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Neutrophil to Lymphocyte Ratio, Cardiac Troponin and D-dimer as Predictors of Outcome in Patients with Cerebral Venous Thrombosis

Amr Kamel, Hadeer S. Esaa*, A. E. Badawy, Nesma A. M. Ghonimi
Neurology Department, Faculty of Medicine, Zagazig University, Egypt
***Corresponding author:** Hadeer Shabaan Abdel-Ati, **Mobile:** (+20) 01032346796, **E-mail:** hadsha_47@gmail.com

ABSTRACT

Background: Cerebral venous thrombosis (CVT) is a neurovascular disorder with a highly variable presentation and clinical course. **Objective:** This study aimed to explore the role of neutrophil to lymphocyte ratio (NLR), cardiac troponin and D-dimer as predictors of short term outcome in patients with cerebral venous sinus thrombosis.

Patients and methods: Thirty patients diagnosed with CVT were included. They were classified into favorable and unfavorable outcome groups based on one-month modified Rankin scale scores (mRS) (0-2: good prognosis, 3-6: poor prognosis). Clinical findings and laboratory markers (NLR, cardiac troponin and d dimer) were compared between the two groups. The correlation between each marker and mRS was assessed.

Results: This study included 30 patients with diagnosis of CVT, 7 (23.3%) were males and 23 (76.7%) were females with mean age 31.63 (SD 11.29) years. Headache was the most common symptom (93.3%) followed by blurring of vision (86.6 %). Left transverse sinus was the most frequent site of sinus thrombosis in 66.66% of patients. A total of 20 (66.7%) patients had favorable outcome and 10 (33.3%) had unfavorable outcome. NLR and D-dimer values were significant predictors of poor outcome in patients with CVT while cardiac troponin (cTn) was found to be non-significant.

Conclusion: On admission, D-dimer and NLR are separate predictors of short-term functional prognosis in CVT patients.

Keywords: CVT, NLR, D-dimer, Cardiac troponin.

INTRODUCTION

CVT is a rare type of stroke, accounting for 0.5%–1% of all strokes [(1)]. The pathophysiology of CVT remains unclear. It is believed that CVT can lead to both vasogenic and cytotoxic edema due to increased venous pressure. The blood-brain barrier may be broken, leading to vasogenic edema, or it may restrict cerebral blood flow, impair cellular metabolism, and lead to cytotoxic edema. ICP and parenchymal hemorrhage can result from an increase in venous pressure [(2)].

There are many CVT risk factors include thrombophilia, infections, inflammation, pregnancy, puerperium and usage of oral contraceptives. Women are more likely than males to develop CVT [(3)]. Despite the wide range of clinical manifestations, CVT frequently results in one or more of the following four syndromes: the increased ICP syndrome (headache, papilledema, visual disturbance), the focal neurologic syndrome (focal deficits, seizures, or both), encephalopathy (impaired cognition, stupor, or coma, with or without focused signs or symptoms), and the cavernous sinus syndrome [(4)].

Inflammation increases the risk of CVT and causes secondary brain damage [(1)]. Many studies examining the connection between CVT and inflammation have found increased initial NLR and CRP baseline levels. The severity of the disease, poor prognosis, and higher inflammatory markers at admission were all linked in some of these studies [(5-7)].

Factor XIIIa acts on the monomers and polymers of fibrin and produce D-dimer units. In people who arrive with clinical symptoms that are thought to be CVT, the D-dimer is an essential screening tool for deciding how quickly neuroimaging should be obtained. It might help to foretell the development of acute or subacute CVT [(8)]. However, there is still debate over whether D-dimer can help to predict outcome and how CVT patients would be managed.

A protein unique to the heart is called cardiac troponin (cTn). It can indicate a bad prognosis since it is increased in acute ischemic stroke and cerebral haemorrhage. Venous stasis brought on by CVT may cause cardiac stress and increased cTn. Patients with arterial ischemic stroke who had elevated plasma cTn levels died more frequently, while their role in CVT still needs to be elucidated [(9)].

The objective of this study was to investigate the function of cardiac troponin, neutrophil to lymphocyte ratio (NLR), and D-dimer as short-term outcome predictors in patients with cerebral venous sinus thrombosis.

PATIENTS AND METHODS

This study was a prospective cohort study conducted in in Neurology Department, Zagazig University Hospitals. All patients diagnosed with CVT during the period from May 2022 to October 2022 were identified.

Inclusion criteria were age >18 years and patients with confirmed diagnosis of CVT by MRV or CT venography.

Exclusion criteria were patients with: arterial stroke, additional causes of optic disc edema, such as ischemic

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optic neuropathy and diabetic papillopathy, Meningoencephalitis, Space-occupying lesion (SOL brain), Known epileptics, Eclampsia and preeclampsia.

