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ORIGINAL RESEARCH

Delayed Diagnosis in Cerebral Venous Thrombosis: Associated Factors and Clinical Outcomes

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BACKGROUND: Identifying factors associated with delayed diagnosis of cerebral venous thrombosis (CVT) can inform future strategies for early detection.

METHODS AND RESULTS: We conducted a retrospective cohort study including all participants from ACTION-CVT (Anticoagulation in the Treatment of Cerebral Venous Thrombosis) study who had dates of neurologic symptom onset and CVT diagnosis available. Delayed diagnosis was defined as CVT diagnosis occurring in the fourth (final) quartile of days from symptom onset. The primary study outcome was modified Rankin Scale score of ≤ 1 at 90 days; secondary outcomes included partial/complete CVT recanalization on last available imaging and modified Rankin Scale score of ≤ 2 . Logistic regression analyses were used to identify independent variables associated with delayed diagnosis and to assess the association of delayed diagnosis and outcomes. A total of 935 patients were included in our study. Median time from symptom onset to diagnosis was 4 days (interquartile range, 1–10 days). Delayed CVT diagnosis (time to diagnosis >10 days) occurred in 212 patients (23%). Isolated headache (adjusted odds ratio [aOR], 2.36 [95% CI, 1.50–3.73]; $P < 0.001$), older age (aOR by 1 year, 1.02 [95% CI, 1.004–1.03]; $P = 0.01$), and papilledema (aOR, 2.00 [95% CI, 1.03–3.89]; $P = 0.04$) were associated with diagnostic delay, whereas higher National Institutes of Health Stroke Scale score was inversely associated with diagnostic delay (aOR by 1 point, 0.95 [95% CI, 0.89–1.00]; $P = 0.049$). Delayed diagnosis was not associated with modified Rankin Scale score of ≤ 1 at 90 days (aOR, 1.08 [95% CI, 0.60–1.96]; $P = 0.79$).

CONCLUSIONS: In a large multicenter cohort, a quarter of included patients with CVT were diagnosed >10 days after symptom onset. Delayed CVT diagnosis was associated with the symptom of isolated headache and was not associated with adverse clinical outcomes.

Key Words: cerebral venous thrombosis ■ diagnostic error ■ venous thromboembolism

Cerebral venous thrombosis (CVT) is a rare cerebrovascular disease, which can result in significant disability.^{1,2} One challenge in diagnosing CVT relates to its often-insidious onset compared with other types of cerebrovascular diseases and the fact that CVT can initially manifest with nonspecific clinical features.^{1,3,4} In the ISCVT (International Study on Cerebral Vein and Dural Sinus Thrombosis), patients

with CVT presented to the hospital after a median of 4 days from symptom onset, and CVT diagnosis was not established until a median of 7 days from symptom onset.^{1,5} In a large multistate cohort study using administrative claims data, nearly 1 in every 30 hospitalized patients with CVT had a potentially missed diagnosis in the emergency department (ED) within 14 days of their CVT diagnosis.⁴

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CLINICAL PERSPECTIVE

What Is New?

- In a large multicenter cohort of patients with cerebral venous thrombosis (CVT), a quarter were diagnosed >10 days after symptom onset.
- Delayed CVT diagnosis was associated with older age patients as well as with isolated headache and papilledema at the time of diagnosis.
- Delayed CVT diagnosis was not associated with adverse clinical outcomes at 90 days or poor venous recanalization.

What Are the Clinical Implications?

- Diagnosis of CVT should be more frequently considered by providers caring for patients with headache complaints, particularly in the presence of CVT risk factors.
- Obtaining a detailed neurologic examination, consideration of known CVT risk factors, and including secondary causes of headache in the differential diagnosis for emergency department patients with headache complaints may help to improve diagnostic accuracy in CVT.

