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RESEARCH

Sinus vein thrombosis and epileptic seizures: outcomes of long term follow-up

Sinüs ven trombozu ve epileptik nöbetler: uzun dönem takip sonuçları

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Abstract

Purpose: In the acute phase of Cerebral Venous Sinus Thrombosis (CVST), approximately 35-50 % of patients diagnosed epileptic seizures. This study aimed to investigate the demographic and clinical characteristics, frequency of seizures, prognosis of patients during a one-year follow-up period.

Materials and Methods: The files of patients who were followed up with the diagnosis of acute ischemic stroke between January 1, 2018 and January 1, 2022 were evaluated in this retrospective study. Demographic features, presence of seizure history and seizure frequency, neuroimaging findings, affected cerebral venous sinuses, and anti-seizure medication use were recorded.

Results: A total of 701 patients with acute stroke had their medical records reviewed. Thirty-two of 701 patients (4.56 %) were diagnosed with CVST; 37.5 % of patients experienced early-onset seizures. Seizure control was achieved with monotherapy in 88.8 % (n:8) of patients with seizures. Involved sinuses in patients with seizures; 50 % (n=6) superior sagittal sinus was the most commonly involved sinus and inferior sagittal sinus and sinus rectus were not involved. In terms of sinus involvement, there was no statistically significant difference between patients with and without seizures. On cerebral magnetic resonance imaging, venous infarcts were detected in 66.7 % (n=8) of patients with seizures, compared to 35 % of patients without seizures.

Conclusion: This retrospective study revealed that seizures typically occur early in the disease, have a favorable prognosis over the long term, and can be managed with monotherapy.

Keywords:. Epilepsy, cerebral venous sinus thrombosis, Anti-seizure medication, prognosis

Öz

Amaç: Serebral Venöz Sinüs Trombozunun (SVST) akut fazında hastaların yaklaşık %35-50'sinde epileptik nöbetler görülmektedir. Bu çalışmada, bir yıllık takip süresi boyunca hastaların demografik ve klinik özellikleri, nöbet sıklığı ve prognozunun araştırılması amaçlanmıştır.

Gereç ve Yöntem: Retrospektif olarak yapılan bu çalışmada 1 Ocak 2018 ile 1 Ocak 2022 tarihleri arasında akut iskemik inme tanısı ile takip edilen hastaların dosyaları değerlendirildi. Demografik özellikler, nöbet öyküsü varlığı ve nöbet sıklığı, nörogörüntüleme bulguları, etkilenen serebral venöz sinüsler ve nöbet önleyici ilaç kullanımı kaydedildi.

Bulgular: Akut inme geçiren toplam 701 hastanın tıbbi kayıtları incelenmiştir. 701 hastanın 32'sine (%4,56) SVST tanısı kondu; hastaların %37,5'inde erken başlangıçlı nöbetler görüldü. Nöbet geçiren hastaların %88,8'inde (n:8) monoterapi ile nöbet kontrolü sağlanmıştır. Nöbet geçiren hastalarda tutulan sinüsler; %50 (n=6) superior sagittal sinüs en sık tutulan sinüs olup, inferior sagittal sinüs ve sinüs rektus tutulumu izlenmemiştir. Sinüs tutulumu açısından nöbet geçiren ve geçirmeyen hastalar arasında istatistiksel olarak anlamlı bir fark yoktu. Beyin manyetik rezonans görüntülemede nöbet geçiren hastaların %66,7'sinde (n=8) venöz enfarkt saptanırken, nöbet geçirmeyen hastaların %35'inde saptanmıştır.

Sonuç: Çalışmamız, nöbetlerin tipik olarak hastalığın erken dönemlerinde ortaya çıktığını, uzun vadede olumlu bir prognoza sahip olduğunu ve monoterapi ile yönetilebileceğini ortaya koymuştur.

