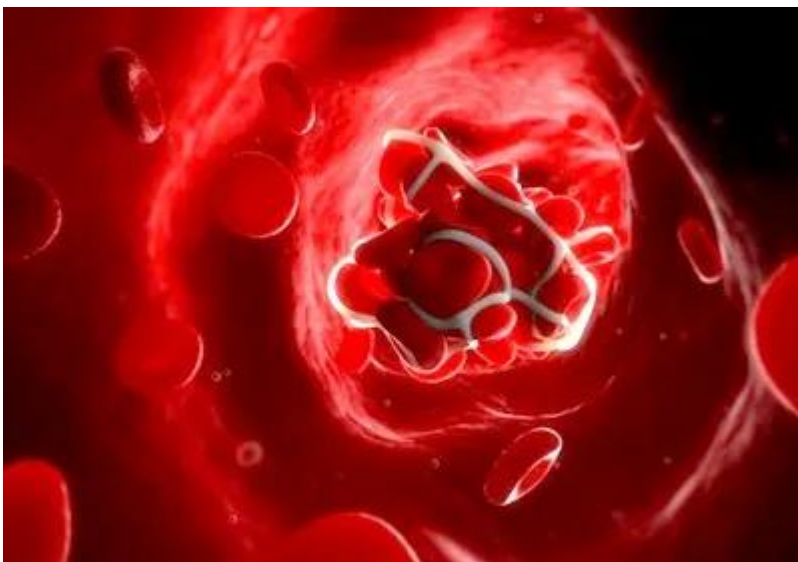


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## Recurrent venous thromboembolism in patients who discontinued anticoagulant therapy for COVID-19-associated venous thromboembolism after at least three months of treatment | 1

Despite research demonstrating a high prevalence of venous thromboembolism (VTE), including deep vein thrombosis (DVT) and/or pulmonary embolism, in acute COVID-19, the clinical significance of recurrent VTE among COVID-19 patients remains unclear. In this study, the authors from Spain and France investigated the incidence and mortality from recurrent VTE in patients with COVID-19-associated VTE who discontinued anticoagulation therapy after at least 3 months of treatment.

According to the authors, their PubMed search using the terms “venous thromboembolism” or “SARS-CoV-2” revealed that existing guidelines have primarily focused on the prevention, diagnosis, and acute treatment of COVID-19-associated VTE. However, there is no consensus regarding the optimal duration of anticoagulant therapy after COVID-19-associated VTE. In the absence of direct randomized trials on treatment duration, the rates and severity of VTE recurrence are considered the most important determinants of therapy duration. In a prospective multinational cohort study by Jara-Palomares et al., conducted on 431 patients with COVID-associated VTE in whom anticoagulant treatment was discontinued, the rate of VTE recurrences was 4.8 per 100 patient-years.





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### **About the study**

In this prospective, multicenter study, the authors used the Registro Informatizado de la Enfermedad Tromboembolica (RIETE) registry, which prospectively collects information on patients with confirmed acute VTE. Patients diagnosed with COVID-19-associated VTE from March 2020 to July 2023, in whom anticoagulation was discontinued after at least 3 months of therapy, were included. A positive COVID-19 test within 30 days of the VTE event confirmed COVID-19-associated VTE. All included patients received at least 3 months of anticoagulation. Follow-up started on the day of anticoagulation stopping and ended in July 2023, or on the day of VTE recurrence, or if the patient died.

The exclusion criteria were: patients with superficial vein thrombosis, those who did not receive at least 3 months of anticoagulant therapy, and those who were followed for less than 15 days after treatment discontinuation.

Pulmonary embolism was confirmed with high probability ventilation-perfusion scintigraphy or positive computed tomography (CT) angiography. Venous thrombosis in any location (lower limb, upper limb, cava, splanchnic, lung vein, jugular, or cerebral vein) was confirmed with positive CT or compression venous ultrasonography.

The primary outcomes were: 1) the rate of symptomatic, confirmed recurrent VTE after anticoagulation discontinuation *per* 100 patient-years, and 2) fatal pulmonary embolism occurring within 30 days following a VTE recurrence. The secondary outcomes were: 1) the incidence of VTE recurrence within the first 30 or 180 days after anticoagulation stopping, 2) the location of VTE recurrence concerning the first VTE event, 3) the risk of VTE recurrence in some predefined subgroups, like age (<65 years vs.  $\geq$  65 years), sex, active cancer (yes/no), VTE location, duration of anticoagulation (<6 months vs.  $\geq$  6 months), year of COVID infection and other multiple risk factors, such as recent surgery, immobilization, recent travel, previous history of VTE, hormonal treatment, pregnancy, and puerperium.

### **Results**

The study included 1106 patients. The mean age was  $62.3 \pm 14.4$  years, and 63% were men. Most of the patients (75%) initially presented as isolated pulmonary embolism, 13% as concomitant pulmonary embolism and DVT, and 12% as isolated DVT. Locations of DVT were: lower limb (n = 208), upper limb (n = 26), vena cava (n = 3), jugular vein (n = 17),



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splanchnic vein (n = 1), lung vein (n = 3), and cerebral venous sinus (n = 1). The median duration of anticoagulant therapy before its discontinuation was 5.6 months (ranging from 3.6 to 7.5 months). Median follow-up after anticoagulation discontinuation was 12.5 months (ranging from 6.3 to 20.1 months).

38 (3.5%) of 1106 patients with COVID-19-associated VTE had recurrent VTE, with a rate of 3.1 *per* 100 patient-years. 26% of VTE recurrences occurred within the first month after anticoagulation stopping, and 76% occurred within 12 months (n = 29). In 58% of patients, VTE recurrences occurred in the form of pulmonary embolism, both in patients who had pulmonary embolism (58%) and DVT (66%) at the first event.

No patient died of recurrent pulmonary embolism. Throughout the follow-up period, 34 (3.1%) of 1106 patients who had COVID-19-associated VTE died.

Subgroup analyses showed that patients diagnosed with COVID-19 in 2021/2022 had significantly higher rates of VTE recurrence than patients diagnosed with COVID-19 in 2020. Also, patients with lower limb DVT had higher rates of VTE recurrence than patients with pulmonary embolism.

### **Conclusion**

This prospective, multicenter, multinational study showed a low incidence of recurrent VTE in patients with COVID-19-associated VTE who discontinued anticoagulation therapy after at least 3 months of treatment. After anticoagulation stopping, recurrent VTE occurred in 3.5% of patients, with a rate of 3.1 per 100 patient-years, and no fatal pulmonary embolism.

According to the authors, it is conceivable that long-term anticoagulant therapy may not be necessary for many patients with COVID-19-associated VTE, although further investigation is required to confirm these findings

This study was published in eClinicalMedicine.

### **Journal Reference**

Jara-Palomares L, Bikdeli B, Jiménez J, et al. Risk of recurrence after discontinuing anticoagulation in patients with COVID-19-associated venous thromboembolism: a prospective multicentre cohort study. eClinicalMedicine, 2024; Volume 73, 102659. (Open



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