Nonstandard Abbreviations and Acronyms

ACTION-CVT	Anticoagulation in the Treatment of Cerebral Venous Thrombosis
CVT	cerebral venous thrombosis
ISCVT	International Study on Cerebral Vein and Dural Sinus Thrombosis
mRS	modified Rankin Scale

The purpose of this current study is to evaluate diagnostic delay in the ACTION-CVT (Anticoagulation in the Treatment of Cerebral Venous Thrombosis) study, to identify factors associated with delayed diagnosis, and to explore the relationship between delayed CVT diagnosis and clinical outcomes.⁶ We hypothesized that the following variables would be associated with delayed CVT diagnosis: male sex, presenting with signs of increased intracranial pressure, encephalopathy, coma, headache complaints, low National Institutes of Health Stroke Scale score, and normal head computed tomography on presentation.⁵ We further hypothesized that well-known CVT risk factors, including oral contraceptive use, cancer, and postpartum state, would be associated with a lack of delay in CVT diagnosis.^{1,7,8} An improved understanding of factors associated with diagnostic delay among

patients with CVT is a key component of future interventions to improve diagnostic accuracy to impact clinical outcomes.

METHODS

Design

This is a substudy of the ACTION-CVT study, a multicenter retrospective international cohort study of consecutive patients with CVT hospitalized from January 1, 2015 to December 31, 2020.⁶ All patients who had available data on their date of CVT symptom onset and their date of CVT diagnosis were included in the current study.

Deidentified data are available on reasonable request to the corresponding author.

Measurements

We defined time to diagnosis of CVT as the interval in days between the onset of CVT symptoms (day of first symptom thought to be related to CVT by the site investigator) and diagnosis of CVT (day of CVT diagnosis reported by the site investigator). We used temporal quartiles to evaluate for factors associated with delayed diagnosis among included study patients.⁵ We defined a delayed diagnosis of CVT as occurring when CVT diagnosis was made in the fourth (final) quartile of days from symptom onset among all study participants, in keeping with prior literature specific to CVT diagnosis⁵ as well as with the National Academies of Science, Engineering, and Medicine definition of diagnostic error as “the failure to establish an accurate and timely explanation of the patient’s health problem,” (p. 4) which has been widely accepted.⁹ In addition, we report the proportion of patients discharged from a hospital/ED encounter with any neurologic symptoms in the 3 months preceding their CVT hospitalization. Although these encounters 3 months before CVT hospitalization may have been unrelated to subsequent CVT detection, some may represent instances of severely delayed or missed CVT diagnosis.

Study Outcomes

Our primary outcome was excellent functional outcome, defined as 90-day modified Rankin Scale (mRS) score of ≤ 1 because recent studies have shown that most patients with CVT have excellent functional outcome.^{1,10} As a secondary outcome, we included good functional outcome, defined as 90-day mRS score of ≤ 2 and any (partial or complete) CVT recanalization on the last available venous imaging study obtained. Presence or absence of any recanalization was abstracted from radiology reports by the local site investigators. Complete recanalization was defined as full

recanalization of the thrombosed vein or sinus without any residual thrombus. Partial recanalization was defined as improved opacification or flow in the affected cerebral sinus or vein, but with residual thrombus present on follow-up imaging. No recanalization was defined as no change or worsening in opacification or flow in the affected cerebral sinus or vein from baseline imaging. We hypothesized that delayed CVT diagnosis would be associated with poor outcomes even after adjustment for patient factors previously known to be predictive of poor outcome in CVT (ie, patient age, active cancer, and CVT with deep vein involvement) in the entire study cohort.¹ We additionally explored the primary study outcome in 3 different patient subgroups: those who presented with (1) isolated headache, (2) focal deficits, or (3) coma.

Subgroup Analysis

Because prior studies have shown an increased risk of delayed diagnosis of cerebrovascular disease in patients with isolated headache complaints,^{4,11,12} we separately evaluated for factors associated with delayed CVT diagnosis in the subset of included patients with isolated headache complaints. We defined isolated headache as having no symptoms other than headache at the time of index CVT hospitalization.

