Cerebral Venous Thrombosis in Older Patients

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Background and Purpose—Cerebral venous thrombosis (CVT) is rare in older patients. We investigated whether clinical features and outcomes differ in older and younger patients.

Methods—We used data from a multicenter observational registry of consecutive adult patients with CVT admitted between 1987 and 2016. We compared demographics, clinical manifestations, and outcomes between older (upper quartile of the age distribution) and younger (lower 3 quartiles of the age distribution) patients.

Results—Data for 843 patients with CVT were available. The median age was 43 years (interquartile range, 30–55 years). Older patients (≥55 years; n=222) were less often women than younger patients (48% versus 71%; $P<0.001$) and less often reported headache (63% versus 87%; $P<0.001$). Cancer was more common in older patients (24% versus 9%; $P<0.001$), especially solid malignancies (19% versus 5%; $P<0.001$). Outcome at follow-up was worse in older patients (modified Rankin Scale, 3–6; adjusted odds ratio, 2.68; 95% confidence interval, 1.78–4.03; mortality, adjusted odds ratio, 2.13; 95% confidence interval, 1.09–4.19).

Conclusions—The sex ratio of CVT is evenly distributed in older patients, probably because of the dissipation of hormonal influences. Malignancy should be considered as a potential precipitant in older patients with CVT. **(*Stroke*. 2018;49:197-200. DOI: 10.1161/STROKEAHA.117.019483.)**

Key Words: aged ■ hormones ■ neoplasms ■ stroke ■ venous thrombosis

Cerebral venous thrombosis (CVT) is an uncommon cause of stroke that mostly affects young adults and children.[1] CVT in older patients may differ in important ways from CVT in the young. In young and middle aged patients, CVT has a female predominance, which is attributed to female hormonal influences such as oral contraceptive use, pregnancy, puerperium, and hormone replacement therapy.[1] We determined the clinical characteristics, risk factors, and outcomes of CVT in older patients in a large international cohort of patients with CVT.

Methods

Study Population

We included adult patients with CVT admitted to 1 of 5 academic hospitals: Academic Medical Center, Amsterdam (2000–2016), Helsinki University Central Hospital (1987–2014), Sahlgrenska University Hospital, Gothenburg (1997–2014), Adelaide Public hospitals (2005–2011), and Toronto Western Hospital (2004–2014). All hospitals maintain a registry of consecutive patients with CVT. For the Amsterdam and Helsinki registries, data have been collected prospectively since 2006 and 2010, respectively. Diagnosis of CVT was confirmed in all patients in accordance with international guidelines.[2] Appropriate research permits were received by local investigators at each study center. The data and analytic methods are available to other researchers. Interested researchers can contract the corresponding author.

Statistical Analysis

We compared demographics, clinical manifestations, and outcomes between older (uppermost quartile of the age distribution) and younger (lower 3 quartiles of the age distribution) patients. For clinical outcome, we used the modified Rankin Scale score at last follow-up. For comparison of categorical data, we used a χ^2 or Fisher exact test, and for continuous data, we used a Mann–Whitney *U* test. We applied multivariate logistic regression analysis to study the association between age and clinical outcome, adjusting for sex, history of cancer, intracerebral hemorrhage, coma, and thrombosis of the deep cerebral venous system.

Results

Within the specified time period, data of 843 adult patients with CVT were available for analysis. The median age was 43 years (interquartile range, 30–55 years).

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Patients aged ≥55 years were less often women (48.2% versus 71.0%; $P<0.001$) and less often reported headache at presentation (62.9% [127/202] versus 87.4% [527/603]; $P<0.001$) compared with patients <55 years (Table 1). Older patients more often used hormone replacement therapy (11.8% [10/85] versus 3.4% [13/387]; $P=0.003$) compared with patients <55 years. A history of cancer occurred more frequently in older patients (24.4% [54/221] versus 9.3% [57/616]; $P<0.001$), especially solid malignancy (16.3% [34/208] versus 3.6% [22/603]; $P<0.001$). The most common types of solid cancer in elderly were lung cancer (3.2%), breast cancer (2.7%), colorectal cancer (2.3%), and skin cancer (2.3%). The time of diagnosis of cancer was known in half of the patients diagnosed with cancer and CVT (52 of 111). Cancer was diagnosed within 1 year before CVT diagnosis in 67.3% (35 of 52). Thirty of 35 patients were treated by chemotherapy. Clinical outcome at follow-up was available for 769 of 843 patients (91.2%; Figure). After adjustment for confounding variables, the risk of poor outcome (modified Rankin Scale, 3–6) was increased in patients aged ≥55 years (adjusted odds ratio, 2.68; 95% confidence interval, 1.78–4.03; Table 2). The risk of mortality was also higher in older patients (adjusted odds ratio, 2.13; 95% confidence interval, 1.09–4.19). Further stratification by age groups showed that the outcome was worse with increasing age strata (Table I in the online-only Data Supplement).

