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Cerebral Venous Thrombosis Prediction Score in a Real-World Setting: A Retrospective Single-Centre Cohort Study of Patients with Confirmed Diagnosis

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Abstract

Background/Objectives: In 2020, a clinical score to predict the risk of cerebral vein thrombosis was published. The score classifies patients into risk categories: low (<3 points), moderate (3–5 points) and high (>5 points). The low-risk result of the score combined with D-dimer level could potentially exclude cerebral vein thrombosis. The main aim of our study was to assess utility of the score in a group of patients with confirmed cerebral vein thrombosis in a real-world setting. **Methods:** A retrospective assessment of patients with a confirmed diagnosis of cerebral vein thrombosis admitted to a department of neurology was performed. Data on patients' demographics and medical history, including the components of the score, were collected. Based on the inclusion criteria from the original publication, the number of patients eligible and ineligible for using the score was calculated. Next, the patients were assessed with the score. **Results**: Thirty-seven patients with newly diagnosed cerebral vein thrombosis were included. Twenty-three (62%) were eligible according to the inclusion criteria of the original study. The sensitivity of the score alone for this group was 52% at a cutoff of three points, and in combination with D-dimer level it was 92%. Two patients were classified as low-risk according to the score and had low D-dimer level. In the remaining symptomatic patients, the score had a sensitivity of 44% without D-dimer testing, and 89% with D-dimer. D-dimer level alone had a sensitivity of 87% and 67%, respectively. **Conclusions**: The score in combination with D-dimer level had higher sensitivity than D-dimer testing alone. However, the score combined with D-dimer level could not exclude cerebral vein thrombosis in the low-risk patients.

Keywords: cerebral venous thrombosis; D-dimer; prediction; CVT clinical score; differential diagnosis; scale; imaging; stroke

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1. Introduction

Cerebral venous thrombosis (CVT) is a frequently underdiagnosed cerebrovascular disease, and accounts for around 0.5–3% of all stroke cases [1].

Delayed diagnosis of CVT is more frequent in patients presenting with isolated headache and lacking other suggestive symptoms [2]. Diagnostic errors also often arise from overlooking thrombosed sinuses or misinterpreting parenchymal lesions as brain contusions, metastases, or hemorrhages of uncertain etiology. D-dimer (DD) is a commonly

used blood marker for CVT, with a sensitivity ranging from 82% to 94%, so DD cannot definitively exclude CVT [3]. These limitations highlight the ongoing need to establish more effective tools for the reliable diagnosis of CVT.

In 2020, Heldner et al. published a study in which they developed a score for predicting CVT (CVT score), based on a cohort of 359 patients with suspected CVT including 94 (25.8%) with radiologically confirmed diagnosis. The inclusion criteria were the presence of one of the following symptoms/findings with a duration of less than 30 days: (1) isolated unexpected headache; (2) headache associated with focal neurological deficits; (3) headache associated with disturbed consciousness; (4) headache associated with seizure(s); (5) unexplained papilledema. The exclusion criteria were: (1) anticoagulant treatment before admission; (2) deep vein thrombosis, pulmonary embolism, myocardial infarction, or stroke in the last 3 months. Finally, the CVT score included: focal or generalized seizure at presentation (4 pts), thrombophilia including any hematological disease known to be associated with an increased tendency to coagulation (4 pts), oral contraception (2 pts), duration of symptoms > 6 days (2 pts), focal neurological deficit at presentation (1 pt), and the worst headache ever declared by a patient (1 pt). The authors divided patients into subgroups according to the risk of CVT: low (<3 pts), moderate (3–5 pts) and high risk of CVT (>5 pts). The addition of DD (3 pts) improved CVT prediction. The authors concluded that none of the patients classified as low-risk by the CVT score and presenting with low DD levels had CVT [4]. The existence of the CVT score potentially allowing for exclusion of CVT in selected patients appears to have important clinical implications. We were interested in the results of using CVT score in the patients admitted to our department with the diagnosis of CVT.

The primary aims of the study were: (1) to assess the sensitivity of the CVT score by Heldner et al. in patients with confirmed diagnosis; and (2) to determine the proportion of patients admitted to the Department of Neurology with CVT who met the inclusion criteria of the original study by Heldner et al., and to compare their characteristics with those of the remaining patients with symptomatic CVT. The secondary aims were: (3) to evaluate factors associated with DD level in the analyzed cohort; and (4) to describe baseline characteristics and identify factors potentially associated with worsening of the modified Rankin Scale score (mRS) between admission and discharge in patients with CVT.

