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ORIGINAL ARTICLE

The effect of recanalization on long-term neurological outcome after cerebral venous thrombosis

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Essentials

- The role of cerebral venous thrombosis (CVT) recanalization on neurologic outcome is still debated.
- We studied a large cohort of 508 CVT patients with 419 patient years of radiological follow-up.
- Recanalization rate is high during the first months after CVT and neurologic outcome is favorable.
- High recanalization grade of CVT independently predicts good neurological outcome.

Summary. *Background:* Studies with limited sample size and with discordant results described the recanalization time-course of cerebral venous thrombosis (CVT). The neurological outcome after a first episode of CVT is good, but the role of recanalization on neurological dependence is still debated. *Objectives:* The aim of the study is to assess the recanalization rate after cerebral venous thrombosis (CVT) and its prognostic role in long-term neurological outcome. *Patients/Methods:* In a retrospective observational multicenter cohort study, patients with an acute first episode of CVT with at least one available imaging test during follow-up were enrolled. Patency status of the vessels was categorized as complete, partial or not recanalized. Neurological outcome was defined using the modified Rankin scale (mRS) as good (mRS = 0–1) or poor (mRS = 2–6). *Results:* Five-hundred and eight patients (median [IQR] age, 39 [28.5–49] years; 26% male) were included. Complete or partial recanalization was not differently represented in patients undergoing scans at different periods of time (from 28-day to 3 month-period up to a 1–3 year-period). mRS at the time of follow-up imaging was available in 483 patients; 92.8% of them had a mRS of 0-1. CVT recanalization (odds ratio [OR], 2.56; 95% confidence interval [CI], 1.59–4.13) was positively associated, whereas cancer (OR, 0.29; 95% CI, 0.09–0.88), and personal history of venous thromboembolism (VTE) (OR, 0.36; 95% CI, 0.14–0.92) were negatively associated as independent predictors of favorable (mRS = 0–1) outcome at follow-up. *Conclusions:* Most patients with a first CVT had complete or partial recanalization at follow-up. Recanalization was independently associated with a favorable neurological outcome.

Keywords: cerebral venous thrombosis; modified Rankin scale; neurological outcome; recanalization; stroke.

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Introduction

Cerebral venous thrombosis (CVT) has long been considered a rare disease with long-term morbidity and mortality rates [1,2]. The actual estimated incidence of CVT ranges from 1.3 to 1.6 cases per 100 000, as reported in recent population-based studies [3]. In the past decades, the improvement of diagnostic techniques and therapeutic strategies has greatly ameliorated the prognosis of CVT [4]. The occurrence of death in CVT patients is estimated at around 4% within the acute phase and reaches up to 8–10% at long-term follow-up [3]. However, up to 12% of surviving patients still have a poor neurological outcome [5].

Only a few studies with a relatively small sample size have investigated frequency, grade and long-term

recanalization rate of CVT [6–16]. Whether the recanalization is associated with a favorable long-term clinical outcome after a first episode of CVT remains controversial [10–16].

The aim of our study was to evaluate the recanalization rate in a large population of patients with a first episode of CVT and to assess the prognostic role of recanalization in the long-term neurological outcome in these patients.

Methods

Study population

The population of this study included white Caucasian patients with CVT enrolled in two published multicenter international cohorts [17,18]. The first cohort of 145 patients was referred to a single thrombosis center after a first episode of CVT and was followed-up for a median time of 6 years after the discontinuation of the anticoagulant treatment [17]. The second cohort of 706 patients was referred to several centers after a first episode of CVT, with a total follow-up of 40 months [18]. Both studies were approved by the local institutional review boards (IRBs). Informed consent was waived because the included patients were part of two international cohorts reported in previously published studies, for which informed consent had been obtained in writing [17] or orally [18]. The present study was carried out in accordance with the code of ethics of the world medical association (Declaration of Helsinki).

For the study purpose, only patients with a radiological follow-up carried out between 28 days and 3 years after the index event were considered. Accepted imaging tests were magnetic resonance (MR) with/without MR venography, computed tomography (CT) with/without CT venography, or conventional angiography. Patients who underwent thrombolysis after the index event were not included in the present study.

Study procedures and outcomes

The choice of timing for the neuroimaging follow-up was left to the treating physicians. CVT recanalization grade was classified into complete, partial or no recanalization according to the imaging technique performed during follow-up and to the neuroradiology report compared with the first radiological imaging evaluation. If thrombosis involved multiple veins or sinuses at the index event, we assigned the recanalization status as determined by the worst recanalization level reported compared with the initial level of thrombosis evaluated at the index event.

