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

SUPPLEMENTAL MATERIAL

Supplemental Methods

We used the same CVT identification protocol as in our previous study,[1] but with an extended time period from January 1, 2005 to December 31, 2017. Briefly, all hospital discharges for patients aged ≥18 years with CVT as the primary diagnosis (ICD-10 codes I63.6 and I67.6) were retrieved from Care Register for Health Care (CRHC), a mandatory registry covering Finland. Admissions with rehabilitation co-diagnosis or invalid follow-up data were excluded. One admission per patient was allowed. Patients with missing overall survival data were excluded.

Cancer diagnoses were obtained from the nationwide Finnish Cancer Registry (FCR, data available 1980-2018) and the CRHC (data beginning from the year 2004). FCR is based on automated reporting of histopathological or cytological diagnosis of malignancy nationwide with an excellent population-based coverage. Outpatient oestrogen prescription data was obtained from The Social Insurance Institution of Finland (KELA), which is the only regulatory authority for outpatient medication reimbursement in Finland, using ATC-codes G03A (excluding G03AD), G03E and G03F (excluding G03EK) to include both contraceptive and hormone replacement therapy (HRT) products.

Patients with a cancer diagnosis in either registry before the CVT were excluded. The primary outcome was a cancer diagnosis (basaliomas excluded, polycythemia vera and myelodysplasic syndrome included) in the FCR within two years after the CVT. Mortality data and causes of death certificates were retrieved from the national Statistics Finland until December 31, 2018. The causes of death diagnoses were also compared to the FCR data of the deceased patients as a sensitivity analysis, which found no additional cancer cases from the death diagnoses. The study was approved by Findata / National Institute for Health and Welfare of Finland (permission no: THL/2245/5.05.00/2019) and Statistics Finland (TK-53-484-20). The legal basis for processing personal data is public interest and scientific research (EU General Data Protection Regulation 2016/679, Article 6(1)(e) and Article 9(2)(j); Data Protection Act, Sections 4 and 6).

The distribution of continuous variables was assessed with the Shapiro-Wilk test and subsequently the Mann-Whitney U-test was used because of skewed distribution in all instances. Charlson Comorbidity Index (CCI) score was calculated as previously described.[1] Chi-square test (χ^2) was used to test if observed frequencies across categories of CCI matched expected frequencies. Cancer risk for CVT is presented with the Kaplan-Meier curve method and log-rank statistics. Non-cancer deaths were censored. All analyses were conducted using SPSS Statistics, version 27.

Table S1. Patient characteristics and comparison by sex.

	Total	Men	Women	p (men vs. women)
N	589	238	351	
Median Age (IQR, range)	44 (30-60, 18-93)	51 (38-62, 18-93)	36 (27-58, 18-90)	<0.0001
Median CCI (and IQR)	0 (0-1)	0 (0-1)	0 (0-1)	0.10
N of CCI 0 (%)	399 (68%)	154 (65%)	245 (70%)	0.10**
Preceding oestrogen *		-	3.1%	-
30-day overall mortality	2.4%	2.5%	2.3%	0.84
2-year overall mortality	5.7%	8.2%	4.0%	0.04
New cancer diagnoses during 2 yrs after CVT	13 (2.3%)	9 (4.0%)	4 (1.2%)	0.027
Median age of patients with a new cancer diagnosis (IQR, range)	67 (59-72, 32-79)	72 (50-73, 32-79)	66 (62-67, 59-67)	0.71
CCI of patients with a new cancer diagnosis (median and IQR)	1 (0-2)	2 (0-3)	0.5 (0-1)	0.25
Preceding estrogen in women with a new cancer diagnosis*		-	25%	-
Patients with co-diagnoses potentially related to CVT in patients with a new cancer diagnosis***	4	2	2	0.53

CCI, Charlson Comorbidity Index; CVT, cerebral venous thrombosis; IQR, interquartile range. *Pharmacy purchase within 90 days prior to CVT; ** χ^2 for difference between sexes across all CCI categories; ***Other specified coagulation defects (ICD-10 code D68.8), Other malformations of cerebral vessels (Q28.3), Arteriovenous fistula, acquired (I77.0), and, Glomerular disorders in blood diseases and disorders involving the immune mechanism (N08.2) + Other specified disorders involving the immune mechanism, not elsewhere classified (D89.8) in the same patient

Table S2. Types of new cancer diagnosed after the CVT by sex and ICD-10 codes

		Men	Women
Cancer type	Bladder (C67)	1	0
	Colorectal (C18-20)	1	0
	Diffuse B-cell lymphoma (C83.3)	2	0
	Follicular B-cell lymphoma (C82)	0	1
	Kidney (C64)	1	0
	Primary liver cancer (C22)	1	0
	Cutaneous Melanoma (C43)	1	0
	Mesothelioma (C45)	1	0
	Myeloma and other plasma cell malignancies (C90)	0	1
	Other endocrine glands (C75)	0	1
	Pancreatic (C25)	0	1
	Thyroid gland (C73)	1	0