2. Materials and Methods

This study is a retrospective analysis of patients admitted to the Department of Neurology with Stroke Subunit of Prof. K. Gibiński University Clinical Centre of the Medical University of Silesia in Katowice, a tertiary care center in the largest city of a highly urbanized region in a highly developed country. The Strengthening the Reporting of Observational studies in Epidemiology (STROBE) checklist was used [5]. Patients admitted between March 2018 and May 2025 due to a first episode of CVT confirmed with computed tomography (CT) venography or magnetic resonance (MR) venography were included. Patients with a relapse of previously diagnosed CVT and/or those using anticoagulants before admission were excluded, as in the study by Heldner et al. [4]. The collected data included gender, age, symptoms and their duration, previous medical history, neurological examination, basic laboratory tests, medical imaging, the Glasgow Coma Scale (GCS) at admission, treatment used, CVT complications including ischemic and hemorrhagic stroke, duration of hospitalization, the National Institutes of Health Stroke Scale (NIHSS) at admission and discharge and mRS before and after admission. DD concentrations were measured using a latex-enhanced immunoturbidimetric assay. The cut-off value for DD was 500 ng/mL. Detailed diagnostic tests for coagulopathies were not included in the study, because in many patients they were completed in outpatient care at other locations not related to the clinic or

the results were no longer available for research purposes. In the study, cancer was defined as a recurrent, regionally advanced, or metastatic cancer diagnosed or treated within the previous 6 months. The CVT score was calculated as previously described by Heldner et al. [4]. A description of very severe headache in medical records was also treated as the worst headache reported by the patient. The number of patients meeting the inclusion criteria of the study by Heldner et al. was determined, and these patients were compared with symptomatic patients who did not meet these criteria [4]. The number of patients with incidentally found CVT was also calculated and their characteristics were described. Poor prognosis was defined as a higher mRS score at discharge than the mRS prior to CVT.

The statistical analysis was performed with STATISTICA 13 PL software (TIBCO Software Inc., Palo Alto, CA, USA). The sensitivity for all patients and particular groups was calculated. Continuous variables are presented as a mean ± standard deviation in the case of normal distribution or a median (lower quartile-upper quartile) when the distribution was not normal. Shapiro–Wilk test, histograms and Q-Q plots were used to assess normality. Categorical data are presented as a number (%). Mann–Whitney U test, Student's *t*-test, Spearman's rank correlation (RS), and Fisher's exact test were utilized appropriately to compare symptomatic patients appropriate and inappropriate for using CVT score. No a priori sample size calculation was performed, as the study retrospectively included all eligible patients with confirmed CVT identified during the predefined study period. Due to the small sample size, multivariable analysis was not performed. The only missing data concerned the exact duration of CVT in one patient, who was therefore excluded from analyses involving this variable, and information on papilledema, which was available only for descriptive purposes.

Due to the retrospective nature of this study and data anonymization, the Ethics Committee confirmed that ethical approval was not required.

3. Results

During the analyzed period, there were 41 admitted patients with radiologically confirmed CVT, but four of them were excluded due to recurrence of previously diagnosed CVT. Finally, 37 patients (18 males and 19 females) were included. The diagnosis of CVT was established or confirmed by CT venography in 32 patients and by MR venography in 5 patients. Brain MR imaging was also performed in seven additional patients after the diagnosis of CVT had been established. The inclusion criteria of the study by Heldner et al. were met by 23 (62.2%) of them. The 14 patients who did not meet the inclusion criteria were four (10.8%) patients who had symptoms lasting longer than 30 days; five (13.5%) patients with asymptomatic CVT incidentally detected on imaging performed for other indications (one demyelinating disease of the central nervous system, one epilepsy, and three oncological diagnostics—two cases of small-cell lung cancer, and one case of a neuroendocrine tumor of the salivary gland with internal jugular vein compression); and five (13.5%) patients with symptomatic CVT without reported headache and without assessed or documented papilledema. However, two of them had severe aphasia, and one of them had late-stage dementia, which might be associated with the lack of a reported headache. The exact duration of symptoms was unknown in one patient, but it was below 30 days and above 6 days. The only significant differences between symptomatic patients who met the criteria from the study by Heldner et al. and symptomatic patients who did not meet them were observed for age, platelet count, and the presence of headache. Detailed patient characteristics are presented in Tables 1–3.

Table 1. Demographics and comorbidities.

	All Patients $N = 37$ **(100%)**	**Meeting Criteria** $N = 23$ **(100%)**	**Other Symptomatic** $N = 9$ **(100%)**	**Asymptomatic** $N = 5$ **(100%)**	***p*-Value** [1]
Gender (% men)	18 (48.7%)	12 (52.2%)	4 (44.4%)	2 (40%)	1
Age (years)	56.5 ± 17.96	50 ± 16.99	64.9 ± 17.69	70.4 ± 7.89	0.038 *
Steroids use	3 (8.1%)	2 (8.7%)	0 (0%)	1 (20%)	1
Active smoking	7 (18.9%)	7 (30.4%)	0 (0%)	0 (0%)	0.149
Cancer	6 (16.2%)	2 (8.7%)	1 (11.1%)	3 (60%)	1
Hematological neoplasm	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-
Surgery/TBI	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-
Lumbar puncture	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-
Diabetes mellitus	6 (16.2%)	2 (8.7%)	2 (22.2%)	2 (40%)	0.557
Arterial hypertension	18 (48.6%)	9 (39.1%)	5 (55.6%)	4 (80%)	0.453
Heart failure	1 (2.7%)	1 (4.3%)	0 (0%)	0 (0%)	1
Previous MI	1 (2.7%)	0 (0%)	1 (11.1%)	0 (0%)	-
DVT/PE	2 (5.4%)	0 (0%)	2 (22.2%)	0 (0%)	0.072
Recent infection	10 (27.0%)	8 (34.8%)	2 (22.2%)	0 (0%)	0.681
Liver cirrhosis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-
Pregnancy/postpartum	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-
HRT	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-
Previous IS/ICH	1 (2.7%)	0 (0%)	1 (11.1%)	0 (0%)	-
ACTD	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-

