Clinical value and prediction efficiency of Neutrophil-to-lymphocyte radio and D-dimer on admission for functional outcome in patients with cerebral venous sinus thrombosis

Rui Sun
Changhai Hospital
Ge Yin
Changhai Hospital
Wen Wu
Changhai Hospital
Qichao Ding
Changhai Hospital
Zhengsheng Gu
Changhai Hospital
Cunxiu Fan
Changhai Hospital
Chenrui Song
Changhai Hospital
Meng Liang (lmzsyd@163.com)
Second Military Medical University First Hospital: Changhai Hospital https://orcid.org/0000-0002-9942-270X
Xiaobei Liu
Changhai Hospital
Xiaoying Bi
Changhai Hospital

Research Article

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Abstract

BACKGROUNDS:

Cerebral venous sinus thrombosis (CVST) is a rare subtype of stroke with a variety of clinical manifestations. This study aimed to explore the role of inflammatory factors and the changes of coagulation function at different stage in the prognosis of cerebral venous sinus thrombosis (CVST).

METHODS

We assessed inflammation and coagulation factors in 137 CVST patients over a 12-year period (2010–2021). The short-term functional outcome was evaluated with the modified Rankin Scale (mRS) at discharge. Patients with CVST were divided into two groups, 102 patients with good functional outcome (mRS score 0–2) and 35 patients with poor functional outcome (mRS score 3–6). Binary logistic regression was performed to identify the potential independent risk factors for functional outcome of patients with CVST. The correlation between each indicator and mRS was assessed. We also use receiver operating characteristic curve (ROC) analysis to evaluate the discriminative ability of significant factors in predicting functional outcome.

RESULTS

Significantly higher neutrophil to lymphocyte ratio (NLR) and D-dimer levels on admission were observed in patients with poor outcome. After adjustments, NLR and D-dimer on admission remained a significant predictor for unfavorable functional prognosis in CVST patients (NLR: OR [95% CI] 1.243 [1.059–1.459], p = 0.008; D-dimer: OR [95% CI] 1.177 [1.021–1.356], p = 0.025). ROC curve of a prediction model showed that NLR ≥ 2.105 and D-dimer ≥ 0.845 could better predict the unfavorable outcome at discharge.

CONCLUSIONS

D-dimer and NLR on admission are independent predicators for short-term functional outcome in CVST patients and may be meaningful for better optimizing treatment decisions.

Background

Cerebral venous sinus thrombosis (CVST) is an uncommon manifestation of thrombosis that occurs mainly in younger individuals [1, 2]. The etiological factors of CVST include haematological diseases, vasculitis, and other inflammatory systemic disorders, as well as several local brain disorders like brain tumors, head trauma, and arteriovenous malformations [3]. The low incidence and atypical presentations of CVST often result in late diagnosis, which has been improved due to the advancement of

neuroimaging techniques in past decades [4, 5]. Nowadays, the earlier diagnosis and the improvement in the therapeutic management has ensured a better prognosis for CVST [1].

However, many patients retain chronic residual symptoms, such as headache, motor deficits, impaired vision or cognition, while some remain severely dependent or even die [6]. A multinational study with 624 patients indicated that 79% presented with complete recovery (defined as the modified Rankin Scale (mRS) 0 to 2) and 13.4% presented with death or dependency (defined as mRS 3 to 6) [7]. Therefore, there is a critical need to develop convenient and reliable indicators for predicting the functional outcome of patients with CVST, identifying those patients who need to be carefully treated.

Blood biomarkers represent an objective measurement of molecular characteristics and have been proposed as a powerful tool to use in CVST.

Previous studies on thrombotic diseases supported the role of inflammation in the pathophysiology of thrombosis, particularly in initiation and amplification of coagulation [8]. In experimental models of cerebral venous thrombosis, inflammatory cellular infiltration has been noted in the sites of thrombosis [9]. Monocytes and neutrophils were reported to provide the initiating stimulus for the development of venous thrombosis [9, 10]. Therefore, inflammation appears to be the link between the risk factors and CVST. Recently, inflammatory biomarkers like neutrophil to lymphocyte ratio (NLR), lymphocyte to monocyte ratio (LMR), platelet to lymphocyte ratio (PLR) and red blood cell distribution width to platelet ratio (RPR) have been confirmed to be related to outcomes of various inflammatory or vascular disease, such as stroke, sepsis and myocardial infarction [11–15]. Nonetheless, researches focused on the role of these inflammatory factors in the prognosis of CVST were limited. As inexpensive and convenient parameters assessing coagulation function, abnormal fibrinogen and elevated d-dimer has been verified in CVST [16, 17], while the dynamic changes of these markers and their effect on prognosis remain unclear. We aim to evaluate if the inflammation indicators and coagulation function indexes are helpful to predict the early diagnosis of patients with CVST. Therefore, this knowledge could guide treatment strategy and prehospital circuits.