Standard Protocol Approvals and Patient Consents

Institutional review board approval was obtained from each participating center to perform the ACTION-CVT study. Patient consent was waived because of the retrospective design of the study.

Statistical Analysis

We report time to diagnosis from symptom onset using median and interquartile range. Predefined patient factors at each quartile of time to diagnosis from symptom onset were described for the entire cohort and for the subgroup of patients experiencing isolated headaches. An ordered logistic regression analysis was performed to evaluate the relationship between these variables and the quartiles of time to diagnosis from symptom onset, with *P* values for trends reported.

A backward stepwise logistic regression model was developed, incorporating all variables from the univariate analyses, with delayed CVT diagnosis as the outcome of interest. Variables were selected using a significance threshold set at *P*<0.05.

To assess the impact of delayed CVT diagnosis on our clinical and radiographic outcomes, we used both unadjusted and adjusted logistic regression models. Factors adjusted for in the models were those identified in the stepwise logistic regression analysis that

were associated with delayed CVT diagnosis in addition to factors previously linked with poor outcomes (ie, patient age, cancer history, and CVT with deep vein involvement) after CVT.¹ We used the same adjusted logistic regression model for patients with (1) isolated headache, (2) focal neurologic symptoms, and (3) coma to evaluate the effect of delayed CVT diagnosis on our primary outcome within each subgroup. Effect estimates were summarized as unadjusted odds ratios (ORs) and adjusted ORs (aORs) with 95% CIs reported. All statistical tests were performed at the 2-sided level. Missing data were not imputed. Data were analyzed using Stata, version 15.1. *P*<0.05 was considered statistically significant.

RESULTS

Of the 1025 patients included in the ACTION-CVT study, a total of 935 were included in this substudy. Median time from symptom onset to diagnosis was 4 days (interquartile range, 1–10 days). The Figure shows the full distribution of time from symptom onset to diagnosis. A total of 84.5% of patients (n=790) had head computed tomography obtained, and 84.7% had brain magnetic resonance imaging (n=792) performed at the time of CVT diagnosis.

Delayed CVT diagnosis occurred in 212 (22.7%) patients (median time to diagnosis, >10 days). A total of 155 patients were discharged from a hospital/ED encounter in the 3 months before their index CVT hospitalization for neurologic symptoms, including 64 of the 212 patients (30.2%) with a delayed CVT diagnosis. Table 1 summarizes the associations between various patient factors and time-to-diagnosis temporal quartiles. We found that the presenting symptoms and signs of CVT associated with delayed diagnosis were low median

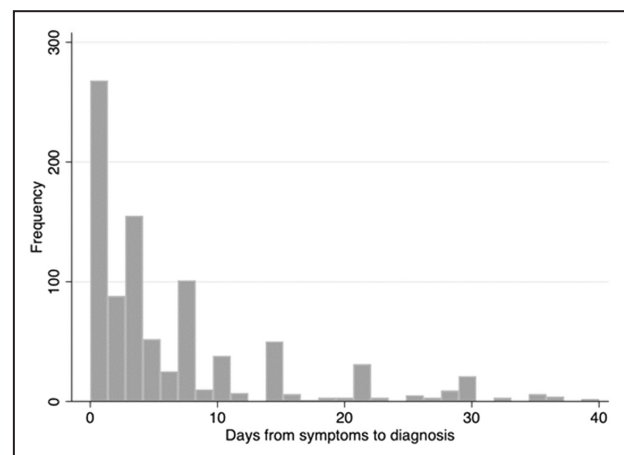


Figure. Time from symptom onset to diagnosis (n=894). A total of 41 patients who were diagnosed >40 days from symptom onset are not shown.