All patients' data were gathered. Age, gender, any neurologic symptoms or signs, the Glasgow Coma Scale (GCS), and the National Institutes of Health Stroke Scale (NIHSS) were among the demographic and clinical information collected at the time of admission. The kind and quantity of affected sinuses on radiographs, as well as the presence of parenchymal lesions, were all noted. On admission, blood samples were regularly taken, and NLR, D-dimer, and cardiac troponin levels were determined. NLR was calculated from complete blood count tests (by dividing neutrophils count by lymphocytes count) performed within 24 hours after admission.

D-dimer levels were estimated on patients' admission time by an automated immunoturbidimetric assay. cTn was measured using a one-step immunoassay sandwich method with a final fluorescent detection (EFLA) with reference values: <100ng/l. For outcome analysis, all patients were subdivided into two groups: favorable and unfavorable outcome groups based on mRS after 1 month (0-2: favorable outcome, 3-6: unfavorable outcome).

Ethical approval:

Zagazig Medical Ethics Committee of the Zagazig Faculty of Medicine gave its approval to this study. All participants gave written consent after receiving all information. The Helsinki Declaration was followed throughout the study's conduct.

Statistical analysis

Data analysis was done using SPSS version 26. Categorical variables were described using absolute frequencies. The means, standard deviations, median, and range of quantitative variables were utilized, depending on the kind of data, to describe it. Quantitative data were compared between two groups using independent sample t tests (for normally distributed data) and Mann-Whitney tests (for not normally distributed data).

The strength and direction of the link between two continuous variables were assessed using Spearman rank correlation coefficients for data that were not normally distributed. The ROC curve was used to find the appropriate cut-off values for outcome prediction and to assess the sensitivity and specificity of relevant indicators. P value was fixed at 0.05 for statistical significance and <0.001 for highly significant results.

RESULTS

A total of 30 patients with CVT were included in our study. The age was 31.63 (SD 11.29) ranging from 18 to 59 years. Twenty-three (76.7%) patients were female. Headache was the most common presenting symptom, occurring in 93.3% of patients, followed by blurred vision in 86.6% of cases.

Seizure and motor weakness were observed in 40% and 33.3% patients, respectively. The most frequent site of sinus thrombosis was left transverse sinus in 66.66% patients followed by right transverse sinus and sagittal sinuses in 43.33%, 40% patients respectively **(Table 1)**.

Table (1): Demographic, clinical, radiologic and risk factors of all CVT patients.

Variables	Studied patients (n=30)
Age	**31.63 ± 11.29**
Sex	
Male	**7 (23.3%)**
Female	**23 (76.7%)**
Clinical presentation	
Headache	**28 (93.3%)**
Blurring of vision	**26 (86.6%)**
Seizures	**12 (40%)**
Motor weakness	**10 (33.3%)**
Disturbed consciousness level	**8 (26.7%)**
Risk factors	
Thrombophilia	**6 (20%)**
Hypertension	**3 (10%)**
Studied female patients (n=23)	
Female related causes : **Pregnancy** **Puerperium** **Oral contraceptive pills**	**16 (69.65%)** **2 (8.69%)** **4 (17.39%)** **10 (43.47%)**
Involved sinuses:	
Superior ±Inferior sagittal Sinus 12 (40%) **Right transverse sinus 13 (43.33%)** **Left transverse sinus 20 (66.66%)** **Right sigmoid sinus 10 (33.3%)** **Left sigmoid sinus 8 (26.6%)** **Right Internal jugular 4 (13.3%)** **Left Internal jugular 2 (6.8%)** **Cortical veins 1 (3.4)**	

As for laboratory parameters, Compared to patients with favorable outcomes, NLR [4.47 (3.34 – 5.23) vs. 2.94 (2.17 – 3.35), P= 0.031], while lymphocyte count was considerably lower in patients with bad results [1.5±0.5 vs. 2.01±0.49, P= 0.012], D-dimer level was significantly higher in patients with poor outcomes [2.25 (1.48 - 2.58) vs. 0.4 (0.29 - 1.1), P= 0.001]. No discernible variations were seen in the other laboratory measurements made **(Table 2)**.

Table (2): Laboratory parameters of the two studied groups.

Laboratory	Poor prognosis (N=10)	Good prognosis (N=20)	t-test	P-value
	Mean ± SD	Mean ± SD		
WBCs count (x10^3 /µL)	10.19 ± 2.36	8.67 ± 2.07	0.953	0.362 (NS)
Neutrophil (x10^3 /µL)	7.71 ± 1.9	5.9 ± 1.39	1.308	0.218 (NS)
Lymphocyte (x10^3 /µL)	1.5 ± 0.36	2.01 ± 0.49	-2.67	0.012 (S)
Variable	**Median (IQR)**	**Median (IQR)**	**Z**	**P-value**
NLR	4.47 (3.34 – 5.23)	2.94 (2.17 – 3.35)	-2.156	0.031 (S)
Cardiac Troponin µg/l	5.45 (2.06 –10.56)	5 (3 – 5.84)	-0.561	0.575 (NS)
D-dimer	2.25 (1.48 – 2.58)	0.4 (0.29 –1.1)	-3.427	0.001 (HS)

Median, IQR: non parametric test.