Methods

Patients

169 patients diagnosed with CVST and been treated in Changhai hospital between September 2010 and August 2021 were retrospectively included in this study. Among the 169 patients included, 7 patients were excluded because of other intracranial lesions, 17 patients were excluded due to a history of inflammatory diseases, anti-inflammatory therapy, or immunosuppressive therapy, and 8 patients were excluded because due to incomplete follow-up data (Fig. 1). As a result, there were 137 patients with CVST included in the final statistical analysis. Permission was approved by the Ethic Committee of Changhai hospital (Shanghai, China) and informed consent was obtained from all patients or their legal guardians.

The inclusion criteria were as follow: (1) all patients meet the clinical diagnostic criteria for CVST [18], (2) the diagnosis of CVST was supported by magnetic resonance venography, operation searching, or digital subtraction angiography, (3) patients didn't have a history of inflammatory disease, and didn't take anti-inflammatory therapy or immunosuppressive therapy. Medical records of all patients were reviewed including clinical record, radiological imaging, and laboratory indicators. Lesions of CVST were identified based on radiological imaging, and all conclusions were obtained by two experienced radiologists. Laboratory samples were routinely collected at admission and at the end of treatment. This study focused on patients' prognosis at discharge. And patients' functional outcome was evaluated by the mRS: mRS 0-2 as good outcome, mRS 3-6 as poor outcome [19].

Statistical method

Quantitative data was described by mean ± standard deviation and analyzed by independent Student's t-test or Mann-Whitney U test. Qualitative data was described as percentages and analyzed by χ^2 test or Fisher's exact test. Binary logistic regression was applied to identify factors that could influence prognosis. The correlation between mRS score and significant clinical indicators was analyzed by the Spearman correlation test. The receiver operating characteristic (ROC) curve was used to test the discrimination capability of D-dimer on admission, NLR, and combined of these two indicators on the functional outcome. P values < 0.05 were considered statistically significant. All data analysis were performed by with SPSS, version 22.0 (Chicago, Illinois, USA).

Results

Baseline Characteristics for two functional outcome groups of CVST patients

The demographic and clinical characteristics of patients were shown in Table 1. Based on mRS, 102 patients were defined as good functional outcome, and the remaining 35 patients had poor functional outcome. The population was comprised of 72 men and 65 women with a mean age of 39.5 years (range, 7 - 80 years). Patients with acute onset were identified frequently in the poor functional outcome group than patients with chronic onset ($P = 0.032$). Besides, headache with nausea and vomiting was more common among patients with unfavorable functional outcome ($P = 0.042$). In addition, there are significant difference between the two groups with respect to type of lesion ($P < 0.001$) and treatment method ($P = 0.031$). However, there was no significant difference in other factors including age, gender, and etiologies.

Laboratory indicators for two groups of CVST patients

Laboratory indicators of patients were described in Table 2. D-dimer level on admission was significantly higher in patients evaluated as poor functional outcome compared with patients evaluated as good functional outcome (5.02 ± 6.18 vs 1.47 ± 2.21, $P = 0.002$). Moreover, neutrophil count was significantly lower in the good functional outcome group than the poor functional outcome group (5.35 ± 2.75 vs 7.15

± 3.54, $P = 0.008$). Furthermore, the difference on NLR and PRP between the two groups reached statistical significance ($P = 0.003$ and $P = 0.013$), but not LMR ($P = 0.355$) and PLR ($P = 0.138$).