[1]—*p*-value for comparison of symptomatic patients with CVT who met and did not meet criteria from original study by Heldner et al. *—statistically significant differences. Abbreviations: TBI—traumatic brain injury during last 3 months, MI—history of myocardial infraction, DVT/PE—history of deep vein thrombosis or pulmonary embolism, HRT—hormonal replacement therapy, IS/ICH—history of ischemic stroke or intercerebral hemorrhage, ACTD—diagnosed autoimmune connective tissue disorders.

Table 2. Symptoms and clinical assessment.

	All Patients $N = 37$ **(100%)**	**Meeting Criteria** $N = 23$ **(100%)**	**Other Symptomatic** $N = 9$ **(100%)**	**Asymptomatic** $N = 5$ **(100%)**	***p*-Value** [1]
Duration of symptoms (days) †:	4 (3–21)	4 (4–13)	3 (2–60)		0.896
Papilledema:					
No data	24 (64.9%)	15 (65.2%)	7 (77.8%)	2 (40%)	
Absent	9 (24.3%)	4 (17.4%)	2 (22.2%)	3 (60%)	-
BL	3 (8.1%)	3 (13.0%)	0 (0%) pt	0 (0%)	
UL	1 (2.7%)	1 (4.3%)	0 (0%) pt	0 (0%)	
Headache:	25 (67.6%)	21 (91.3%)	4 (44.4%)	0 (0%)	0.010 *
BL	15 (40.5%)	12 (52.2%)	3 (33.3%)		
UL	10 (27.0%)	9 (39.1%)	1 (11.1%)		
Nausea/vomiting	14 (37.8%)	12 (52.2%)	2 (22.2%)	0 (0%)	0.235
Visual symptoms	9 (24.3%)	7 (30.4%)	1 (11.1%)	1 (20%) †	0.386
Vertigo/dizziness	6 (16.2%)	5 (21.7%)	1 (11.1%)	0 (0%)	0.648
GCS < 15 pts	8 (21.6%)	5 (21.7%)	3 (33.3%)	0 (0%)	0.654

Table 2. *Cont*.

	All Patients $N = 37$ (100%)	Meeting Criteria $N = 23$ (100%)	Other Symptomatic $N = 9$ (100%)	Asymptomatic $N = 5$ (100%)	*p*-Value [1]
NIHSS at admission	0 (0–2)	0 (0–2)	1 (0–3)	0 (0–0)	0.476
NIHSS at discharge	0 (0–1.5)	0 (0–2)	0 (0–2)	0 (0–0)	0.617
mRS before admission > 0	7 (18.9%)	5 (21.7%)	2 (22.2%)	0 (0%)	1
mRS after discharge > 0	16 (43.2%)	11 (47.8%)	5 (55.5%)	0 (0%)	1
ΔmRS	10 (27.0%)	7 (30.4%)	3 (33.3%)	0 (0%)	1
Time of hospitalization (days)	10 (8–15)	11 (8–15)	12 (8–15)	8 (7–8)	0.917

[1]—*p*-value for comparison of symptomatic patients with CVT who met and did not meet criteria from original study by Heldner et al., *—statistically significant differences. †—exact duration of the symptoms was absent in one patient. Abbreviations: UL—unilateral, BL—bilateral, GCS—Glasgow Coma Scale, mRS—modfied Rankin scale, ΔmRS—mRS worse at discharge than prior to the disease, NIHSS—National Institutes of Health Stroke Scale, [†]—a patient was a few months after optic neuritis and CVT was absent in contrast enhanced MRI performed during optic neuritis, but found in next contrast enhanced MRI and subsequent angioCT.

Table 3. Basic laboratory and medical imaging findings.