Table 1. Clinical and Radiographic Factors, Stratified According to Time to Diagnosis Quartiles

Variables	First quartile (<1 d) (n=149)	Second quartile (1–4 d) (n=362)	Third quartile (5–10 d) (n=212)	Fourth quartile (>10 d) (n=212)	P value for trend
Demographics					
Age, mean±SD, y	50.71 (17.35)	45.13 (15.94)	43.6 (17.79)	46.4 (16.65)	0.036
Women, n/total (%)	74/149 (49.7)	233/362 (64.4)	146/212 (68.9)	139/212 (65.6)	0.004
Race or ethnicity, n/total (%)					
White	110/147 (74.8)	255/361 (70.6)	142/210 (67.6)	142/210 (67.6)	0.117
Black	24/147 (16.3)	56/361 (15.5)	30/210 (14.3)	40/210 (19.0)	0.522
Asian	7/147 (4.8)	12/361 (3.3)	16/210 (7.6)	5/210 (2.4)	0.907
Hispanic	8/146 (5.5)	39/361 (10.8)	33/210 (15.7)	15/207 (7.2)	0.435
Medical history, n/total (%)					
Active cancer	21/148 (14.2)	14/362 (3.9)	9/211 (4.3)	17/212 (8.0)	0.125
12 wk Postpartum	6/148 (4.1)	12/358 (3.4)	10/211 (4.7)	8/209 (3.8)	0.797
Recent mastoiditis/sinusitis	5/149 (3.4)	31/362 (8.6)	18/212 (8.5)	26/212 (12.3%)	0.009
Oral contraceptive use	14/145 (9.7)	94/356 (26.4)	63/209 (30.1)	48/207 (23.2)	<0.015
Presenting symptoms/signs					
NIH Stroke Scale score on arrival, median (interquartile range)	1 (0–5)	0 (0–4)	0 (0–2)	0 (0–0)	<0.001
Isolated headache, n/total (%)	11/149 (7.4)	123/362 (34.0)	83/212 (39.2)	108/212 (50.9)	<0.001
Focal deficit, n/total (%)	76/149 (51.0)	149/362 (41.2)	81/212 (38.2)	72/212 (34.0)	0.002
Seizure, n/total (%)	60/149 (40.3)	98/362 (27.1)	49/212 (23.1)	24/212 (11.3)	<0.001
Encephalopathy/coma, n/total (%)	49/149 (32.9)	90/362 (24.9)	38/212 (17.9)	33/212 (15.6)	<0.001
Papilledema, n/total (%)	4/135 (3.0)	26/335 (7.8)	24/194 (12.4)	36/206 (17.5)	<0.001
Increased intracranial pressure, n/total (%)	27/147 (18.4)	74/357 (20.7)	43/208 (20.7)	59/211 (28.0)	0.034
Imaging findings, n/total (%)					
Computed tomography of the head normal	11/134 (8.2)	77/322 (23.9)	57/182 (31.3)	52/151 (34.4)	<0.001
Deep location of cerebral venous thrombosis	30/149 (20.1)	99/361 (27.4)	55/212 (25.9)	52/211 (24.6)	0.629

NIH indicates National Institutes of Health.

National Institutes of Health Stroke Scale score, isolated headache, nonfocal deficit, lack of seizure, lack of encephalopathy, presence of papilledema, and increased intracranial pressure (Table 1). In a stepwise regression analysis, presence of isolated headache (aOR, 2.36 [95% CI, 1.50–3.73]; $P<0.001$), older age (aOR by 1 year, 1.02 [95% CI, 1.004–1.03]; $P=0.01$), and papilledema (aOR, 2.00 [95% CI, 1.03–3.89]; $P=0.04$)

were associated with diagnostic delay. Presenting with a higher National Institutes of Health Stroke Scale score was inversely associated with diagnostic delay (aOR by 1 point, 0.95 [95% CI, 0.89–1.00]; $P=0.049$).