NLR (R=0.469, P=0.009) and D-dimer level (R=0.716, P=0.001) were strongly correlated with mRS score at one month, according to the analysis's findings. However, the relationship between mRS and cardiac troponin is statistically insignificant **(Table 3)**.

Table (3): Correlation between laboratory parameters and outcome.

Variable	mRS		
	R	P-value	(Sig.)
WBCs (x10^3/mm3)	0.268	0.152	NS
NLR	0.469	0.009	S
D-dimer	0.716	<0.001	(HS)
Cardiac Troponin	0.273	0.16	(NS)

According to the ROC curve, NLR and D-dimer levels at admission might statistically predict the short-term outcome of CVT. The NLR AUC was 0.745, and the optimum cut-off value was ≥3.6035 (sensitivity 80%, specificity 85%) (**Figure 1**). The best cut-off value for D-dimer was ≥1.3 (sensitivity 88.9%, specificity 85%) (**Figure 2**).

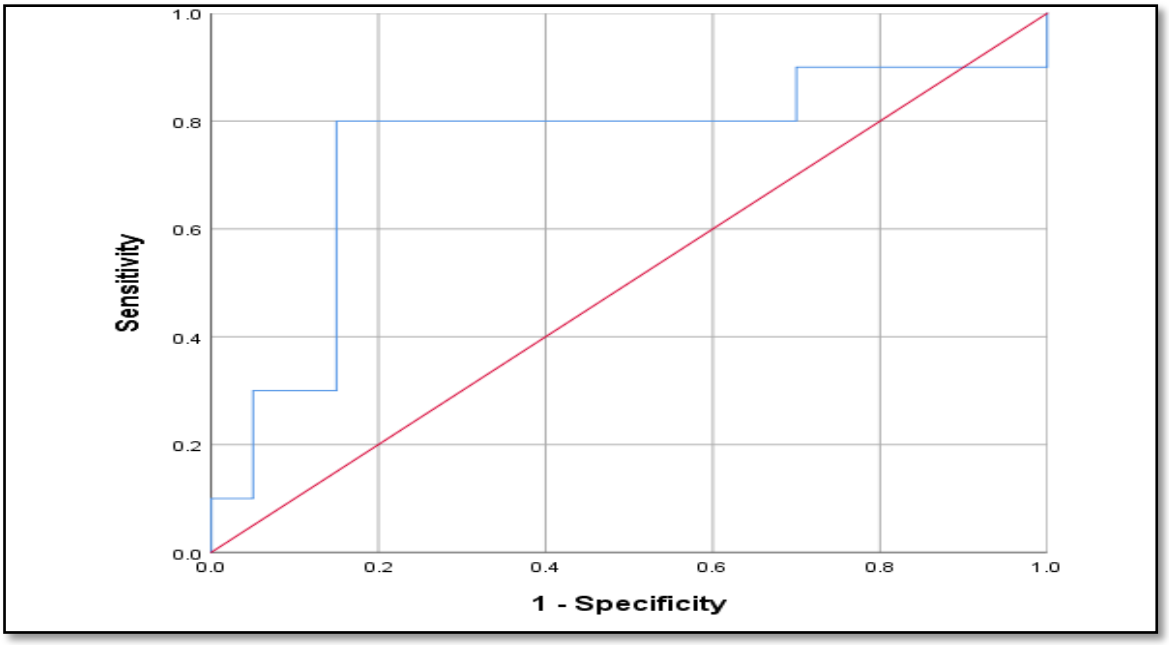

Figure (1): ROC curve demonstrating the performance of NLR in predicting bad outcomes in the patients investigated.