	All Patients $N = 37$ (100%)	Meeting Criteria $N = 23$ (100%)	Other Symptomatic $N = 9$ (100%)	Asymptomatic $N = 5$ (100%)	*p*-Value [1]
Basic Laboratory Findings					
Glycemia (mg/dL)	117 (91.7–162)	115.5 (91.7–163)	127 (115–146)	82.5 (77.1–167.9)	0.805
CRP (mg/L)	8.1 (2.5–20.7)	12.9 (2.8–35.8)	4.0 (1.6–16.9)	4.7 (4.0–6.6)	0.176
Hemoglobin (g/L)	14.0 (12.7–15.9)	14.0 (12.7–16.0)	14.3 (13.3–14.9)	12.7 (11.9–13.4)	0.883
Elevated hemoglobin	5 (13.5%)	3 (13.0%)	2 (22.2%)	0 (0%)	0.604
Thrombocytes (k/μL)	274 (211–327)	314 (239–367)	254 (190–267)	245 (211–254)	0.040 *
Thrombocytosis	3 (8.1%)	3 (13.0%)	0 (0%)	0 (0%)	0.541
DD (ng/mL)	1162 (625–1972)	1162 (625–3527)	994 (398–1887)	1303 (1232–1972)	0.400
MDRD GFR < 60 mL/min	2 (5.4%)	0 (0%)	2 (22.2%)	0 (0%)	0.072
Medical Imaging					
No. of affected vessels	2 (2–3)	3 (2–3)	2 (1–3)	2 (2–3)	0.180
No. of patients with >3 affected vessels	6 (16.2%)	4 (17.4%)	2 (22.2%)	0 (0%)	1
Affected vessels:					
Transverse sinus	27 (73%), 3 BL	18 (78.3%), 2 BL	5 (55.6%), 1 BL	4 (80%)	0.226
Sigmoid sinus	26 (70.3%)	17 (73.9%)	4 (44.4%)	5 (100%)	0.213
Internal jugular vein	15 (40.5%), 1 BL	9 (39.1%), 1 BL	3 (33.3%)	3 (60%)	1
Superior sagittal sinus	12 (32.4%)	10 (43.5%)	2 (22.2%)	0 (0%)	0.422
Straight sinus	3 (8.1%)	3 (13.0%)	0 (0%)	0 (0%)	0.541
Cortical veins	3 (8.1%)	1 (4.3%)	2 (22.2%)	0 (0%)	0.184
Deep cerebral vein	2 (5,4%)	1 (4.3%)	1 (11.1%)	0 (0%)	0.490
Great vein of Galen	2 (5,4%)	1 (4.3%)	1 (11.1%)	0 (0%)	0.490
Cavernous sinus	2 (5,4%)	1 (4.3%)	1 (11.1%)	0 (0%)	0.490
Ophthalmic vein	1 (2.7%)	1 (4.3%)	0 (0%)	0 (0%)	1
Left site	17 (45.9%)	8 (34.8%)	5 (55.6%)	4 (80%)	0.426
Right site	13 (35.2%)	10 (43.5%)	2 (22.2%)	1 (20%)	0.422

Table 3. *Cont*.

	All Patients $N = 37$ (100%)	Meeting Criteria $N = 23$ (100%)	Other Symptomatic $N = 9$ (100%)	Asymptomatic $N = 5$ (100%)	*p*-Value [1]
Both sites	5 (13.5%)	4 (17.4%)	1 (11.1%)	0 (0%)	1
No lateralization	2 (5.4%)	1 (4.3%)	1 (11.1%)	0 (0%)	0.490
ICH	12 (32.4%)	9 (39.1%)	3 (33.3%)	0 (0%)	1
Venosus infraction	9 (24.3%)	4 (17.4%)	5 (55.6%)	0 (0%)	0.075

[1]—*p*-value for comparison of symptomatic patients with CVT meeting and not meeting criteria from original study by Heldner et al. *—statistically significant differences. Abbreviations: No.—number, UL—unilateral, BL—bilateral, ICH—intercerebral hemorrhage, DD—d-dimer level, CRP—C-reactive protein.

Ten patients had an infection within 1 month prior or during CVT: one patient with C2 spondylodiscitis with concomitant spinal epidural and retropharyngeal abscesses; one case of influenza, two cases of COVID-19, three cases of unidentified upper respiratory tracts infections, one patient with a knee joint infection, and two cases of an unspecified infection.

There was no difference in the CVT score and its components between the two groups of symptomatic patients defined by whether they met the inclusion criteria of the study by Heldner et al. The CVT score had sensitivity of 43.2% at the cut point of 3 points in all patients. The CVT score combined with DD testing was negative in three patients in the analyzed population, so its sensitivity was 91.8%. After exclusion of patients who did not meet the criteria of the original study by Heldner et al., the sensitivity of the scale without DD was 52.2% and with DD it was 91.3%. DD (with a cut-off value of 500 ng/mL) alone had the sensitivity of 83.8% in all patients, and 87% in patients meeting criteria from the study by Heldener et al. Details about patients in the particular categories of the risk and the sensitivity of the score are shown in Table 4.

Table 4. CVT Clinical score with and without DD in analyzed groups.

CVT Clinical Score					
	All Patients $N = 37$ (100%)	Meeting Criteria $N = 23$ (100%)	Other Symptomatic $N = 9$ (100%)	Asymptomatic $N = 5$ (100%)	*p*-Value [1]
Coagulopathy	0 (0%)	0 (0%)	0 (0%)	0 (0%)	-
Oral contraceptives	6 (16.2%)	5 (21.7%)	1 (11.1%)	0 (0%)	0.648
Seizures	8 (21.6%)	6 (26.1%)	2 (22.2%)	0 (0%)	1
Focal neurological signs	17 (45.9%)	12 (52.2%)	5 (55.6%)	0 (0%)	1
Severe headache	16 (43.2%)	14 (60.9%)	2 (22.2%)	0 (0%)	0.113
Duration of symptoms > 6 days	12 (32.4%)	8 (34.8%)	4 (44.4%)	0 (0%)	0.696
DD > 500 ng/mL	31 (83.8%)	20 (87.0%)	6 (66.7%)	5 (100%)	0.314
CVT score without DD	2 (1–4)	3 (2–5)	2 (1–4)	0 (0–0)	0.600
Low risk (without DD)	21 (56.8%)	11 (47.8%)	5 (55.6%)	5 (100%)	
Moderate risk (without DD)	11 (29.7%)	7 (30.4%)	4 (44.4%)	0 (0%)	
High risk (without DD)	5 (13.5%)	5 (21.7%)	0 (0%)	0 (0%)	
Sensitivity for ≥3 points (without DD)	16 (43.2%)	12 (52.2%)	4 (44%)	0 (0%)	
CVT score with DD	5 (3–6)	5 (4–8)	4 (4–5)	3 (3–3)	0.216
Low risk (with DD)	3 (8.1%)	2 (8.7%)	1 (11.1%)	0 (0%)	
Moderate risk (with DD)	21 (56.8%)	10 (43.5%)	6 (66.7%)	5 (100%)	