A total of 628 included patients had 90-day mRS data available, of whom 481 (51%) had an excellent functional outcome. In a regression model adjusted for factors associated with delayed diagnosis in our logistic regression

Table 2. Unadjusted and Adjusted Logistic Regression Assessing the Association of Delayed Diagnosis With Excellent 90-Day Outcome (mRS Score ≤ 1), Good 90-Day Outcome (mRS Score ≤ 2), and Recanalization

	Unadjusted	Adjusted
Excellent 90-d outcome (mRS score ≤ 1)	n=628; OR, 1.34 (95% CI, 0.85–2.11); $P=0.21$	n=530; aOR, 1.08 (95% CI, 0.6–1.96); $P=0.79$
Good 90-d outcome (mRS score ≤ 2)	n=628; OR, 1.17 (95% CI, 0.68–1.99); $P=0.57$	n=530; aOR, 0.69 (95% CI, 0.34–1.4); $P=0.30$
Partial or complete recanalization	n=601; OR, 1.12 (95% CI, 0.66–1.89); $P=0.68$	n=496; aOR, 1.44 (95% CI, 0.76–2.73); $P=0.26$

Regression analysis is adjusted (aOR) for variables significant from stepwise regression analysis (headache, age, papilledema, and National Institutes of Health Stroke Scale score) as well as deep location of cerebral venous thrombosis and cancer. aOR indicates adjusted OR; mRS, modified Rankin Scale; and OR, odds ratio.

model as well as known predictors of functional outcome after CVT, delayed diagnosis was not associated with good functional outcome (mRS score ≤ 2) (aOR, 0.69 [95% CI, 0.34–1.4]; $P=0.30$), excellent functional outcome (mRS score ≤ 1) (aOR, 1.08 [95% CI, 0.60–1.96]; $P=0.79$), or any (complete or partial) recanalization (aOR, 1.44 [95% CI, 0.76–2.73]; $P=0.26$) (Table 2). Similarly, there were no significant associations between diagnostic delay and mRS score of ≤ 1 at 90 days in the subgroups of patients presenting with isolated headache (aOR, 1.71 [95% CI, 0.54–5.45]; $P=0.36$), focal neurologic deficits (aOR, 1.27 [95% CI, 0.51–3.15]; $P=0.61$), or coma.

Subgroup Analysis of Patients With Isolated Headache

Headache was the most common symptom, reported in 705 patients (75.4%), and was the only presenting symptom (isolated headache) for 325 patients (34.8%). Among patients with isolated headache, the median time to diagnosis was 6 days (interquartile range, 3–14 days). Factors associated with delayed diagnosis in the subgroup of patients with isolated headache included increased intracranial pressure, papilledema, and normal head computed tomography imaging at the time of CVT diagnosis (Table 3).

DISCUSSION

In this large, multicenter retrospective cohort study of patients with CVT, we found that those with isolated headache complaints, older age, and papilledema at the time of index CVT hospitalization were at increased odds of delayed diagnosis. We did not detect a relationship between delayed CVT diagnosis and functional outcomes or recanalization.

Headache complaints are present in $\approx 90\%$ of patients with CVT.^{1,13,14} In the ED setting, diagnosing cerebrovascular conditions among patients who present with headache and mild or minimal clinical deficits is particularly challenging.^{11,15} In a study of CVT misdiagnosis using administrative claims data, patients with a missed diagnosis of CVT at index ED visit were more often given a benign headache diagnosis than a diagnosis of seizure.⁴ In ISCVT, diagnostic delay was longer in patients with isolated intracranial hypertension syndrome (defined as any combination of headache, vomiting, and papilledema with/without visual loss or sixth nerve paresis, without other neurologic symptoms or signs) and those with papilledema.^{1,5} Although we did not specifically capture patients who presented with the syndrome of isolated intracranial hypertension, our findings of diagnostic delay among patients with

Table 3. Clinical and Demographic Factors, Stratified According to Time to Diagnosis Quartiles for the Subgroup of Patients With Isolated Headache (N=325)