Independent risk factors for functional prognosis of CVST patients

Potentially significant demographic, clinical, and laboratory indicators extracted in Table 1 and Table 2 were submitted to binary logistic regression analysis, and the details were shown in Table 3. The results demonstrated that chronic onset (OR, 0.211, 95CI%, 0.048-0.933, $P = 0.040$), D-dimer on admission (OR, 1.177, 95CI%, 1.021-1.356, $P = 0.025$) and NLR (OR, 1.243, 95CI%, 1.059-1.459, $P = 0.008$) were significantly associated with patients' functional outcome, respectively.

The correlation between short-term outcome and significant clinical indicators

The correlation between functional outcome evaluated by mRS score and significant clinical indicators was described in Table 4. The results showed that the functional outcome was positively associated with treatment method (rho=0.221, $P = 0.010$), D-dimer on admission (rho=0.394, $P < 0.001$), neutrophil count (rho=0.258, $P = 0.002$), NLR (rho=0.357, $P < 0.001$), and PRP(%) (rho=0.298, $P < 0.001$), among which D-dimer on admission had the closest correlation. However, acute onset was negatively related with patients' functional outcome (rho=-0.196, $P = 0.021$).

ROC curves analysis for NLR, D-dimer on admission, and combined detection

Patients with poor functional outcome had higher D-dimer level on admission and NLR than those with good functional outcome. Therefore, ROC curves of the predictive value of D-dimer on admission, NLR, and combined detection were shown in Fig 2. Simultaneously, the outcome of ROC curves for D-dimer on admission, NLR, and combined detection was described in Table 5. The area under the curve (AUC) of D-dimer on admission was 0.696, the optimal cut-off value was 0.845, the sensitivity was 0.743, the specificity was 0.598, and the Youden's index was 0.341. AUC of NLR was 0.707, the optimal cut-off value was 2.105, the sensitivity was 0.971, the specificity was 0.392, and the Youden's index was 0.364. In addition, AUC of combined detection was 0.703, the optimal cut-off value was 12.52, the sensitivity was 0.486, the specificity was 0.833, and the Youden's index was 0.319.

Discussion

From all the blood indicators screened, the main findings of this study are that higher NLR and D-dimer level on admission were independently associated with worse CVST functional outcome. Our study aimed at determining the predictive factors for the neurological recovery after CVST. The optimal cut-off to predict poor recovery for D-dimer was 0.845 with a sensitivity of 74%, a specificity of 60% and an AUC of 0.696. The optimal cut-off for NLR was 2.105 with a sensitivity of 97%, a specificity of 39% and an AUC of 0.707.

D-dimer is a circulating peptide degradation product of the cross-linked fibrin after being degraded by plasmin, reflecting systemic fibrin formation, with higher levels reflecting more systemic fibrin formation

and a tendency for thrombosis [20, 21]. As resistant to ex vivo activation and relatively stable, D-dimer has a long half-life, becoming an appropriate biomarker for thrombotic diseases. For example, D-dimer test has been widely used in the diagnosis of deep vein thrombosis and pulmonary embolism [22]. Recent research indicated that D-dimer at admission was independent predictor of large vessel occlusion in stroke, and higher D-dimer was significantly associated with a stroke severity scale [23]. It was also reported that plasma D-dimer may help to predict the occurrence of acute or subacute CVST [16, 24]. The relation between D-dimer and CVST might be based on two features: composition and quantity of thrombus. Higher increase in D-dimer levels means fibrin-rich and larger thrombus, which predicts poor outcome for patients with thrombosis [25]. However, investigations on the correlation of D-dimer at different stage and the functional outcome of patients with CVST were limited. Our study observed the dynamic monitoring of D-dimer level, which would be more valuable. We found that elevated D-dimer level on admission were predictive of unfavorable recovery, while D-dimer level at discharge didn't affect the outcome after CVST.

