



# Cancer Occurrence After a Cerebral Venous Thrombosis: A Nationwide Registry Study

Jussi O.T. Sipilä<sup>1</sup>, MD, PhD; Jori O. Ruuskanen<sup>2</sup>, MD, PhD; Eetu Heervä<sup>3</sup>, MD, PhD; Jussi P. Posti<sup>4</sup>, MD, PhD; Päivi Rautava, MD, PhD; Ville Kytö<sup>5</sup>, MD, PhD

The incidence of cerebral venous thrombosis (CVT) decreases with age in women but increases in men, suggesting that age and sex affect CVT etiology.<sup>1</sup> Cancer is a possible cause of CVT, but the risk of occult malignancy is unknown.<sup>2</sup> We combined data from 4 nationwide mandatory registries to identify all patients with a CVT in 2005 to 2017 in Finland<sup>1</sup> and to investigate the occurrence of new cancer diagnoses within 2 years of CVT in patients without prior malignancy (Supplemental Methods). This was a retrospective register study, and thus no ethical board review or informed consent was required, and the participants were not contacted. We are not permitted to disclose data to third parties. Requests to access the data set may be sent to Findata (<https://findata.fi/en/>).

We included 589 CVT patients without cancer (Table S1). Thirteen (2.3%) patients had a new cancer diagnosis during the follow-up. Only 2 patients (both male) were <50 years of age at the time of the CVT (1.8% of all male patients aged <50 years). The risk of a new cancer diagnosis was higher in men compared with women in this age group ( $P=0.035$ ) and overall ( $P=0.027$ ), but there was no sex difference in the older patients ( $P=0.41$ ; Figure). No particular cancer type was predominant (Table S2). Four of the new cancer diagnoses had occurred within a year of the CVT, 3 in men and 1 in women (all in different organs). Four of the 13 patients with cancer died within 2 years, all because of cancer.

Age and sex were associated with the occurrence of a new cancer diagnosis in these CVT patients. In

patients under 50 years of age, the risk was absent in women and very low in men, and none of these cancers was diagnosed within a year of the CVT. New cancer diagnoses were more common in patients >50 years of age, and it seems reasonable to maintain clinical vigilance for signs of malignancy when treating patients, especially men, of this age group. Comprehensive screening of all CVT patients for cancers appears unwarranted, although more data are needed to confirm this. The situation could be much the same as after unprovoked venous thromboembolism.<sup>3</sup> Given the difference in perspectives, the current results are not directly comparable to previous studies that reported no sex differences in cancer as a predisposing factor for CVT.<sup>4,5</sup> Importantly, it appears there is no specific type of occult cancer to look for after a CVT.

## ARTICLE INFORMATION

Presented in part at the European Stroke Organisation Conference, virtual, September 1–3, 2021.

### Affiliations

Department of Neurology, North Karelia Central Hospital, Joensuu, Finland (J.O.T.S.). Clinical Neurosciences, University of Turku, Finland (J.O.T.S., J.O.R., J.P.P.). Neurocenter, Department of Neurology (J.O.R.) and Department of Public Health, University of Turku and Turku Clinical Research Centre (P.R.), Turku University Hospital, Finland. Department of Oncology (E.H.), Department of Neurosurgery (J.P.P.), and Heart Center and Center for Population Health Research (V.K.), Turku University Hospital and University of Turku, Finland.

### Sources of Funding

This study was supported by the Government's Special Financial Transfer tied to academic research in Health Sciences (Finland).