Variables	First quartile (<1 d) (n=11)	Second quartile (1–4 d) (n=123)	Third quartile (5–10 d) (n=83)	Fourth quartile (>10 d) (n=108)	P value for trend
Demographics					
Age, mean \pm SD, y	46.45 \pm 16.23	40.15 \pm 13.77	38.22 \pm 15.55	43.01 \pm 15.51	0.392
Women, n/total (%)	2/11 (18.2)	87/123 (70.7)	55/83 (66.3)	75/108 (69.4)	0.340
Race or ethnicity, n/total (%)					
White	9/11 (81.8)	94/123 (76.4)	57/83 (68.7)	74/106 (69.8)	0.186
Black	2/11 (18.2)	16/123 (13.0)	11/83 (13.3)	15/106 (14.2)	0.933
Asian	0/11 (0.0)	1/123 (0.8)	4/83 (4.8)	2/106 (1.9)	0.474
Hispanic	1/11 (9.1)	13/122 (10.7)	15/83 (18.1)	9/107 (8.4)	0.775
Medical history, n/total (%)					
Active cancer	2/11 (18.2)	0/123 (0.0)	1/83 (1.2)	3/108 (2.8)	0.890
12 wk Postpartum	0/11 (0)	5/121 (4.1)	5/83 (6.0)	5/106 (4.7)	0.646
Recent mastoiditis/sinusitis	0/11 (0)	14/123 (11.4)	7/83 (8.4)	14/108 (13.0)	0.476
Oral contraceptive use	0/11 (0)	45/120 (37.5)	27/83 (32.5)	25/106 (23.6)	0.173
Presenting symptoms/signs, n/total (%)					
Papilledema	0/10 (0)	6/118 (5.1)	9/79 (11.4)	19/105 (18.1)	0.001
Increased intracranial pressure	2/11 (18.2)	14/123 (11.4)	16/81 (19.8)	30/108 (27.8)	0.003
Imaging findings, n/total (%)					
Computed tomography of the head normal	1/8 (12.5)	33/103 (32.0)	25/71 (35.2)	34/76 (44.7)	0.040
Deep location of cerebral venous thrombosis	3/11 (27.3)	29/122 (23.8)	16/83 (19.3)	23/107 (21.5)	0.568

headache symptoms are consistent with these ISCVT results. Similarly, we found that the presence of increased intracranial pressure and papilledema at index CVT admission was associated with delayed diagnosis in the overall cohort as well as in the subgroup of patients with isolated headache. In both our study and the ISCVT, papilledema is likely best understood as a result of delayed diagnosis rather than as a risk factor for diagnostic delay. We suspect that patients with CVT with minor or nonspecific symptoms who are not promptly diagnosed went on to develop papilledema and increased intracranial pressure before their CVT was properly diagnosed and treated. This is important because papilledema has been associated with permanent visual field deficits, which can impact patients' quality of life.^{5,16} Nevertheless, we are unable to confirm whether delayed diagnosis resulted in a greater risk of vision loss as we did not systematically capture the occurrence of visual deficits in our study.

On the basis of our study findings, obtaining a detailed neurologic examination, consideration of known CVT risk factors, and including secondary causes of headache in the differential diagnosis for ED patients with headache complaints may help to improve diagnostic accuracy in CVT. Headache complaints in CVT are notoriously diverse. Some key clinical features of CVT-associated headache include exacerbation by valsalva maneuver and recumbency as well as subacute onset of headaches with often diffuse rather than unilateral location.¹⁷ However, acute presentations consistent with migraine or thunderclap headache may also occur in CVT.¹⁸

The lack of relationship between delayed CVT diagnosis and our chosen outcomes is in keeping with prior literature. In ISCVT, no significant differences in mRS scores were found between patients with CVT diagnosed earlier versus later after symptom onset.⁵ Because we accounted for important predictors of functional outcome in our adjusted models, it is possible that delay in diagnosis may contribute to a small, but clinically important, difference in outcomes following CVT. In particular, it remains possible that for certain patients, there is a threshold wherein early treatment initiation with anticoagulation is associated with better outcomes, which our study failed to detect because of local adjudication of recanalization and variable timing of follow-up imaging at each study site. The PRIORITY-CVT (Pathophysiology of Venous Infarction—Prediction of Infarction and Recanalization in CVT) study found that 68% of patients had at least partial recanalization within 8 days of initiation of anticoagulation, and early recanalization was associated with early regression as well as lower risk of enlargement of nonhemorrhagic lesions.¹⁹