Table 4. *Cont*.

	CVT Clinical Score				
	All Patients $N = 37$ **(100%)**	**Meeting Criteria** $N = 23$ **(100%)**	**Other Symptomatic** $N = 9$ **(100%)**	**Asymptomatic** $N = 5$ **(100%)**	***p*-Value** [1]
High risk (with DD)	13 (35.1%)	11 (47.8%)	2 (22.2%)	0 (0%)	
Sensitivity for ≥3 points (with DD)	34 (91.9%)	21 (91.3%)	8 (88.9%)	5 (100%)	

[1]—*p*-value for comparison of symptomatic patients with CVT meeting and not meeting criteria from original study by Heldner et al. Abbreviations: CVT—cerebral vein thrombosis, DD—dimers.

Detailed characteristics of two patients meeting the inclusion criteria of the study by Heldner et al., who had negative results of CVT score combined with DD are presented in Table 5.

Table 5. Characteristic of patients with negative results of CVT clinical score with D-dimer.

	Patient 1	**Patient 2**
Age	32 years	54 years
Sex	men	men
D-dimer	334 ng/mL	469 ng/mL
Symptoms	Admitted to the hospital due to a 4-day history of left-sided headache described as the worst headache ever experienced, tenderness in the left mastoid region, nausea and vomiting, vertigo, blurred vision, and newly developed partial bilateral hearing loss.	Referred to the hospital due to bilateral papilledema diagnosed in ophthalmological outpatient care. Patient symptoms had been started for 4 days before admission. The patient complained of blurry vision in right eye, loss of vision in upper temporal quadrant in a visual field of the right eye and feeling of foreign body in the eyeball, but foreign body was not found by ophthalmologist.
Comorbidities	None	Arterial hypertension, epilepsy and smoking.
Neurological examination	Bilateral papilledema, mild ataxia and partial bilateral hearing loss.	Loss of vision in upper temporal quadrant in visual field of the right eye.
Neuroimaging	Head CT without contrast–hyperdensity of the left transverse and straight sinuses. CT venography–thrombosis of left sigmoid, left transverse, straight and superior sagittal sinuses and left internal jugular vein.	Head CT—unremarkable. CT venography—superior sagittal and right transverse sinuses thrombosis
Laboratory findings	Unremarkable	Slightly elevated platelets 480,000/µL
Other abnormalities	Unremarkable	Two thyroid nodules (EU-TIRADS 4, and EU-TIRADS 3), and two oncologically suspected lymph nodes nearby; enlarged heterogeneous prostate gland with normal PSA.
Treatment	UFH, switched to LMWH after 2 days and acetazolamide.	LMWH
Outcome	Discharged from the hospital without neurological deficits, mRS 0, NIHSS 0 pts.	Discharged from the hospital without neurological deficits, mRS 0, NIHSS 0 pts
CVT score	2 points: 1 point for worst headache ever –one point 1 point for focal neurological signs (mild ataxia and partial bilateral hearing loss)–one point.	1 point for focal neurological signs (loss of vision in upper temporal quadrant in a visual field of the right eye).

Abbreviations: CT—computer tomography, UFH—unfractionated heparin, LMWH—low-molecular-weight heparin, EU-TIRADS—European Thyroid Imaging Reporting and Data System, PSA—prostate specific antigen, mRS—modified Rankin Scale, NIHSS—National Institutes of Health Stroke Scale.

DD level was higher in patients with cancer, seizures, intracerebral hemorrhage (ICH) and GCS below 15 points. There was a positive correlation of DD level with C-reactive protein (CRP) and the NIHSS score and negative correlation with CVT duration. Details are presented in Table 6.

Table 6. Association of variables with D-dimer level (ng/mL).