According to the clinical practice of the involved centers, patients were clinically re-evaluated by the physician after neuroimaging and were assigned a score to characterize the presence of any residual clinical disability according to the modified Rankin scale (mRS). The mRS ranges from the absence of any symptom (mRS = 0) to death (mRS = 6).

A good outcome was classified as complete recovery (mRS, 0–1), whereas poor outcome was categorized as partial recovery, dependence or death (mRS, 2–6) [14,16,18,19].

To identify factors associated with recanalization and functional clinical outcome, we analyzed the presence of different co-existing CVT risk factors at diagnosis (if present in at least 5% of the study population), as well as neuroimaging findings at onset, including: (i) age (median age); (ii) male sex; (iii) personal history of venous thromboembolism (VTE); (iv) thrombophilic abnormalities (antithrombin, proteins C and S deficiency, lupus anticoagulant, anticardiolipin antibodies, factor V Leiden and G20210A prothrombin mutation) [20]; (v) hormonal use (oral contraceptive, hormonal replacement therapy or hormonal therapy for cancer); (vi) cancer; (vii) head trauma or neurosurgical operation; (viii) local or systemic infection; (ix) pregnancy or puerperium; (x) deep venous system CVT; (xi) single site (vessel or sinus) CVT; (xii) concomitant intracranial hemorrhage; (xiii) unprovoked CVT (defined if none of the clinical variables v-ix was present) [21]; and (xiv) duration of anticoagulation (parenteral and/or oral anticoagulant therapy).

Statistical analysis

Normality of data distribution was assessed using the Shapiro–Wilk test. Continuous variables were expressed as mean plus or minus standard deviation (SD) or as median with interquartile range (IQR), as appropriate. Range was used to describe days of follow-up. Categorical data were reported as counts and percentages. Patients' follow-up was stratified into four different periods, defined as: early (28 days to 3 months), intermediate (3–6 months), late (6–12 months) and chronic (1–3 years).

Complete and partial vs. no recanalization and good vs. poor clinical functional outcome were compared between the different follow-up periods with the chi-squared test.

Univariate ordered logistic or logistic regression was used to examine: (i) the association between a higher recanalization level (outcome variable) and different possible predictors of CVT recanalization; and (ii) the association between good clinical outcome (outcome variable) and different possible predictors of residual disability.

Each single variable that was correlated with a higher recanalization status or good clinical outcome with a P-value < 0.10 was a candidate for testing in a multivariate ordered logistic or logistic regression. Backward elimination was performed to finalize the independent predictors of the multivariate models.

All patients had complete data for the CVT recanalization level (diagnostic imaging evaluation). Neurological outcome information was missing in less than 5% of our patient population; therefore, no data imputation was used to replace it.

Statistical significance was reached when the *P*-value was < 0.05 (two-tailed). Statistical analyses were performed using STATA-14/MP (StataCorp LP, College Station, TX, USA), GraphPad Prism 7.0a (GraphPad Software, San Diego, CA, USA) and Microsoft Excel for Mac 2017, Version 15.32.

The study was carried out and reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for observational studies [22].

Results

Baseline characteristics and CVT therapeutic management

Of the 851 patients with a first episode of CVT included in the two cohort studies, 508 (59.7%) had at least one radiological follow-up between 28 days and 3 years after the index event and were therefore included in this study. Patients' baseline characteristics, risk factors for CVT and main neuroradiological findings at the time of the index event are summarized in Table 1.

Almost all patients were treated with anticoagulant therapy: low-molecular-weight heparin, unfractioned heparin alone or followed by vitamin K antagonists (86.1%), or vitamin K antagonists alone (9%). Less than 5% of our patient population ($n = 25$) received antiplatelet therapy or did not receive any therapy. The median duration of the anticoagulant therapy in our population was 187 days (IQR, 92–358) (Table 2).