Overall, our results indicate that patients with CVT with delayed diagnosis might initially present with less

severe signs and symptoms of CVT than those diagnosed more quickly. Having a higher National Institutes of Health Stroke Scale score at presentation was inversely associated with delayed CVT diagnosis in our model. This point may impact how our results with regard to clinical outcomes should be interpreted. As others have noted, when assessing the effects of diagnostic delay, misdiagnosis, or both, the counterfactual of what would have happened had a diagnostic delay not occurred for a specific patient, particularly those with initially mild disease manifestations, is of central importance.²⁰ Although this counterfactual is difficult to evaluate, even in our subgroup analysis of patients with isolated headache who, by definition, have mild symptoms, we did not find any relationship between diagnostic delay and 90-day outcomes. Because delayed diagnosis in our study could have related to delayed presentation of patients for medical evaluation, community education for stroke should include information to help patients and family members recognize signs and symptoms of CVT, particularly in high-risk patients.

Our study has several important limitations. First, there is no consensus about the definition of what constitutes diagnostic delay in patients with CVT. Indeed, our definition of delay in diagnosis as time from symptom onset to diagnosis in the final temporal quartile (>10 days from symptoms to diagnosis) was shorter than both the interval used in ISCVT (>16 days), which was based on temporal quartiles,⁵ and a 14-day interval used to measure missed CVT diagnosis in the ED.⁴ Although we report the proportion of included patients who were seen in an acute care setting for neurologic complaints within 3 months of CVT diagnosis, we did not capture encounters closer in time to CVT diagnosis or encounters that occurred in other medical settings. Second, information on factors associated with delayed CVT diagnosis is limited by the retrospective design of the ACTION-CVT study as accurate documentation of presenting symptoms and other key clinical features may have been imperfect and likely differed at each participating site. Third, we did not measure hospital or provider factors associated with timely CVT diagnosis or perform detailed chart review of included patients with CVT to identify potential causes of diagnostic delay. It is, therefore, uncertain what the reasons for delayed CVT diagnosis were in our cohort; patient factors, errors in judgment by providers, flawed interpretation of neuroimaging, and failure to request expert consultation are all possible. Whether or not sources of delay in CVT are similar to previously identified sources of delay in detecting acute stroke (eg, failure to use screening tools, incomplete neurologic examination, and too narrow a differential diagnosis) requires further study.^{21–23} To understand current and ideal clinical pathways

for CVT detection, methods other than retrospective chart review are likely warranted.²⁴ Fourth, the mRS score might not be sensitive enough to study CVT-specific clinical disability. Prior studies have shown long-term persistent symptoms and difficulty returning to work after CVT, despite good outcome, as measured using the mRS score.^{25,26} It is, therefore, possible that we did not detect important differences in clinical outcomes, including vision loss, between patients with CVT with delayed versus nondelayed diagnosis in our cohort because of our reliance on mRS score. Future studies should include more detailed outcome measures among patients with CVT. Fifth, our study findings may have limited generalizability, despite the large sample size, insofar as the ACTION-CVT study excluded patients with antiphospholipid antibody syndrome, active cancer, and pregnancy.⁶ Finally, we do not know if a heightened awareness of clotting disorders associated with COVID-19 and the phenomenon of vaccine-induced immune thrombotic thrombocytopenia has led to reductions in time from symptom onset to CVT diagnosis because our study time period was before the COVID-19 pandemic.^{27–29}

CONCLUSIONS

In a large, multicenter study, we found that a substantial number of patients with confirmed CVT were diagnosed after 10 days of symptom onset. Delayed diagnosis was associated with isolated headache symptoms and was not associated with clinical outcomes at 90 days or radiographic recanalization. On the basis of our findings, the diagnosis of CVT should be more frequently considered by providers caring for patients with headache complaints, particularly in the presence of CVT risk factors.

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