Variable	Correlations and Comparisons	*p*-Value
Age	$R_S = 0.306$	0.065
Gender (♂ vs. ♀)	1193 (602–1972) vs. 1162 (625–2442)	0.891
Active smoking	1022 (550–1527) vs. 1197 (675–3527)	0.323
Cancer	1901 (1554–4582) vs. 994 (589–1887)	0.031 *
Diabetes mellitus	1415 (994–4582) vs. 1083 (602–1972)	0.313
Arterial hypertension	1223 (796–1887) vs. 944 (550–2442)	0.421
Recent infection	1527 (791–1829) vs. 1223 (607–2985)	0.986
Oral contraceptives	1473 (625–3577) vs. 1083 (602–1972)	0.726
Glycemia (mg/dL)	$R_S = 0.053$	0.764
CRP (mg/L)	$R_S = 0.475$	0.003 *
Hemoglobin (g/L)	$R_S = -0.144$	0.396
Thrombocytes (k/µL)	$R_S = -0.309$	0.063
Duration of symptoms (days) †	$R_S = -0.428$	0.009 *
Headache	1022 (589–1829) vs. 1268 (895–2207)	0.307
Severe headache	868 (474–2630) vs. 1303 (796–1972)	0.175
Focal neurological signs	1213 (796–3577) vs. 1053 (614–1692)	0.385
Seizures	4069 (2985–10,213) vs. (589–1303)	<0.001 *
Nausea/vomiting	994 (550–4560) vs. 1162 (791–1887)	0.888
Visual symptoms	675 (469–944) vs. 1415 (783–2985)	0.058
Vertigo/dizziness	1781 (1213–1887) vs. 1022 (602–2442)	0.422
GCS < 15	2165 (1275–4044) vs. 944 (589–1732)	0.031 *
NIHSS at admission	$R_S = 0.441$	0.006 *
Low risk in CVT score	1022 (602–1554) vs. 1473 (711–4069)	0.276
CVT score	$R_S = 0.163$	0.336
No. of affected vessels	$R_S = 0.113$	0.505
>3 affected vessels	1707 (602–13,585) vs. 1083 (625–1972)	0.446
ICH	2087 (1008–4069) vs. 944 (589–1554)	0.046 *
Venosus infraction	1162 (994–1887) vs. 1127 (614–2207)	0.763

*—statistically significant values, Abbreviations: ♂—men, ♀—women, †—exact duration of the symptoms was absent in one patient, NIHSS—National Institutes of Health Stroke.

The factors significantly associated with poor prognosis, defined as worsening of mRS were: GCS score < 15, neurological deficit and higher NIHSS score, thrombosis in cortical veins on medical imaging and presence of ICH (Table 7). During hospitalization. one patient was initially treated with unfractionated heparin, which was switched to low-molecular-weight heparin (LMWH) after 2 days. All other patients were treated with

LMWH. Ten (27.0%) patients had a worse mRS score at discharge than before the disease, including one death associated with massive ICH in the posterior cranial fossa.

Table 7. The factors related to a worsening of mRS between admission and discharge (ΔmRS).

Variable	Without ΔmRS $N = 27$	With ΔmRS $N = 10$	*p*-Value
Age	58 (39–71)	66.5 (43–74)	0.494
Gender (% ♂)	13 (48.1%)	5 (50%)	1
Active smoking	3 (11.1%)	4 (40%)	0.069
Cancer	6 (22.2%)	0 (0%)	0.162
Diabetes mellitus	4 (14.8%)	2 (20%)	0.653
Arterial hypertension	11 (40.7%)	7 (70%)	0.151
Recent infection	7 (25.9%)	2 (20%)	1
Oral contraceptives	3 (11.1%)	3 (30%)	0.313
Duration of symptoms (days) †	4.5 (3–21)	2 (2–4)	0.151
No symptoms	5 (18.5%)	0 (0%)	0.295
GCS < 15	3 (11.1%)	5 (50%)	0.021 *
NIHSS at admission	0 (0–1)	2 (0–6)	0.016 *
Headache	19 (70.4%)	6 (60%)	0.696
Severe headache	12 (44.4%)	4 (40%)	1
Focal neurological signs	9 (33.3%)	8 (80%)	0.023 *
Seizures	6 (22.2%)	2 (20%)	1
Nausea/vomiting	11 (40.7%)	3 (30%)	0.710
Visual symptoms	6 (22.2%)	3 (30%)	0.679
Vertigo/dizziness	4 (14.8%)	2 (20%)	0.653
Glycemia (mg/dL)	107 (88–161)	131 (114–178)	0.097
Hemoglobin (g/L)	14.0 (12.7–16.0)	14.0 (12.3–14.9)	0.801
CRP (mg/L)	6.6 (2.2–16.4)	22.8 (5.5–35.8)	0.295
Thrombocytes (k/μL)	259 (202–316)	322 (267–367)	0.130
D-dimer level (ng/mL)	1162 (550–2442)	1148 (994–1887)	0.596
No. of affected vessels	2 (2–3)	3 (2–3)	0.374
No. of patients with >3 affected vessels	4 (14.8%)	2 (20%)	0.653
Transverse sinus	20 (74.1%)	7 (70%)	1
Sigmoid sinus	21 (77.8%)	5 (50%)	0.125
Internal jugular vein	13 (48.1%)	2 (20%)	0.153
Superior sagittal sinus	8 (29.6%)	4 (40%)	0.696
Straight sinus	2 (7.4%)	1 (10%)	1
Cortical veins	0 (%)	3 (30%)	0.015 *
ICH	6 (22.2%)	6 (60%)	0.049 *
Venous infarction	5 (18.5%)	4 (40%)	0.214

*—statistically significant differences, Abbreviations: ♂—men, †—exact duration of the symptoms was absent in one patient. NIHSS—National Institutes of Health Stroke Scale, GCS—Glasgow Coma Scale, ICH—intercerebral hemorrhage, CRP—C-reactive protein.