**Key Words:** humans ■ neoplasms ■ risk ■ thrombotic stroke ■ venous thrombosis

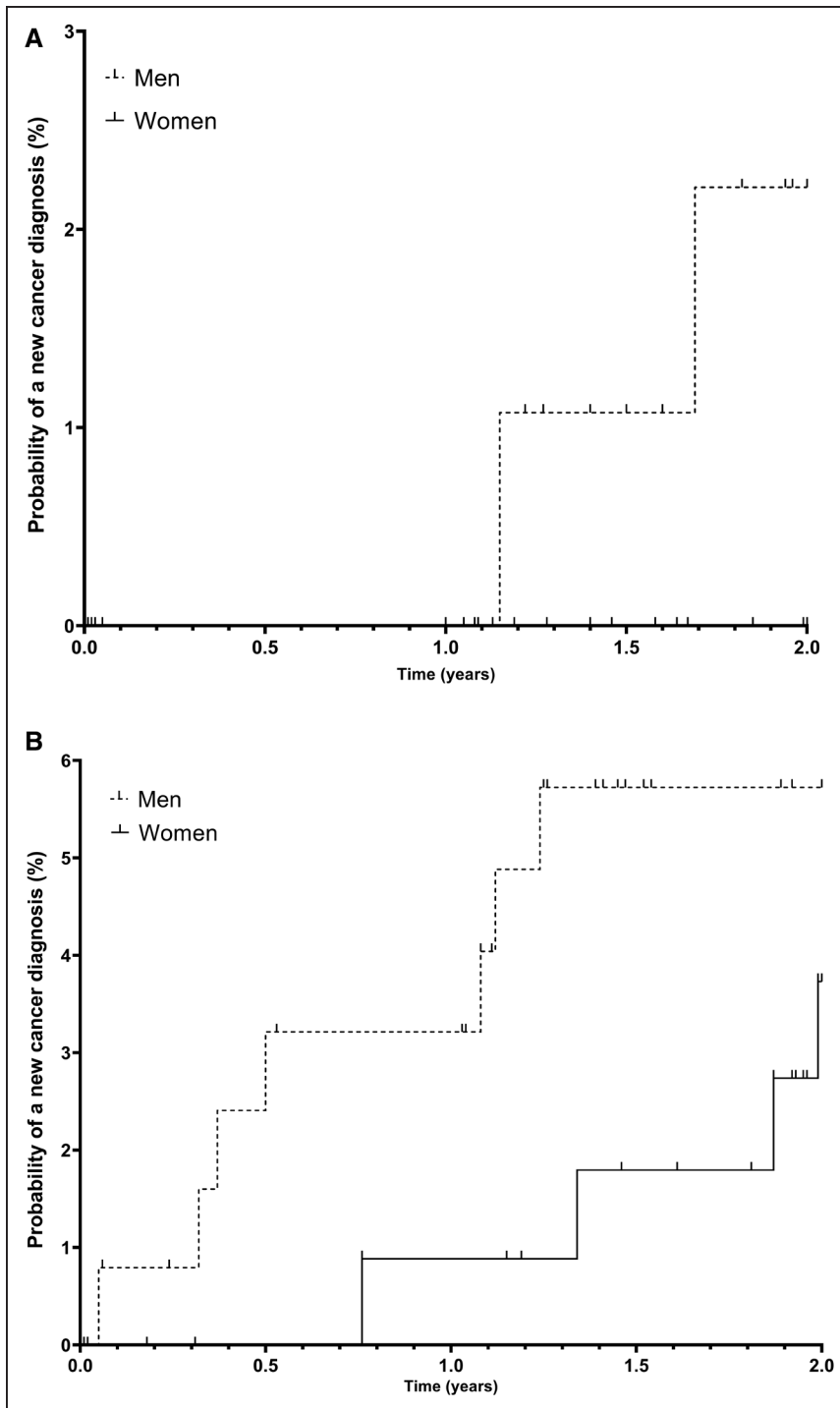
Correspondence to: Jussi O.T. Sipilä, MD, PhD, Department of Neurology, North Karelia Central Hospital, Tikkamäentie 16, FI-80521 Joensuu, Finland. Email [jussi.sipila@utu.fi](mailto:jussi.sipila@utu.fi)

Supplemental Material is available at <https://www.ahajournals.org/doi/suppl/10.1161/STROKEAHA.122.038685>.

For Sources of Funding and Disclosures, see page e189–e190.

© 2022 The Authors. *Stroke* is published on behalf of the American Heart Association, Inc., by Wolters Kluwer Health, Inc. This is an open access article under the terms of the [Creative Commons Attribution Non-Commercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use, distribution, and reproduction in any medium, provided that the original work is properly cited, the use is noncommercial, and no modifications or adaptations are made.

*Stroke* is available at [www.ahajournals.org/journal/str](http://www.ahajournals.org/journal/str)



**Figure.** Probability of a new cancer diagnosis after a cerebral venous thrombosis by age and sex.

Cumulative probability of new cancer diagnosis after a cerebral venous thrombosis in (A) patients <50 y of age and (B) patients ≥50 y of age.

### Disclosures

Dr Sipilä reports shares (Orion Corporation). Dr Ruuskanen reports scientific consultancy fee (Sandoz), speaker fee (Merck) travel/congress sponsorship (Bristol Myers Squibb and Bayer), and shares (Medbase, Ltd). Dr Heervä reports advisory board fees and travel grants (Roche/Genentech, Amgen, AstraZeneca, Bayer, MSD, Merck, Sanofi, and Pierre Fabre). Dr Posti reports academy of Finland grant funding (No. 17379). Dr Kytö reports scientific consultancy fee (AstraZeneca), speaker fee (Bayer), and funding (Finnish Foundation for Cardiovascular Research). The other author reports no conflicts.

### Supplemental Material

Supplemental Methods  
Tables S1–S2

### REFERENCES

1. Ruuskanen JO, Kytö V, Posti JP, Rautava P, Sipilä JOT. Cerebral venous thrombosis: Finnish nationwide trends. *Stroke*. 2021;52:335–338. doi: 10.1161/STROKEAHA.120.031026
2. Ferro JM, Bousser MG, Canhão P, Coutinho JM, Crassard I, Dentali F, di Minno M, Maino A, Martinelli I, Masuhr F, et al; European Stroke Organization. European Stroke Organization guideline for the diagnosis and treatment of cerebral venous thrombosis - endorsed by the European Academy of Neurology. *Eur J Neurol*. 2017;24:1203–1213. doi: 10.1111/ene.13381
3. van Es N, Ay C, Jara-Palomares L. Screening for occult cancer in patients with venous thromboembolism: past, present, and future. *Hamostaseologie*. 2020;40:270–279. doi: 10.1055/a-1150-2286

4. Alet M, Ciardi C, Alemán A, Bando L, Bonardo P, Cea C, Cirio J, Cossio J, Cuculic M, Esnaola MM, et al; Argentinian Stroke and Cerebrovascular Diseases Study Group - Argentine Neurological Society. Cerebral venous thrombosis in Argentina: clinical presentation, predisposing factors, outcomes and literature review. *J Stroke Cerebrovasc Dis.* 2020;29:105145. doi: 10.1016/j.jstrokecerebrovasdis.2020.105145
5. Porceddu E, Rezoagli E, Poli D, Magliocca A, Scoditti U, Di Minno MND, De Stefano V, Siragusa S, Ageno W, Dentali F; CEVETIS (Cerebral Vein Thrombosis International Study) Investigators. Sex-related characteristics of cerebral vein thrombosis: a secondary analysis of a multi-center international cohort study. *Thromb Res.* 2020;196:371–374. doi: 10.1016/j.thromres.2020.09.023