Anahtar kelimeler: Epilepsi, serebral venöz sinüs trombozu, nöbet önleyici ilaçlar, prognoz

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INTRODUCTION

The incidence of cerebral venous sinus thrombosis (CVST) is reported to be 3-4/1,000,000 and accounts for 1% of all strokes[1]. CVST, which occurs in younger age groups compared to other stroke types, may present with headache alone or with focal neurologic findings, seizures, and coma. In patients presenting with isolated headaches, the diagnosis may sometimes be delayed, leading to a poor prognosis in a disease that usually has a good prognosis[2,3].

Although CVST is rare, it gains special importance because it affects young adults, children, and women of childbearing age and causes epileptic seizures. Seizures at the time of diagnosis and in the first seven days after the diagnosis are called acute symptomatic seizures and are reported with a rate of 24-50% in the literature[4-6]. Epileptic seizures are known to be more frequent as a presenting symptom in CVST than in other types of stroke[7]. Approximately 35-50% of patients diagnosed with CVST have focal onset or generalized seizures in the acute period, and in approximately 9% of these patients, seizures may persist in the long term[5]. Seizures occurring 7 days after CVT are termed late seizures and should be considered unprovoked seizures. These seizures may affect quality of life as they require long-term use of anti-seizure medication (ASM)[8]. The group of patients in whom a late seizure occurs should be diagnosed with epilepsy because, according to the International League Against Epilepsy (ILAE), it is possible to diagnose epilepsy after a single unprovoked seizure in certain cases with a greater than 60% risk of seizure recurrence in the following 10 years[9]. Ferro JM et al. reported focal neurologic deficit, parenchymal lesions, and superior sagittal sinus involvement as risk factors for epileptic seizure development[6]. The incidence of epileptic seizures is higher in these patients with venous infarction compared to arterial strokes. In addition, the presence of epileptic seizures has been reported as a poor prognostic factor. Seizures in patients with SVST have been reported as an indicator of poor prognosis, and mortality was found to be three times higher in patients with seizures compared to those without seizures[4,10].

In this study, we aimed to to investigate the frequency, prognosis and type of seizures and to define the risk factors for acute seizures in patients with CVST in 1-year follow-up. Thus, it will raise awareness in primary and secondary health care physicians, especially in clinicians dealing with stroke and epilepsy, in terms of the treatment and long-term prognosis of epileptic seizures associated with SVT. Knowing the risk factors for and long-term prognosis of acute seizures after CVST may be helpful in both the early detection of patients at risk for epileptic seizures and in providing patients with proper treatment and information.

MATERIALS AND METHODS

This retrospective study reviewed the electronic archive files of patients diagnosed with acute ischemic stroke between January 1, 2018 and December 31, 2022 in the Stroke Unit of the Department of Neurology, Çukurova University Faculty of Medicine. Approval for the study was obtained from the Non-Interventional Clinical Research Ethics Committee of Çukurova University Faculty of Medicine (135/2023).

The electronic files of patients diagnosed with acute ischemic stroke were reviewed, and those diagnosed with CVST were identified. Inclusion criteria were as follows: having a diagnosis of CVST for the first time, having a follow-up of at least 12 months, not having a diagnosis of epilepsy before the diagnosis of CVST, or not using anti-seizure medication (ASM). Patients with a follow-up of less than 12 months, patients with a known diagnosis of epilepsy before the diagnosis of CVST, patients not receiving ASM regimen appropriate for their seizure type, patients diagnosed with recurrent stroke, patients with insufficient file data, and patients with a history of epilepsy were excluded from the study.

Age, gender, history of pregnancy in the last year, whether in the postpartum period, history of oral contraceptive drug use in the last year, history of miscarriage, stillbirth, in utero ex, whether hormone replacement therapy in the last year, Seizure history after the diagnosis of CVST, time of first seizure, seizure frequency at 1-year follow-up, cerebral magnetic resonance imaging (MRI), cerebral MRI venography findings, electroencephalography findings, involved sinuses, and ASM use were recorded. The patients were examined by a neurologist and these structured data were collected from a tertiary epilepsy center (Çukurova University).