4. Discussion

Our study suggests that some patients with confirmed CVT were manifesting nonspecific clinical features, who did not meet the inclusion criteria used by Heldner et al., such as asymptomatic patients, those with long-lasting symptoms and atypical symptomatic presentation of CVT. The older age observed in these patients may suggest a lower diagnostic utility of CVT score in older patients due to atypical presentations of the disease. In the original study, the sensitivity of a CVT score ≥ 3 points was 78.7%, and none of the patients classified as having a low probability of CVT (<3 points) with a D-dimer level <500 ng/mL were diagnosed with CVT [4]. Two recently published studies evaluated the score [6,7]. Dahl et al. retrospectively analyzed data from 578 patients with suspected CVT; however, due to missing data, only 444 patients were ultimately included, among whom 27 had confirmed CVT. Eighteen of these 27 patients (66%) had the CVT score ≥ 3 points [7]. In the study by Dahl et al. only three of nine patients classified as having a low-risk CVT score had the DD measured, and all three had elevated DD [7]. Ranjan et al. prospectively evaluated the CVT score in 75 patients with suspected CVT including 40 (53%) whose diagnosis was confirmed by MR venography. Thirty-two (80%) CVT patients had a CVT score ≥ 3 points. Among eight patients with a low risk of CVT, five of them had elevated DD; therefore, the score combined with DD sensitivity was 37/40 (92.5%) for all patients in the cohort [6]. In our study, sensitivity of CVT score in the patients eligible to be included to the study by Heldner et al. at the cutoff of 3 points was only 52.2%, which was lower than the sensitivity reported in the previous studies [4,6,7]. In combination with DD, CVT score sensitivity increased to 91.8% in this group. Among hospitalized patients meeting the inclusion criteria used by Heldner et al., two of them had low risk in CVT score, low DD level, and a confirmed diagnosis of acute CVT. This finding is consistent with a study by Ranjan et al. but in contrast to the original study and the study by Dahl et al., because it suggests that low CVT score (<3 points) combined with low DD might not be sufficient to exclude CVT [4,6,7]. However, CVT score plus DD still had high sensitivity, which was better than DD level alone in all symptomatic patients, so although it might be potentially useful as a screening tool, it should not replace clinical judgment. Based on the findings of our study and the original approach proposed by Heldner et al., patients with moderate or high CVT scores and elevated DD levels may warrant further evaluation with CT or MR venography. In patients with low scores, the decision to perform venography should be individualized, taking into account the clinical presentation and presence of bilateral papilledema, regardless of the DD level. However, this proposed approach should be interpreted cautiously, as our study was not designed to develop or validate a diagnostic algorithm.

According to the literature, DD sensitivity for CVT diagnosis is between 81% and 93%, similar to our study [4,8]. There is a weak recommendation for measuring DD before neuroimaging in the European Stroke Organisation/European Academy of Neurology guidelines and Polish Neurological Society recommendations with some exceptions, such as isolated headache and prolonged duration of symptoms [8,9]. However, newer guidelines do not recommend using DD to rule out CVT or recommend their use only in selected cases [10,11]. One of the factors limiting the utility of DD is a presence of multiple factors influencing their level including pregnancy, aging, physical exercise, inflammation, cancer, cardiovascular diseases, diabetes, hemorrhages, trauma, surgery, renal and liver diseases [12]. Cancer and inflammation were related to DD level in our study. No statistically significant associations were observed for the other factors, probably due to small sample size or low prevalence in the studied group. DD level in CVT is also related to the disease characteristics. Some data suggest that CVT patients might have low DD if the presentation is an isolated headache [8]. Also, low DD level was observed in patients with long lasting CVT, which is consistent with the findings of our study and potentially limits

the utility of DD in patients with extended time between the onset of CVT and the clinical evaluation [8,13]. In our study, there was a statistically significant association between DD and factors related to larger severity of the CVT, like abnormal GCS, higher NIHSS, seizures and ICH, which is in agreement with previous publications [14–16]. The DD level was correlated with the amount of sinus involvement in venography in part of the studies or only in cases with elevated DD [13,17,18]. This association was absent in our study, which might be associated with inclusion of asymptomatic and chronic cases, small cohort, as well as the structure of the studied population, as explained below.

Thrombophilia is an important risk factor of CVT, and previously known thrombophilia defined as any hematological disease known to be associated with increased tendency of coagulation was used in the score by Heldner et al. [4]. In our study, we used the same definition, and probably some patients had undiagnosed thrombophilia as may have been the case in the study by Heldner et al. [4]. During the study period, thrombophilia testing was performed according to current standards [8,9]. However, in our cohort, the diagnostic tests for thrombophilia were frequently completed in outpatient settings outside the clinic and not cooperating with our hospital, or the results were not available for research purposes. Consequently, our data do not allow us to determine the prevalence of thrombophilia based on comprehensive laboratory testing or to assess whether additional investigations would have identified previously unrecognized thrombophilia.