The increased NLR level may attribute to the excessive neuroinflammation [26]. CVST is a local event of venous occlusion characterized by the reduction of oxygen and failure of cellular metabolism, which triggers a local inflammatory immune response [27, 28]. Previous studies have found that inflammation is closely linked with thrombosis, particularly in the amplification of coagulation, which could shift the haemostatic balance towards a prothrombotic state [8, 29]. In the acute phase, neutrophil granulocyte counts elevate and lymphocyte counts decrease, which could be the primary nonspecific reaction of the immune system [30]. The inflammatory response triggered by acute stress then leads to a disruption of the neutrophil-to-lymphocyte ratio in peripheral circulation. Our study also found the difference of neutrophil counts between the patients with good or poor functional outcome. As a systemic inflammatory indicator, NLR has been reported to be associated with outcomes of various cerebrovascular diseases and may be useful as a prognostic factor, such as ischemic stroke, acute intracerebral hemorrhage and subarachnoid hemorrhage [26, 31, 32]. However, the studies related to the neutrophil-to-lymphocyte ratio and CVST were limited. Akboga, Y. E et al. reported that higher NLR on admission was independently related to the presence of CVST [33]. Recently, Wang, L et al. explored the relationship between inflammation and prognosis in cerebral venous thrombosis, and reported that higher NLR was significantly correlated with short-term poor outcome [34]. Consistent with their results, our findings demonstrated that elevated NLR was associated with higher incidence of neurologic deficit at discharge in CVST patients, suggesting a more common inflammatory state in poor functional outcome.

It was reported that longer disease duration at onset was associated with better physical function of CVST patients [35]. In addition, acute onset was reported to be the predictor of the expansion of early intracranial hemorrhage after CVST, suggesting the effect of onset form on the prognosis [36]. These conclusions mentioned above explained our findings of acute onset being associated with higher incidence of neurological deficits in patients with CVST.

Brain parenchymal injury lesion, treatment method, and levels of RPR (red blood cell distribution width to platelet ratio) were also found significantly different in patients with poor recovery compared to those

with good recovery. Local brain lesions like intracranial hemorrhage followed by herniation, seizures can be fatal [1]. Intracranial hemorrhage on imaging was reported to be a marker for worse long-term prognosis of CVST [2]. The present study also observed more local brain lesions in patients with unfavorable outcomes, consistent with these previous studies. Meanwhile, we observed the association between the treatment method and functional outcome of patients with CVST. Patients with good functional outcome tend to receive more anticoagulant therapy than those with adverse functional outcome. Since currently available data about the safety and efficacy of thrombolysis and endovascular treatment in patients remains controversial [37], further analysis is warranted to determine the treatment options. In addition, the elevation of RPR in CVST may be partially attributed to the inflammatory response [38]. The inflammatory cytokines might suppress erythrocyte maturation and accelerate newer, larger reticulocytes entering into the peripheral circulation, which lead to the increase of red blood cell distribution width [38]. Platelets produce proinflammatory molecules and lead to the formation and progression of pathological thrombosis [21]. As a novel index, RPR has been shown to reflect the severity of inflammation and is used to predict fibrosis and severity of chronic liver disease progresses [39]. To our knowledge, this is the first study to indicate that the elevated RPR is associated with the unfavorable outcome in CVST patients. Although there was no statistical significance after binary logistic regression analysis, the role of RPR remains uncertain. Further investigations are required to clarify the correlation and mechanisms of the process.

NLR and D-dimer are both simple laboratory parameters easily obtained with the whole blood count, suggesting them as stable and suitable predictor of functional prognosis after CVST. The rapid, objective, inexpensive, and easy evaluation of NLR and D-dimer on admission could become an opportunity to develop a prehospital point-of-care test. The combination between point-of-care test and CVST severity could improve prehospital assessment accuracy and guide treatment decisions. During the inflammatory process, the release of plasminogen activators is increased with subsequent plasmin generation [8], which may suggest the relationship between extension of thrombosis and increased inflammatory markers. However, the mechanism behind these observations is still poorly understood, and so are potential therapeutic targets in these patients. This study had several limitations. Firstly, it was a single-center study and the number of patients was not enough. Secondly, other inflammatory indicators such as C-reactive protein and erythrocyte sedimentation rate were not provided due to missing data in some patients. Thirdly, the association between these indicators and long-term outcome still need to be further explored.

Conclusion

Among CVST patients, D-dimer and NLR on admission are independent predicators of short-term functional outcome. This supports the opinion that coagulation and inflammation may play an important role in the development of thrombotic diseases. Further understanding on the process of the immune orchestra and the potential mechanism are required to assess the future risk and identify the therapeutic strategies.