Statistical analysis

Categorical variables are expressed as numbers

(percentage), and continuous variables are expressed as mean ± standard deviation or median minimum–maximum, where appropriate. The chi-square test was performed to compare categorical variables between the groups. In the comparison of numerical measurements between two groups, independent samples T test was used if the conditions were provided. The degree of association between variables was determined based on odds ratios (ORs) and 95% confidence intervals (CIs). All analyses were performed using the IBM SPSS Statistics Version 20.0 statistical software package. The statistical significance level for all tests was set at $p \leq 0.05$.

RESULTS

The files of 701 patients with acute ischemic stroke were reviewed. Descriptive statistics of demographic and clinical characteristics of the patients are presented in Table 1. The mean age of the 32 patients diagnosed with CVST and meeting the inclusion criteria was 31.6 ± 5.4 years (range: 19-47). Notably, 84.4% of the patients were under 35 years of age. There was no statistically significant relationship between patient age and seizure risk.

The rate of CVST was found to be 4.56% among all ischemic stroke cases. It was determined that 37.5% (n:12) of the patients, 93.8% of whom were women, had seizures during or after the diagnosis of CVST. It was determined that 93.8% (n:11) of the patients with seizures presented to the emergency department complaining of seizures, and only one patient had the first seizure on the fourth day after the diagnosis.

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Table 1. Demographic and clinical characteristics of the study population

Variable	All patients(n=32)
Age (years) a	31.6±5.4 31.0(19.0-47.0)
Age, n (%) <35 ≥35	 27(84.4) 5(15.6)
Gender, n (%)	
Female	30(93.7)
Male	2(6.3)
Seizure, n (%)	
Yes	12(37.5)
No	20(62.5)
Infarct on MRI, n (%) (Yes)	15(46.8)
Anti-seizure medications, n (%)	
Drug-free	3(25)
Monotherapy	8(66.6)
Polytherapy	1(8.4)
Seizure frequency, n (%)	
Seizure-free	9(75)
More than once a month	1(8.3)
1 in 6 months	1(8.3)
1 per year	1(8.3)
Sinüs vein involvement, n (%)	
Superior sagittal sinus Transverse sinus Inferior sagittal sinus Sigmoid sinus Sinus rectus Internal jugular vein Cavernous sinus	14(43.7) 6 (18.7) 1 (3.1) 4 (12.5) 2 (6.2) 3 (9.3) 2 (6.2)

aData were expressed as mean±standard deviation, median (min-max)

Table 2. Comparison of seizure group and seizure-free patient group

	Groups		OR (p)
	Seizure-free group (n=20)	Seizure group (n=12)	
Age, n,% <35 years ≥35 years	17 (85) 3 (5)	10 (83.3) 2 (16.7)	1.11 (0.133) Ref.
Sinus involvement, n,%			
Superior sagittal sinus Transverse sinus	8 (40) 4 (20)	6 (50) 2 (16.6)	1.39 (0.251) 1.12 (0.421)
Inferior sagittal sinus Sigmoid sinus Sinus rectus Internal jugular vein Cavernous sinus	1 (5) 2 (10) 2 (10) 2 (10) 1 (5)	0 2 (16.6) 0 1 (8.3) 1 (8.3)	- 1.16 (0.081) - 1.2 (0.90) Ref.
Venous infarct, n,%			
No	13(65)	4 (33.3)	Ref.
Yes	7 (35)	8 (66.7)	2.14 (0.08)

OR, odds ratio

The mean follow-up period was 2.1 years (range 1-5 years). Seizure control was achieved with monotherapy in 88.8% (n:8) of the patients who were found to have seizures secondary to CVST and with polytherapy in 1 patient, while three patients did not use ASM. In the group of patients who had seizures, 75% were seizure-free, but seizures continued in 3 patients who did not use ASM (Table 1). Involved sinuses in patients with seizures; 50% (n=6) superior sagittal sinus was the most commonly involved sinus, and inferior sagittal sinus and sinus rectus were not involved (Table 2). No statistically significant difference existed between patients with and without CVST-related seizures regarding involved sinuses. Venous infarcts were detected on cerebral MRI in 66.7% (n=8) of patients with seizures and 35% without seizures. The presence of venous infarction on cerebral MRI increased seizure risk 2.14 times (Table 2). This was found to be statistically borderline significant (P = 0.08)

DISCUSSION

CVST is a type of stroke frequently occurring in young or middle-aged populations and is less common than arterial strokes [11]. In our study, approximately 93.8% of the patients with CVST were female, and 86.6% were under 35. One of the most important reasons for the high prevalence in young adult women is that pregnancy and oral contraceptive use significantly increase the risk of cerebral venous thrombosis in women[12]. Although CVST has been reported with a frequency of 0.5-1% in studies in the literature, this rate was higher at 4.56% because we included only ischemic strokes in our study[13]. When this frequency is considered, CVST should definitely be considered in the etiology of young ischemic strokes.