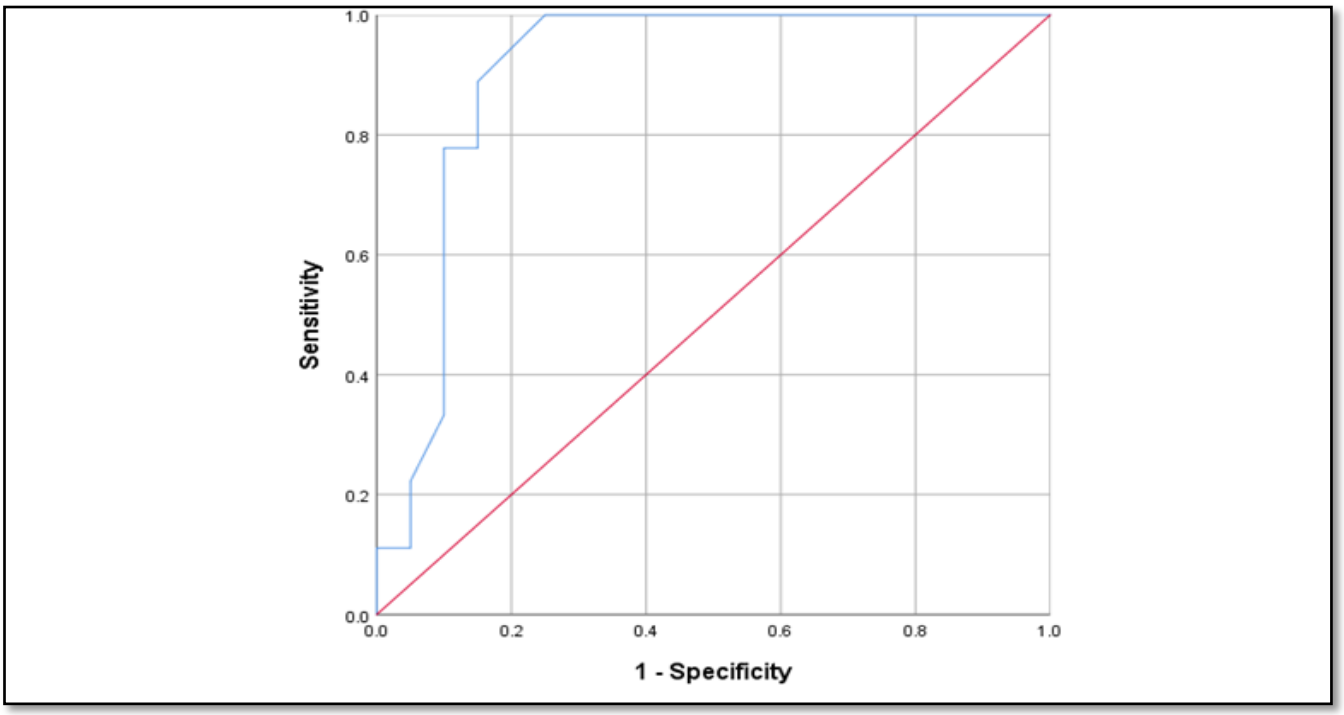

Figure (2): ROC curve demonstrating D dimer performance in predicting poor outcome in the patients investigated.

DISCUSSION

CVST results might range from complete recovery to death. The majority of CVST patients, according to the ISCVT, are released with a successful outcome; nonetheless, mortality and reliance are observed in 18.9% of people [10].

Clinical, laboratory, and radiographic factors can serve as predictors of an unfavorable outcome [10-12]. In this study we evaluated simple laboratory biomarkers (NLR, D dimer and cTn) as predictors of outcome in CVT patients.

NLR has been shown to be able to predict the prognosis in acute MI and numerous cancer types. A higher NLR is typically associated with high mortality and a bad prognosis [13-15].

In our study, which examined the relationship between NLR admission values and outcomes in patients with CVT, we discovered that NLR was considerably greater in the group of patients with bad results, with a median NLR (4.47 vs. 2.94) suggesting a more prevalent inflammatory condition in patients with poor outcome. This is in agreement with the results reported by **Wang *et al.*** [16] **and Kim *et al.*** [17].

Several studies have found that D-dimer levels rise was linked to a variety of inflammatory and thrombotic vascular diseases [8,18,19]. D-dimer is frequently used to diagnose CVST [20]. Moreover, in individuals with CVT, high D-dimer levels are associated with increased thrombus extension and a risk of cerebral hemorrhage [21].

In concordance with these data, we found elevated levels of D-dimer in our patients, with higher level in patients with unfavorable outcome than in those with favorable outcome with median (2.25 vs. 0.4), and these results were supported by the high statistically significant positive correlation between D-dimer values and mRS score.

We also found that there was non-statistically significance correlation between cTn and mRS score in CVT patients. A bad prognosis may be indicated by cTn increase, which occurs in acute ischemic stroke [21], as well as cerebral hemorrhage [22]. But there are still few studies examining how cTn affects the clinical course of CVT patients, nevertheless **Johansen *et al.*** [23] in their cohort study on 81 CVT patients demonstrated that there is an increased odds of cTn in patients with acute sever CVT.

The minor drawbacks of our investigation were the limited sample size, the short duration of our trial, and the dearth of information regarding the long-term prognosis of our patients.

CONCLUSION

High D-dimer levels and NLR upon admission were linked to a higher probability of a poor outcome in CVT patients. These two indications may also be useful in predicting the CVST prognosis in the near future.

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Competing interests: Nil.

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