Table 1 Baseline characteristics of study participants

Number, *n*	508
Sex, M/F, *n* (%)	132/376 (26/74)
Age, years, median (IQR)	39 (28.5–49.0)
Age > 39 years, *n* (%)	248/508 (48.8)
Personal history of VTE, *n* (%)	42/508 (8.3)
Unprovoked CVT, *n* (%)	195/508 (38.4)
Hormonal therapy, *n* (%)	218/508 (42.9)
Known thrombophilia abnormality, *n* (%)	181/508 (35.6)
Cancer, *n* (%)	27/508 (5.3)
Trauma of the head or neurosurgery, *n* (%)	14/508 (2.8)
Local or systemic infection, *n* (%)	46/508 (9.1)
Pregnancy or puerperium, *n* (%)	64/376 (17.0)
Intracerebral hemorrhage, *n* (%)	151/508 (29.7)
Deep venous system CVT, *n* (%)	102/499 (20.4)
Single site CVT, *n* (%)	225/499 (45.1)

n, sample size; M, male; F, female; IQR, interquartiles (25–75% percentiles); VTE, venous thromboembolism; CVT, cerebral venous thrombosis.

Table 2 Recanalization grade up to 3-year follow-up after cerebral venous thrombosis

Recanalization, *n* (%)	
28 days–3 months	
1. Complete	43/100 (43.0)
2. Partial	38/100 (38.0)
3. Not recanalized	19/100 (19.0)
3–6 months	
1. Complete	42/101 (41.6)
2. Partial	33/101 (32.7)
3. Not recanalized	26/101 (25.7)
6–12 months	
1. Complete	72/150 (48.0)
2. Partial	48/150 (32.0)
3. Not recanalized	30/150 (20.0)
1–3 years	
1. Complete	62/157 (39.5)
2. Partial	55/157 (35.0)
3. Not recanalized	40/157 (25.5)
Imaging at follow-up, *n* (%)	
CT	20/508 (3.9)
Angio-CT	16/508 (3.2)
MRI	162/508 (31.9)
Angio-MRI	302/508 (59.4)
Angiography	8/508 (1.6)
Total follow-up, days (range)	152758 (28–1091)
Follow-up, days, median (IQR)	245 (116–395)
Follow-up, patient years	419
Therapy, *n* (%)	
Antiplatelet therapy	17 (3.3)
Alone, *n*	13
Followed by OAT, *n*	4
LMWH	327 (64.4)
Alone, *n*	39
Followed by OAT, *n*	278
Followed by antiplatelet therapy, *n*	10
UFH	110 (21.7)
Alone, *n*	2
Followed by LMWH, *n*	4
Followed by OAT, *n*	104
OAT	46 (9.0)
None	8 (1.6)
Duration of anticoagulation, median (IQR)	187 (92–358)

CT, computed tomography; MRI, magnetic resonance imaging; IQR, interquartiles (25–75% percentiles); LMWH, low-molecular-weight heparin; UFH, unfractioned heparin; OAT, oral anticoagulant therapy.

Recanalization rates within 3 years after a first episode of CVT

More than 90% of imaging tests performed at follow-up were MRI (either with or without angio-sequence).

Because imaging tests were available at different time-points after the index event, we defined four different time-frames: early (28 days to 3 months), intermediate (3–6 months), late (6–12 months) and chronic (1–3 years).

Patients were followed for a total of 152 758 days (range, 28–1091) and 419 patient years.

Recanalization rate (either complete or partial) was high in each study period (early, 81.0%; intermediate, 74.3%; late, 80.0%; chronic, 74.5%), despite the

radiological follow-up being performed at different periods of time in different CVT patients. No significant differences in CVT recanalization were reported among different timings (overall $P = 0.452$) (Table 2).

Clinical outcome within 3 years after a first episode of CVT

Clinical outcome was evaluated in 483 of 508 (95.1%) patients and it was analyzed, as for recanalization rates, according to the four time-frames of follow-up. A good outcome was observed in each study group of patients (early, 88.3%; intermediate, 94.8%; late, 94.5%; chronic, 93.7%). No significant difference in terms of good vs. poor clinical functional outcome was observed among the groups (overall $P = 0.263$) (Table 3).

Predictors of CVT recanalization

At the univariate analysis, three clinical variables were associated with a lower CVT recanalization grade: age > 39 years (odds ratio [OR], 0.45; 95% confidence interval [CI], 0.32–0.63; $P < 0.001$), deep venous system CVT (OR, 0.57; 95% CI, 0.38–0.84; $P = 0.005$) and unprovoked CVT (OR, 0.69; 95% CI, 0.49–0.96; $P = 0.027$). Two variables were associated with a higher grade of CVT recanalization: single site CVT (OR, 1.92; 95% CI, 1.37–2.69; $P < 0.001$) and CVT during pregnancy or puerperium (OR, 2.73; 95% CI, 1.61–4.64; $P < 0.001$) (Table 4A). These results were confirmed by the multivariate analysis for age > 39 years (OR, 0.55; 95% CI, 0.39–0.78; $P = 0.001$), single site CVT (OR, 1.81; 95% CI, 1.29–2.55; $P = 0.001$) and CVT during pregnancy or puerperium (OR, 2.24; 95% CI, 1.28–3.92; $P = 0.005$) (Table 4B).