Table 1. Clinical Characteristics

	Age <55 y (n=621)	Age ≥55 y (n=222)	*P* Value
Demographics			
Female	441/621 (71.0%)	107/222 (48.2%)	<0.001
Median age (IQR)	37.0 (26–45)	63.0 (59–70)	<0.001
Symptoms and signs			
Headache	527/603 (87.4%)	127/202 (62.9%)	<0.001
Focal neurological deficits	344/611 (56.3%)	140/216 (64.8%)	0.029
Seizure(s)	178/614 (29.0%)	55/216 (25.5%)	0.321
Coma (GCS <9)	46/565 (8.1%)	19/200 (9.5%)	0.554
Risk factors			
Cancer	57/616 (9.3%)	54/221 (24.4%)	<0.001
Solid types	22/603 (3.6%)	34/208 (16.3%)	<0.001
Hematologic types	22/603 (3.6%)	7/208 (3.4%)	0.850
Oral contraceptives*	238/377 (58.3%)	3/91 (3.3%)	<0.001
Pregnancy and puerperium*	44/438 (10.0%)	0/105 (0%)	0.001
Hormone replacement therapy*	13/387 (3.4%)	10/85 (11.8%)	0.003
Previous venous thrombosis	45/536 (8.4%)	18/176 (10.2%)	0.426
Genetic thrombophilia	54/389 (13.9%)	9/160 (5.6%)	0.006
Thrombosed sinuses/veins			
Superior sagittal sinus	340/620 (54.8%)	97/222 (43.7%)	0.004
Lateral sinus left	280/618 (45.3%)	109/222 (49.1%)	0.331
Lateral sinus right	268/618 (43.4%)	91/222 (41.0%)	0.540
Deep cerebral venous system†	125/619 (20.2%)	28/222 (12.6%)	0.012
Parenchymal lesions			
Nonhemorrhagic lesion	199/613 (32.5%)	63/219 (28.8%)	0.312
Intracerebral hemorrhage	199/616 (32.3%)	74/219 (33.8%)	0.687
Therapy			
Anticoagulation	571/612 (93.3%)	180/218 (82.6%)	<0.001
Endovascular treatment	56/616 (9.1%)	13/221 (5.9%)	0.137
Hemicraniectomy	31/615 (5.0%)	14/221 (6.3%)	0.465

GCS indicates Glasgow Coma Scale; and IQR, inter quartile range.

*Women only.

†Thrombosis in ≥1 of the following veins or sinuses: straight sinus, internal cerebral veins, vein of Galen, and basal vein of Rosenthal.

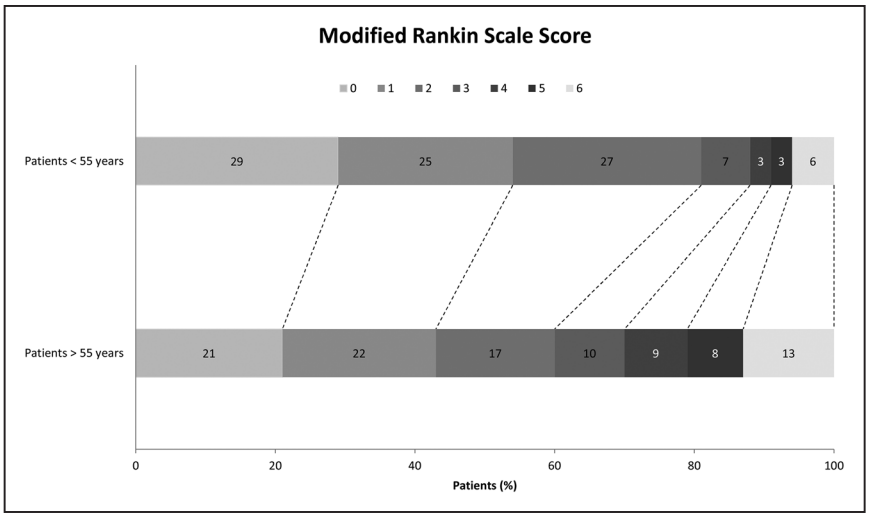

Figure. modified Rankin Scale (mRS) distribution for older patients and patients <55 years. The numbers in the Figure represent percentages. The scores on the mRS at last follow-up are shown for older patients and patients <55 years. For each score, the percentage is shown in the bars. Outcome data were not available for 74 patients.