Transverse sinus (44-73%) and superior sagittal sinus (39-62%) have been reported to be the most commonly affected sinuses by thrombosis, and in our study, transverse sinus involvement was 18.7%, and superior sagittal sinus involvement was 43.7%[14]. Ferro JM et al. reported that superior sagittal sinus involvement increased the risk of epileptic seizure development [6]. Similarly, in our study, 50% of the patients with epileptic seizures had superior sagittal sinus involvement. In addition, despite the low number of patients, the absence of inferior sagittal sinus and sinus rectus involvement in the group of patients with seizures is also noteworthy.

CVST-related seizures are mostly acute symptomatic (35-50%), occurring within the first 7 days[5,15]. Seizures occurring after seven days are called late seizures and are less common [16]. In our study, it was observed that all of the patients with seizures had acute symptomatic seizures. In Lidgren et al. study of 1281 patients, the frequency of acute symptomatic seizures was 34%, and 81% of these patients presented with seizures similar to our study[17].

Supratentorial cerebral infarcts have been reported to be one of the important factors in the development

of CVST-related seizures[8,18]. Similar to the literature, our study found cerebral infarction due to venous thrombosis significant as a seizure marker (P = 0.08). Ferro JM. et al. found that ASM treatment reduced the development of acute symptomatic seizures in patients with cerebral lesions[16]. In this context, the high risk of CVST-related acute symptomatic seizure development, especially in patients with cerebral lesions, raises the issue of preventive ASM drug initiation in this patient group. European and American guidelines recommend the initiation of ASM in patients with acute symptomatic seizures to prevent seizure recurrence[18,19].

Beghi et al. reported that mortality was higher in patients with CVST accompanied by epileptic seizures than in patients without seizures [20]. On the contrary, Sha et al. reported that epileptic seizures did not make a difference in mortality[21]. In the VENOST study, acute symptomatic seizures were reported to be effective on prognosis and mortality, especially in the first 1 month[12]. In our study, although mortality was not specifically excluded, there were no patients who resulted in mortality. Even if they do not increase mortality, epileptic seizures should be managed correctly as they impair patients' life quality. In the literature, the frequency of status epilepticus has been reported between 0.5-11% in CVST patients and 1-22% in patients with acute symptomatic seizures[4,6,16]. In our study, status epilepticus did not develop in any of our patients during follow-up.

In conclusion, although epileptic seizures are common and occur early in the disease, the prognosis is favorable in the long term. Patients with cortical vein thrombosis and associated hemorrhagic lesions have a high risk of epileptic seizures. Therefore, considering these risk factors, this patient group should be closely monitored and evaluated for prophylactic ASM treatment. In addition, three patients who did not use ASM and whose seizures could not be controlled draw attention to the importance of ASM use in this patient group.

The limitations of our study include the low number of patients, short follow-up periods of some patients even though follow-up was at least one year, and the retrospective nature of the study. Further prospective studies with a larger patient population and longer follow-up periods will guide clinicians in this regard.