Table 3 Neurologic outcome up to 3 years of follow-up after cerebral venous thrombosis

msRankin	
28 days–3 months	
0	64/94 (68.1)
1	19/94 (20.2)
2	5/94 (5.3)
3	4/94 (4.3)
4	2/94 (2.1)
5	0/94 (0)
6	0/94 (0)
msRankin	
3–6 months	
0	72/95 (75.8)
1	18/95 (19.0)
2	2/95 (2.1)
3	1/95 (1.1)
4	2/95 (2.1)
5	0/95 (0)
6	0/95 (0)
msRankin	
6–12 months	
0	109/145 (75.2)
1	28/145 (19.3)
2	2/145 (1.4)
3	5/145 (3.4)
4	1/145 (0.7)
5	0/145 (0)
6	0/145 (0)
msRankin	
1–3 years	
0	95/149 (63.8)
1	43/149 (28.9)
2	4/149 (2.6)
3	1/149 (0.7)
4	5/149 (3.3)
5	1/149 (0.7)
6	0/149 (0)

msRankin, modified Rankin scale.

Predictors of good clinical outcome after a first episode of CVT

At the univariate analysis, CVT recanalization (OR, 2.67; 95% CI, 1.67–4.28; $P < 0.001$) and the presence of hormonal therapy (OR, 2.65; 95% CI, 1.18–5.96; $P = 0.019$) were significantly associated with a good neurological outcome. Conversely, a personal history of VTE (OR, 0.31; 95% CI, 0.12–0.76; $P = 0.011$), the presence of cancer (OR, 0.25; 95% CI, 0.09–0.72; $P = 0.010$), a deep venous system CVT (OR, 0.47; 95% CI, 0.23–0.99; $P = 0.047$) and unprovoked CVT (OR, 0.50; 95% CI, 0.25–0.99; $P = 0.047$) were significantly associated with a poor neurological outcome. This association was marginally significant for concomitant trauma of the head or the neck or neurosurgical procedures (OR, 0.27; 95% CI, 0.07–1.01; $P = 0.052$ with a significance level of $P < 0.05$, two-tailed) (Table 5A). These results were confirmed by the multivariate analysis for

Table 4 Univariate (A) and multivariate (B) analyses of variables associated with CVT recanalization

	OR	*P*	95% CI
(A)			
Age > 39 years	**0.45**	**< 0.001**	**0.32-0.63**
Male	0.87	0.449	0.60–1.25
Personal history of VTE	0.71	0.252	0.40–1.27
Thrombophilia	1.00	0.977	0.72–1.41
Hormonal therapy	1.25	0.188	0.90–1.73
Cancer	0.55	0.110	0.27–1.14
Trauma/neurosurgery	1.43	0.485	0.53–3.86
Local/systemic infection	1.23	0.475	0.67–2.17
Deep system CVT	**0.57**	**0.005**	**0.38–0.84**
Single site CVT	**1.92**	**< 0.001**	**1.37–2.69**
Hemorrhage	1.05	0.792	0.74–1.48
Pregnancy/puerperium	**2.73**	**< 0.001**	**1.61–4.64**
Unprovoked	0.69	0.027	0.49–0.96
Duration of anticoagulation	1.00	0.351	1.00–1.00
(B)			
Age > 39 years	**0.55**	**0.001**	**0.39–0.78**
Single sinus CVT	**1.81**	**0.001**	**1.29–2.55**
Pregnancy/puerperium	**2.24**	**0.005**	**1.28–3.92**

VTE, venous thromboembolism; CVT, cerebral venous thrombosis; OR, odds ratio; CI, confidence interval. Positive or negative significant association with CVT recanalization is highlighted in bold.

