varies based on the risk factor but is estimated to be around 5% and 15% at one and five years. The challenge is that a patient may have multiple risk factors [1]. Thus, it is not surprising that patients with unprovoked VTE and those with minor risks are often grouped together. This grouping is supported by cumulative data from the EINSTEIN EXTENSION and EINSTEIN CHOICE studies, which show that patients with unprovoked VTE have recurrence rates similar to those with persistent or transient minor risk factors [7]. One tool used by clinicians to assess treatment interruption is the D-dimer test. D-dimer positivity after Oral Anticoagulant Therapy (OAT) can identify VTE patients at higher risk of recurrence. Recent studies have supported these findings [8]. These considerations are taken into account by physicians monitoring patients, and it might be interesting to consider data from a study examining complications over two years of follow-up in patients with a first VTE [9]. First, the nature of the index events, whether provoked or unprovoked, did not dominate the decision to prolong or interrupt

anticoagulation. Second, the decision to extend anticoagulation was more likely in patients with proximal DVT (62.2%) compared to those with distal DVT, where discontinuation was more common (82.2%).The most common reasons for extending anticoagulation included the patient's general condition (high perceived recurrence risk), elevated D-dimer levels, persistent residual venous thrombosis, or thrombophilic changes. In practice, the risk of recurrent VTE increases continuously in the minds of clinicians due to a combination of risk factors. This concept has been suggested by Albertsen and others [10]. Another significant finding of the study is that the incidence of recurrent VTE did not differ between patients who extended anticoagulation (2.2% per year) and those who stopped (3.0% per year). From Marvelous 2 [4] we know that high-risk patients have a relapse rate despite effective anticoagulant therapy. Relapses are expected, but what is notable is the few relapses in patients on anticoagulant therapy (either full or reduced dose) and those off therapy, indicating that physicians have managed to appropriately categorize patients through comprehensive assessment. Among those who discontinued anticoagulation, 4.5% were prescribed aspirin (100 mg daily), while 20.3% were recommended sulodexide cycles [9].

Finally, it is important, though rarely considered in real-life studies, that the patient's preference is thoroughly taken into account.

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