Abbreviations

APTT, Activated partial thromboplastin time
Apo, Apolipoprotein
AUC, Area under the curve
CI, Confidence interval
Cr, Creatinine
CVST, Cerebral venous sinus thrombosis
Hb, Hemoglobin
HDL-C, High density lipoprotein cholesterol
LDL-C, Low density lipoprotein cholesterol
LMR, Lymphocyte to monocyte ratio
MCHC, Mean corpuscular hemoglobin concentration
MCV, Mean corpuscular volume
MPV, Mean platelet volume
mRS, The modified Rankin Scale
MRV, Magnetic resonance venogram
NLR, Neutrophil to lymphocyte ratio
OR
Odds ratio
PLR, Platelet to lymphocyte ratio
PLT, Platelet
PT, Prothrombin time
RDW, Red cell distribution width
ROC, Receiver operating characteristic
RPR, Red blood cell distribution width to platelet ratio
TC, Total cholesterol
TG, Triglyceride
TT, Thrombin time
UA, Uric acid.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Changhai hospital affiliated to Navy Military Medical University. Written informed consent was obtained from all patients or their legal guardians, and the study was conducted in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analysed during this study are included in this article.

Competing interests

All authors declare that they have no competing interests to disclosure.

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Authors' contributions

X B, offered the research direction. M L, and X L, designed the study and gave us several meaningful suggestions. Q D, Z G, C F, and C S reviewed and collected the medical records. W W, G Y, and R S analyzed and interpreted the patient data. R S was a contributor in writing the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1 Demographic and clinical characteristics of the two functional outcome groups in CVST patients.

Parameter	Good mRS≤2	Poor mRS>2	t/χ^2	*P* value
	n=102	n=35		
Age (y)	38.06±15.41	43.57±14.98	-1.839	0.955
Gender (male/female)	56/46	16/19	0.882	0.348
Onset			5.288	0.032*
Acute	5 (4.9%)	6 (17.1%)		
Chronic	97 (95.1%)	29 (82.9%)		
Etiologies				
Oral contraceptives	10 (9.8%)	1 (2.9%)	1.703	0.289
Thrombosis and blood diseases	17 (16.7%)	3 (8.6%)	1.370	0.242
Surgery	6 (5.9%)	2 (5.7%)	0.001	1.000
Infection	5 (4.9%)	1 (2.9%)	0.260	1.000
Immunological diseases	3 (2.9%)	2 (5.7%)	0.570	0.602
Puerperium	3 (2.9%)	3 (8.6%)	1.973	0.174
Pregnancy	5 (4.9%)	2 (5.7%)	0.035	1.000
Others	53 (52.0%)	21 (60.0%)	0.678	0.438
Signs and symptoms				
Headache with nausea and vomiting	82 (80.4%)	22 (62.9%)	4.382	0.042*
Visual disturbance	8 (7.8%)	4 (11.4%)	0.419	0.502
Muscle weakness	6 (5.9%)	4 (11.4%)	1.185	0.277
Seizures	5 (4.9%)	4 (11.4%)	1.808	0.233
Cognitive deficit	1 (1.0%)	1 (2.9%)	0.638	0.447
From onset to diagnostic time (d)	1.20±3.19	0.80±1.66	0.699	0.486
Lesion site on MRV				
Superior sagittal sinus	10 (9.8%)	4 (11.4%)	0.075	0.754
Inferior sagittal sinus	6 (5.9%)	0 (0.0%)	2.153	0.338
Straight sinus	4 (3.9%)	1 (2.9%)	0.084	1.000
Transverse and sigmoid sinus	31 (30.4%)	9 (25.7%)	0.276	0.671
Others	51 (50.0%)	21 (60.0%)	1.045	0.333

Type of lesion			23.296	<0.001*
Hemorrhage	33 (32.4%)	13 (37.1%)		
Infarct	31 (30.4%)	12 (34.3%)		
Both	1 (1.0%)	7 (20.0%)		
None	37 (36.3%)	3 (8.6%)		
Treatment method			8.876	0.031*
Anticoagulant therapy	82 (80.4%)	20 (57.1%)		
Interventional therapy	1 (1.0%)	2 (5.7%)		
Both	15 (14.7%)	9 (25.7%)		
Conventional therapy	4 (3.9%)	4 (11.4%)		
*Indicates statistical significance ($P < 0.05$).				
y, year; d, day; MRV, magnetic resonance venogram				

Table 2. Laboratory indicators of two functional outcome groups in CVST patients.