Table 5 Univariate (A) and multivariate (B) analyses of variables associated with good neurologic outcome (mRS = 0–1)

	OR	*P*	95% CI
(A)			
Recanalization	**2.67**	**< 0.001**	**1.67–4.28**
Age > 39 years	0.88	0.733	0.45–1.77
Male	0.66	0.268	0.32–1.37
Personal history of VTE	**0.31**	**0.011**	**0.12–0.76**
Thrombophilia	0.63	0.189	0.31–1.26
Hormonal therapy	**2.65**	**0.019**	**1.18–5.96**
Cancer	**0.25**	**0.010**	**0.09–0.72**
Trauma/neurosurgery	0.27	0.052	0.07–1.01
Local/systemic infection	3.70	0.202	0.49–27.71
Deep system CVT	**0.47**	**0.047**	**0.23–0.99**
Single site CVT	0.75	0.424	0.38–1.50
Hemorrhage	1.07	0.868	0.50–2.28
Pregnancy/puerperium	5.36	0.101	0.72–39.87
Unprovoked	0.50	0.047	0.25–0.99
Duration of anticoagulation	1.00	0.180	1.00–1.00
(B)			
CVT recanalization	**2.56**	**< 0.001**	**1.59–4.13**
Cancer	**0.29**	**0.029**	**0.09–0.88**
Personal history of VTE	**0.36**	**0.033**	**0.14–0.92**
Hormonal therapy	2.30	0.050	1.00–5.29

VTE, venous thromboembolism; CVT, cerebral venous thrombosis; OR, odds ratio; CI, confidence interval. Positive or negative significant association with good neurologic outcome is highlighted in bold.

CVT recanalization (OR, 2.56; 95% CI, 1.59–4.13; $P < 0.001$), presence of cancer (OR, 0.29; 95% CI, 0.09–0.88; $P = 0.029$) and personal history of VTE (OR, 0.36; 95% CI, 0.14–0.92; $P = 0.033$). A trend toward significance was observed for the hormonal therapy (OR, 2.30; 95% CI, 1.00–5.29; $P = 0.050$) (Table 5B).

Discussion

In our study, high rates of recanalization were already detected in most patients with CVT when neuroimaging tests were performed within the first months after the index event. Furthermore, as suggested by a number of previous studies, the long-term neurological outcome of these patients appeared favorable. Our findings suggest that partial or complete recanalization is independently associated with a favorable clinical outcome. Thanks to the large sample size, we were able to reliably assess the role of several other potential factors associated with CVT recanalization and neurological outcome.

A number of previous retrospective and prospective cohorts have described the time course of recanalization after the first episode of CVT. These studies had a limited sample size and their results were not consistent [6,9,12–14,16]. In a study on 33 patients, Baumgartner *et al.* reported that CVT recanalization occurred until 4 months after the diagnosis, irrespective of duration of oral anticoagulation [6]. Their results were confirmed by Stolz and colleagues in a study of 37 patients who had a high CVT recanalization rate at discharge that did not further increase in the subsequent year [12]. Conversely, other investigators observed a later onset of CVT recanalization during anticoagulant treatment [13,14,16], with a median time after CVT diagnosis of 6 months [14], which could continue until 11 months [16].

The duration of anticoagulant treatment after the acute phase from the onset of CVT has not been established yet, due to the lack of a high level of supportive evidence [23].

In our study, we report that the duration of anticoagulant therapy did not predict the rate of CVT recanalization. Furthermore, the majority of patients showed a high CVT recanalization within 3 months of follow-up, suggesting that patients treated with anticoagulant therapy need a relatively short period of time to obtain cerebral venous patency. The patients' age was inversely associated with CVT recanalization in our study and in two previous studies [13,16], suggesting a prothrombotic deviance of the thrombolytic balance in elderly patients. On the other hand, in our study, the involvement of a single site and the presence of pregnancy or puerperium as risk factors for CVT were independently associated with CVT recanalization.

As a second finding, we observed that the neurological outcome after a first episode of CVT was good in most of the patients within 3 months of follow-up. This finding was comparable with the neurological outcome evaluated in different patient groups followed for longer periods of time (up to 3 years). Our results confirm the findings of several previous cohort studies and of a large meta-analysis, which showed a good functional outcome with a low rate of dependence even years after the index event [13,14,16,24,25].