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REFERENCES

1. Mu S, Li J, Lin K, Fang Y, Lin F, Li Z, Xu Y, Wang S. Predictive factors for early-onset seizures in patients with cerebral venous sinus thrombosis. Front Neurol. 2022;29;13:842807.
2. Luo Y, Tian X, Wang X. Diagnosis and treatment of cerebral venous thrombosis: a review. Front Aging Neurosci.2018;30:10-2.
3. Sassi S B, Touati N, Baccouche H, Drissi C, Romdhane, NB, and Hentati, F Cerebral venous thrombosis: a tunisian monocenter study on 160 patients. Clin Appl Thromb Hemost. 2016; 23:1005–09.
4. Masuhr F, Busch M, Amberger N, Ortwein H, Weih M, Neumann K et al. Risk and predictors of early epileptic seizures in acute cerebral venous and sinus thrombosis. Eur J Neurol.2006;13:852–6.
5. Habibabadi JM, Saadatnia M, Tabrizi N. Seizure in cerebral venous and sinus thrombosis. Epilepsia Open. 2018;3:316–22.
6. Ferro JM, Canhão P, Bousser MG, Stam J, Barinagarrementeria F. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Venous Sinus Thrombosis (ISCVT). Stroke. 2004;35:664–70.
7. Gazioglu S, Yildirim A, Kokturk EG, Seker D, Altunayoglu Cakmak V, Velioglu SK.. Acute seizures in cerebral venous sinus thrombosis risk factors and prognosis. Neurologist. 2020 ;25:126-30.
8. Gasparini S, Neri S, Brigo F, Cianci V, Mammì A, Pascarella A et al. Late epileptic seizures following cerebral venous thrombosis: a systematic review and meta-analysis. Neurol Sci. 2022;43:5229-36.
9. Fısher RS, Acevedo C, Arzimanoglou A, Bagacz A, Cross HJ, Elger CE et al. ILAE official report: a practical clinical definition of epilepsy. Epilepsia.2014;55:475-82.
10. Uluduz D, Midi I, Duman T, Yayla V, Karahan AY, Afsar N et al. Epileptic seizures in cerebral venous sinus thrombosis: subgroup analysis of VENOST study. Seizure. 2020;78:113-7.
11. Daghriri HM, Alrajhi AA, Aburasain KS, Ateya EA, Hakami MA, Gosadi IM. An assessment of cerebral venous thrombosis risk factors and associated clinical outcomes in Jazan region, Saudi Arabia. Neurosciences (Riyadh).2021;26:15-20.
12. Roeder HJ, Lopez JR, Miller EC. Ischemic stroke and cerebral venous sinus thrombosis in Pregnancy. Handb Clin Neurol.2020;172:3–31.

13. Alimohammadi A, Kim DJ, Field TS. Updates in cerebral venous thrombosis. Curr Cardiol Rep. 2022;24:43-50.
14. Moraes Junior AAA, Conforto AB. Cerebral venous thrombosis. Arq Neuropsiquiatr. 2022;80:53-9.
15. Kalita J, Chandra S, Misra UK. Significance of seizure in cerebral venous sinus thrombosis. Seizure.2012;21:639-42.
16. Ferro JM, Correia M, Rosas MJ, Pinto AN, Neves G. Cerebral venous thrombosis portuguese collaborative study group [venoport]. seizures in cerebral vein and dural sinus thrombosis. Cerebrovasc Dis. 2003;15:78–83.
17. Lindgren E, Silvis SM, Hiltunen S, Heldner MR, Serrano F, de Scisco M et al. Acute symptomatic seizures in cerebral venous thrombosis. Neurology. 2020;95:1706-15.
18. Ferro JM, Bousser MG, Canhao P, Coutinho JM, Crassard I, Dentali F et al. European stroke organisation guideline for the diagnosis and treatment of cerebral venous thrombosis - endorsed by the European Academy of Neurology. Eur J Neurol.2017;24:1203-13.
19. Saposnik G, Barinagarrementeria F, Brown RD, Bushnell CD, Cucchiara B, Cushman M et al. Diagnosis and management of cerebral venous thrombosis: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2011;42:1158-92.
20. Beghi E, D'Alessandro R, Beretta S, Consoli D, Crespi V, Delaj L et al. Incidence and predictors of acute symptomatic seizures after stroke. Neurology. 2011;77:1785-93.
21. Sha D, Qian J, Gu S, Wang L, Wang F, Xu Y. Cerebral venous sinus thrombosis complicated by seizures: a retrospective analysis of 69 cases. J Thromb Thrombolysis. 2018;45:186-91.