Discussion

We found that CVT was equally prevalent in older men and women. Our data substantiate the hypothesis that the overrepresentation of women among patients with CVT in general is explained by female hormonal influences.[3,4]

One in 4 patients with CVT who were >55 years had a history of cancer, making this one of the most common risk factors in this age group. Cancer is a well-known risk factor for more common locations of venous thrombosis, such as deep vein thrombosis of the leg and pulmonary embolism.[5] Cohort studies suggest that, overall, ≈7% of adult patients with CVT have a history of cancer.[6,7] Unfortunately, our data cannot be used to determine the (cost)-effectiveness of screening for cancer in older patients with CVT because the frequency of diagnosis of cancer at follow-up was not systematically recorded. Nevertheless, given the high prevalence, it seems appropriate to have a low threshold to search for the most common types of cancer in older patients with CVT. The only previous study on CVT in older patients is a post hoc analysis of the ISCVT (International Study on Cerebral Vein and Dural Sinus Thrombosis).[8] Our results are mainly concordant with this study. In both studies, CVT was equally prevalent in older men and older women, and headache was less common in older. This latter information is valuable to clinicians because it shows that the possibility of CVT should not be disregarded in the absence of headache in this age group. Mortality was substantially higher in ISCVT (27% versus 13%). In part, this might be explained by a more stringent elderly definition (>65 years) in ISCVT. In addition, improvements in management of patients with CVT, especially decompressive surgery, may have led to a lower mortality rate in our study.[9,10] Finally, there is an overall trend over time of declining mortality in CVT.[6,11] A strength of our study is the large number of older CVT patients (51 in ISCVT versus 202 in our study). Useful information on hormonal influence is added by a postmenopausal age cutoff of 55 years. A weaknesses is that baseline modified Rankin Scale score and withdrawal of care information, which may differed between older and younger patients, were not available. In summary, CVT has a divergent clinical profile in older patients. Female predominance is absent in this age group, and ≈1 in 4 patients harbors an underlying malignancy. The prognosis of older CVT patients is worse than younger patients but better than previously characterized.

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Disclosures

Dr Coutinho is a steering committee member of the RESPECT-CVT trial (Randomised, Open-Label, Exploratory Trial With Blinded Endpoint Adjudication, Comparing Efficacy and Safety of Oral Dabigatran Etexilate Versus Oral Warfarin in Patients With Cerebral Venous and Dural Sinus Thrombosis Over a 24-Week Period), and Dr Silver is a national coordinator of the RESPECT-CVT trial, a study funded by Boehringer Ingelheim in which the efficacy and safety of dabigatran are assessed in patients with cerebral venous thrombosis. Dr Hiltunen has a research grant to disclose from the Helsinki University. The other authors report no conflicts.

Table 2. Association Between Age and Clinical Outcome

Outcome at Last Follow-Up	No. (%) of Patients*		OR (95% CI)	
	Age <55 y	Age ≥55 y	Unadjusted	Adjusted†
mRS 3–6	107/571 (18.7%)	78/198 (39.4%)	2.82 (1.98–4.02)	2.68 (1.78–4.03)
Mortality	34/571 (6.0%)	26/198 (13.1%)	2.39 (1.39–4.09)	2.13 (1.09–4.19)

CI indicates confidence interval; mRS, modified Rankin Scale; and OR, odds ratio.

*The number of study participants was divided by the total number (unknown and missing cases excluded) to calculate the percentage.

†The multivariate model is adjusted for sex, intracerebral hemorrhage, coma, history of cancer, and thrombosis of the deep cerebral venous system.

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SUPPLEMENTAL MATERIAL

Table I. Association between age strata and mRS 3-6.

	No. (%) of patients*	**OR (95% CI)**	
	mRS 3-6	**Unadjusted**	**Adjusted†**
Age < 55 years	107/571 (18.7%)	Reference	Reference
55-64 years	37/108 (34.3%)	2.26 (1.44-3.54)	2.08 (1.24-3.48)
65-74 years	24/62 (38.7%)	2.74 (1.58-4.76)	2.21 (1.17-4.20)
≥75 years	17/28 (60.7%)	6.70 (3.05-14.72)	6.26 (2.67-14.70)

mRS, modified Rankin Scale; OR, odds ratio; CI, confidence interval.
* The number of study participants was divided by the total number (unknown and missing cases excluded) to calculate the percentage.
† The multivariate model is adjusted for sex, intracerebral hemorrhage, coma, history of cancer, and thrombosis of the deep cerebral venous system.

Table II. Association between age strata and mortality.

	No. (%) of patients*	**OR (95% CI)**	
	Mortality	**Unadjusted**	**Adjusted†**
Age < 55 years	34 /571 (6.0%)	Reference	Reference
55-64 years	11 /108 (10.2%)	1.79 (0.88-3.66)	1.41 (0.58-3.43)
65-74 years	7 /62 (11.3%)	2.01 (0.85-4.75)	1.39 (0.49-3.97)
≥75 years	8 /28 (28.6%)	6.32 (2.59-15.39)	6.15 (2.07-18.31)

mRS, modified Rankin Scale; OR, odds ratio; CI, confidence interval.
* The number of study participants was divided by the total number (unknown and missing cases excluded) to calculate the percentage.
† The multivariate model is adjusted for sex, intracerebral hemorrhage, coma, history of cancer, and thrombosis of the deep cerebral venous system.