When we evaluated the presence of factors associated with the neurological outcome, we found that a high recanalization grade independently predicted a good prognosis. The association between CVT recanalization and clinical outcome is still uncertain because, to date, this has been assessed in only a few studies with a relatively small sample size and short follow-up. Stolz *et al.*, in a small study with 26 CVT patients followed for up to 90 days, reported that CVT recanalization, quantified by means of venous transcranial duplex sonography, was associated with a favorable functional outcome [10]. However, the same group did not find a significant association between recanalization and patient outcome in another small series of patients with a previous CVT prospectively followed with MRI, CT or conventional angiography [12]. In 2010, Putaala *et al.* reported a positive correlation by univariate analysis between no recanalization and unfavorable functional outcome (mRS 2–6), after 6 months follow-up [13]. More recently, in a cohort of 102 patients with CVT, Arauz and colleagues observed that complete CVT recanalization predicted good functional outcome (mRS 0–1), when compared

with patients who had no recanalization [16]. Conversely, in another study with a similar sample size (99 patients), Herweh *et al*. did not find a significant association of outcome and recanalization status with the MRI [14].

The present study, with a larger sample size and a longer follow-up, may have overcome some of the limitations of the existing literature, and suggests that CVT recanalization contributes to the neurological outcome during follow-up. Furthermore, we observed that the presence of cancer and a history of VTE was correlated with a poor functional outcome. These variables were previously found to be associated with an increased risk of recurrent VTE after the first event of CVT [17] and with increased mortality rates [24]. Our results confirm the findings of a small study by Breteau and colleagues, who highlighted the detrimental role of cancer in clinical outcome at 3-year follow-up, in terms of dependence or death (mRS 3–6) [25].

We also reported that hormonal therapy is associated with a good clinical outcome at univariate analysis, with a significant trend shown at multivariate analysis. The positive effect of the use of oral contraceptives and hormonal replacement therapy (representing the majority of patients on hormonal therapy, and a 'sex-specific risk factor'), together with a young age (i.e. $\leq$ 39 years), confirms that CVT in young women is generally associated with a more favorable clinical outcome, as suggested in a subanalysis of the International Study on Cerebral Vein and Dural sinus Thrombosis (ISCVT) [26]. However, the interpretation of the effect of hormonal therapy on the type of clinical outcome after a first episode of CVT is still debatable. Indeed, in the study by Hiltunen *et al*., the use of estrogen was associated with an unfavorable long-term clinical outcome at follow-up, although this was only detected at univariate analysis [19].

Our results may have some potential clinical implications. Because the greatest CVT recanalization rate occurred in most patients within the first months after the index event and CVT recanalization appears to be an independent predictor of functional outcome, repeating imaging tests after this period of time does not appear to add relevant information.

The present study has some limitations. First, this is a retrospective study and the decision on type and time of radiological follow-up was left to the discretion of the treating physician. Second, radiological examinations were not centrally adjudicated, leaving a potential heterogeneity in their evaluation. Furthermore, data on cerebral hemodynamics were not collected in our patients. Future investigations on CVT recanalization associated with the evaluation of cerebral hemodynamics in large population studies might add relevant information on the pathophysiology of CVT progress and its effect on outcome. As a third limitation, we do not have multiple follow-up data for the same patient at different periods of time; therefore, in this study we have no information on the patterns of recanalization over time in each patient. Fourth, thrombophilia abnormalities were not systematically searched for in all the included patients. Thus, the results of the analysis of their association with recanalization and functional outcome should be interpreted with caution. As a fifth limitation, the present study may not have included the sickest CVT patients who died within the acute phase (mRS=6) or who were too critical to undergo a subsequent follow-up imaging evaluation. Therefore, generalization of our results in patients with no follow-up imaging could not be confirmed.

Study strengths include the very large sample of patients, making this the largest report on recanalization rates of CVT ever published, with 508 patients and 419 patient-years of follow-up.

Conclusions

After a first episode of CVT, recanalization rates during follow-up are already high in the early phases after the index event. Most patients have a good functional outcome, which is independently predicted by CVT recanalization. Conversely, the presence of cancer and a personal history of VTE independently predict a poor functional clinical outcome. Large prospective management studies are necessary to confirm our findings and to guide the optimal timing of follow-up imaging.

Addendum

E. Rezoagli and F. Dentali conceived the study, followed-up the patients, collected, analyzed and interpreted the data, searched the literature and wrote the manuscript. I. Martinelli, D. Poli, U. Scoditti, S.M. Passamonti, P. Bucciarelli and W. Ageno followed-up the patients, collected the data, interpreted the results and revised the manuscript for important intellectual content. All authors have read and approved the manuscript for submission to *JTH*™.

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Disclosure of Conflict of Interests

The authors state that they have no conflict of interest.

Appendix

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