Parameter	Good mRS≤2	Poor mRS>2	t	*P* value
	n=102	n=35		
Coagulation indicator				
D-dimer on admission (mg/L)	1.47±2.21	5.02±6.18	-3.330	0.002*
D-dimer at last (mg/L)	0.72±1.66	1.32±1.65	-1.876	0.063
PT on admission (s)	14.32±2.86	15.71±7.65	-1.056	0.298
PT at last (s)	19.77±5.86	19.11±6.33	0.566	0.572
APTT on admission (s)	37.92±5.52	38.16±10.48	-0.129	0.898
APTT at last (s)	42.91±8.92	44.12±12.73	-0.607	0.545
TT on admission (s)	17.31±3.48	18.11±6.66	-0.903	0.368
TT at last (s)	16.98±2.58	17.41±3.05	-0.811	0.419
Fibrinogen on admission (g/L)	3.52±1.06	3.43±1.09	0.419	0.676
Fibrinogen at last (g/L)	3.20±1.73	3.65±1.29	-1.405	0.162
Biochemical indexes				
Apo-A1 (g/L)	1.22±0.30	1.26±0.30	-0.554	0.580
Apo-B (g/L)	0.90±0.30	0.98±0.30	-1.300	0.196
TC (mmol/L)	4.59±1.26	4.93±1.33	-1.356	0.177
TG (mmol/L)	1.61±1.03	1.51±0.89	0.486	0.628
LDL-C (mmol/L)	2.78±0.93	2.98±1.07	-1.034	0.303
HDL-C (mmol/L)	1.26±0.65	1.35±0.36	-0.744	0.458
Cr (mmol/L)	62.63±15.49	57.03±14.70	1.868	0.064
UA (mmol/L)	59.50±124.60	49.15±97.05	0.447	0.656
Blood routine examination				
Hb (g/L)	135.26±25.35	129.97±28.01	1.036	0.302
MCV (fL)	87.95±7.02	88.23±6.86	-0.206	0.837
MPV (fL)	10.41±1.30	10.42±1.19	-0.068	0.946
MCHC (g/L)	336.00±16.04	333.74±16.45	0.714	0.477
RDW (%)	14.54±13.02	13.97±2.14	0.253	0.800
Neutrophil (× 10^9/L)	5.35±2.75	7.15±3.54	-2.746	0.008*

Lymphocyte (× 10^9/L)	1.92±0.68	1.65±0.97	1.493	0.142
Monocyte (× 10^9/L)	0.64±0.46	1.63±6.33	-0.928	0.360
PLT (× 10^9/L)	242.70±88.71	219.60±119.02	1.212	0.227
NLR	3.16±2.09	5.79±4.85	-3.115	0.003*
LMR	3.53±1.56	3.23±1.74	0.928	0.355
PLR	140.94±78.06	178.75±140.70	-1.512	0.138
RPR %	6.32±3.09	9.34±6.62	-2.606	0.013*
*Indicates statistical significance (P < 0.05).				

PT, prothrombin time; APTT, activated partial thromboplastin time; TT, thrombin time; Apo, apolipoprotein; TC, total cholesterol; TG, triglyceride; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; Cr, creatinine; UA, uric acid; Hb, hemoglobin; MCV, mean corpuscular volume; MPV, mean platelet volume; MCHC, mean corpuscular hemoglobin concentration; RDW, red cell distribution width; PLT, blood platelet; NLR, neutrophil-to- lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; PLR, platelet-to-lymphocyte ratio; RPR, red blood cell distribution width to platelet ratio.

Table 3. Binary logistic regression analysis of risk factors for functional outcome in CVST patients.

Parameters	B	SE(β)	Wald χ^2	OR	95%CI	P value
Onset	-1.554	0.757	4.207	0.211	0.048-0.933	0.040*
Type of lesion	-0.218	0.204	1.133	0.805	0.539-1.201	0.287
Treatment method	0.444	0.229	3.752	1.559	0.995-2.442	0.053
D-dimer on admission (mg/L)	0.163	0.072	5.047	1.177	1.021-1.356	0.025*
NLR	0.218	0.082	7.063	1.243	1.059-1.459	0.008*
RPR %	0.101	0.069	2.153	1.106	0.967-1.266	0.142
*Indicates statistical significance (P < 0.05).						
NLR, neutrophil-to-lymphocyte ratio; RPR, red blood cell distribution width to platelet ratio						
CI indicates confidence interval						