The typical CVT population consists mainly of patients younger than 55 years, with a predominance of women [1]. That classical sex and age distribution was present in the study by Heldner et al. and some previous studies. The different demographic distribution observed in our study might be partly explained by the different study periods and inclusion criteria [4,19–21]. However, according to some newer data, the profile of CVT patients in developed countries is changing, and some studies report increasing prevalence of CVT in male and/or similar male to female proportions [14,22,23]. Also, prevalence in older women seems to be increasing [24,25]. These changes might be partly explained by the improved availability of neuroimaging, which may be associated with more frequent diagnosis of atypical, less severe, or even asymptomatic cases [22–24]. Data from a Canadian population suggest quite high prevalence of CVT found incidentally during medical imaging related to other reasons [26]. Additionally, asymptomatic cases accounted for 10% of cases in one Polish study [19]. Other factors potentially related to this shift in the epidemiology of CVT are overall higher survival of prothrombotic diseases like a cancer, higher prevalence of obesity and common use of low-estrogen contraception [23,25]. Aging of the population might also play a role. These trends may partly explain the older age and relatively balanced sex distribution observed in our cohort. Our study might also suggest that better availability of neuroimaging may play a role in the increasing prevalence of CVT in older patients—the mean age of patients with atypical and asymptomatic presentations was higher than that of patients with classical symptoms. However, our study was small and did not assess the availability of neuroimaging, so larger studies with neuroimaging availability assessment should be performed to verify this hypothesis.

Several factors were associated with a poor prognosis, defined as an adverse mRS score at discharge. One such factor was the presence of neurological symptoms on admission, reflected by a higher NIHSS score. These findings are consistent with prior studies, which linked a higher NIHSS score on initial evaluation to worse clinical outcomes [27–29]. Impaired consciousness in our study was also associated with poor outcome as in previous studies [1,27–31]. ICH, which is frequently associated with focal deficits and impaired consciousness, is a known negative prognostic factor [1,31,32]. Association between cortical vein thrombosis in medical imaging and worse outcome was also noted previously [33].

Overall, our findings regarding factors associated with an unfavorable outcome were broadly consistent with previous reports.

The study had several limitations. The retrospective nature of our study was associated with missing data, potential selection bias, and reliance on medical records. Eye fundus examination records were unavailable for many patients, which might have affected the study results and their interpretation. Furthermore, some potential risk factors were not assessed. Detailed coagulopathy diagnostics were frequently performed after hospital discharge or the results were unavailable for research purposes; therefore, they were not analyzed. Due to the limited sample size and the use of only univariate statistical analyses, our findings should be interpreted with caution, as they may be subject to bias. We assessed a relatively small group of patients at a single tertiary care center located in a highly urbanized region of a developed European country. The relatively small sample size, single-center design, and sex distribution different from that typically reported in patients with CVT may limit the generalizability of our findings to other populations and healthcare settings. The study included only patients with the confirmed diagnosis; therefore, we could evaluate the sensitivity of CVT score, but not its specificity, positive and negative predictive value. Therefore, the utility of the CVT score for the differential diagnosis of CVT could not be assessed in this study. Due to the study design and limited sample size, we were also unable to formulate recommendations for improving the CVT score proposed by Heldner et al. Finally, the association of factors related to poor prognosis based on change in mRS at discharge. However, a long-term outcome is the most important, and mRS does not adequately reflect the subtle cognitive, physical, and psychosocial problems [34,35].

5. Conclusions

In summary, in our cohort of patients, the CVT score combined with DD testing showed relatively high sensitivity. However, the original study inclusion criteria did not capture a meaningful subset of patients encountered in our practice such as those with atypical presentations or a long duration of CVT. Our study suggests, in line with previous findings, that some patients meeting the inclusion criteria of the study by Heldner et al., may have confirmed CVT despite a low DD level and a low-risk CVT score. Therefore, the combination of CVT score and DD might not be sufficient to exclude the need to perform CT or MR venography. Prediction tools should therefore be applied with caution and always interpreted within the broader clinical and radiological context. Further prospective, multicenter studies including both suspected and confirmed CVT patients are warranted to better define the utility of the score proposed by Heldner et al., especially for CVT screening [4]. The sensitivity of DD testing and the associations between DD levels and related factors observed in our study, as well as the factors associated with poor prognosis, were similar to those reported in the literature. The demographic characteristics of our cohort, including the relatively high proportions of older patients and males, differed from those reported in most previous CVT populations. These differences may reflect changes in the demographic profile of patients with CVT in developed countries and may potentially be related to improved availability of neuroimaging. However, given the small, single-center nature of our study, these findings should be interpreted cautiously and should not be considered representative of broader changes in the epidemiology of CVT.

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Abbreviations

The following abbreviations are used in this manuscript:

CVT	Cerebral venous thrombosis
DD	D-dimer level
CT	Computed tomography
MR	Magnetic resonance
GCS	Glasgow Coma Scale
NIHSS	National Institutes of Health Stroke Scale
mRS	Modified Rankin Scale
LMWH	Low-molecular-weight heparin
CRP	C-reactive protein
ICH	Intracerebral hemorrhage

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