Table 4. The correlation between functional outcome and significant clinical indicators

Parameter	rho value	*P* value
Onset	-0.196	0.021*
Type of lesion	-0.148	0.084
Treatment method	0.221	0.010*
D-dimer on admission (mg/L)	0.394	<0.001*
Neutrophil (× 10^9/L)	0.258	0.002*
NLR	0.357	<0.001*
RPR %	0.298	<0.001*
*Indicates statistical significance (*P* < 0.05).		
RPR, red blood cell distribution width to platelet ratio		

Table 5. Outcome of ROC for D-dimer on admission, NLR, and combined detection

Diagnostic indicators	AUC	cut-off value	95% *CI*	Sensitivity	Specificity	YI
D-dimer on admission (mg/L)	0.696	0.845	0.591~0.800	0.743	0.598	0.341
NLR	0.707	2.105	0.611~0.802	0.971	0.392	0.364
Combined detection	0.703	12.52	0.607~0.799	0.486	0.833	0.319
AUC, area under curve; NLR, neutrophil-to-lymphocyte ratio; YI, Youden's index						
CI indicates confidence interval						

Figures

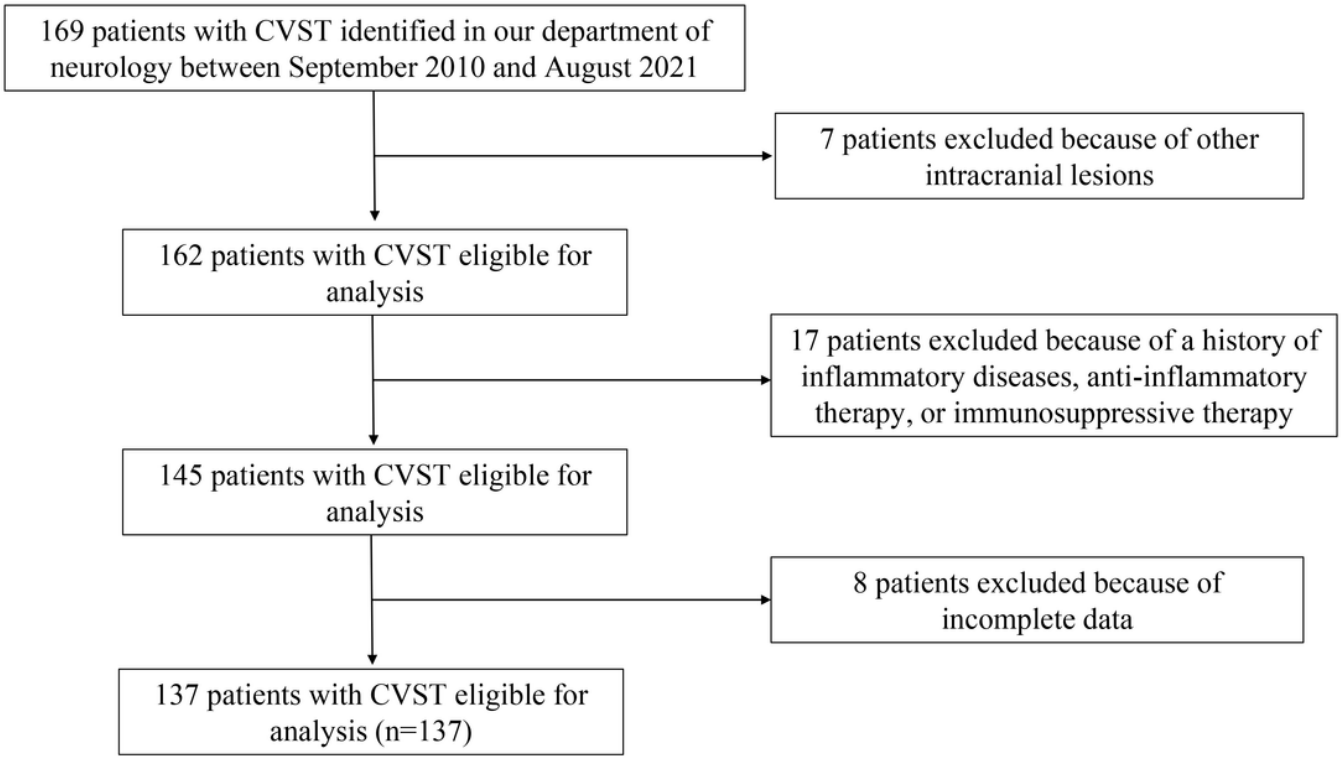

Figure 1

Flow chart of the study

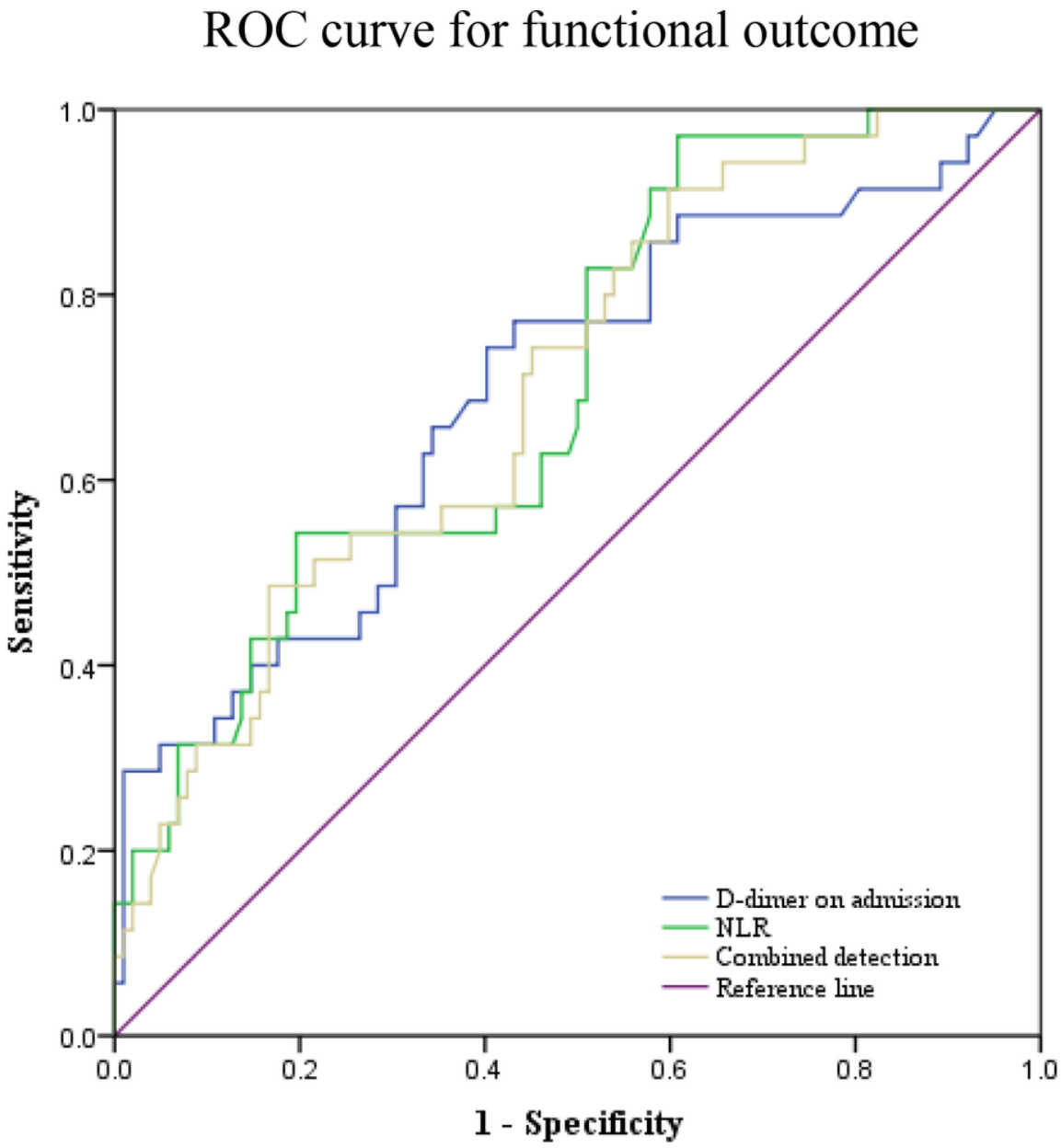

Figure 2

Receiver operating characteristic curve for D-dimer on admission, NLR, and combined detection to predict the functional outcome in CVST patients.