Jinekoloji - Obstetrik ve Neonatoloji Tıp Dergisi
The Journal of Gynecology-Obstetrics and Neonatology

ÖZGÜN ARAŞTIRMA / ORIGINAL ARTICLE

DOI: 10.38136/jgon.1578867

The Utility of the Systemic Immune-Inflammation Index (SII) and the Systemic Immune-Response Index (SIRI) in predicting pregnancy-related cerebral venous sinus thrombosis: An experience from a tertiary center

Sistemik İmmün-İnflamasyon İndeksi (SII) ve Sistemik İnflamatuar-Yanıt İndeksi'nin (SIRI) gebelikle ilişkili serebral venöz sinüs trombozunu öngörme etkisi: Üçüncü basamak merkez deneyimi

Ezgi BAŞARAN[1], Atakan TANAÇAN[2], Nihat FARİSOĞULLARI[1], Zahid AĞAOĞLU[1], Hakkı ŞERBETÇİ[1], Özgür KARA[1], Namık Nebi ÖZCAN[3], Dilek ŞAHİN[2]

[1]Department of Obstetrics and Gynecology, Division of Perinatology, Turkish Ministry of Health Ankara City Hospital, Ankara, Türkiye
[2]University of Health Sciences, Department of Obstetrics and Gynecology, Division of Perinatology, Turkish Ministry of Health Ankara City Hospital, Ankara, Türkiye
[3]Department of Anesthesiology and Reanimation, Turkish Ministry of Health Ankara City Hospital, Ankara, Türkiye

ABSTRACT

Aim: Our aim in this study was to investigate the difference of systemic immune inflammatory index (SII) and systemic inflammatory response index (SIRI) indices between pregnancy-related cerebral venous sinus thrombosis (CVST) patients and healthy pregnant and postpartum women and to evaluate the association between these indices and disease severity and prognosis in the CVST group.

Materials and Methods: This retrospective study included 21 patients with CVST and 80 healthy pregnant and postpartum patients as the control group. We looked at whether there was a statistical difference in demographic and clinical characteristics and laboratory results between the groups. Then we compared the SII and SIRI values, whose prognostic value has been studied as new inflammatory indices in many subjects.

Results: Neutrophil, monocyte, lymphocyte and platelet counts were similar between the groups. SII and SIRI were significantly higher in the CVST group (p:0.006, p:0.043; respectively). It was found that the SII and SIRI indices were higher in the group with severe disease and the poor prognosis, but the results were not statistically significant.

Conclusion: These results showed us that the SII and SIRI indices can be used as a supporting factor for the diagnosis in patients with suspected CVST. Studies with more patients may help to demonstrate the impact of SII and SIRI indices on disease severity and prognosis.

Keywords: Cerebral venous sinus thrombosis, pregnancy, systemic inflammatory response index, systemic immune inflammation index, thrombo-inflammatory markers

ÖZ

Amaç: Gebelikle ilişkili serebral venöz sinüs trombozu (SVST) hastaları ile sağlıklı gebe ve doğum sonrası kadınlar arasında sistemik immün inflamasyon indeksi (SII) ve sistemik inflamatuar yanıt indeksi (SIRI) arasındaki farkı araştırmak ve bu indeksler ile hastalık şiddeti ve prognoz arasındaki ilişkiyi değerlendirmektir.

Gereç ve Yöntemler: Bu retrospektif çalışmaya 21 SVST hastası ve kontrol grubu olarak 80 sağlıklı gebe ve postpartum hasta dahil edildi. Grupların demografik ve klinik özellikleri, laboratuvar sonuçları, SII ve SIRI indeksleri karşılaştırıldı. SVST grubunda SII ve SIRI indekslerinin hastalığın şiddeti ve prognozu ile ilişkisi araştırıldı.

Bulgular: Gruplar arasında nötrofil, monosit, lenfosit ve trombosit sayıları benzerdi. SII ve SIRI değerleri SVST grubunda daha yüksekti ve fark istatistiksel olarak anlamlı olarak anlamlıydı (sırasıyla; p:0,006, p:0,043). Şiddetli hastalık ve kötü prognozlu grupta SII ve SIRI indekslerinin daha yüksek olduğu görüldü ancak sonuçlar istatistiksel olarak anlamlı değildi.

Sonuç: SVST için klinik şüphe olan hastalarda tanıyı destekleyici bir faktör olarak SII ve SIRI değerleri kullanılabilir. Daha fazla hasta sayılı çalışmalar SII ve SIRI indekslerinin hastalık şiddeti ve prognozundaki etkisini göstermeye yardımcı olabilir.

Anahtar Kelimeler: Serebral venöz sinüs trombozu, gebelik, sistemik inflamatuar yanıt indeksi, sistemik immün inflamasyon indeksi, trombo-inflamatuar belirteçler

Cite as: Başaran E, Tanaçan A, Farisoğulları N, Ağaoğlu Z, Şerbetçi H, Kara Ö et al. The Utility of the Systemic Immune-Inflammation Index (SII) and the Systemic Immune-Response Index (SIRI) in predicting pregnancy-related cerebral venous sinus thrombosis: An experience from a tertiary center. Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi 2025;22(3):255–261.

Geliş/Received: 04.11.2024 • **Kabul/Accepted:** 11.12.2024

Sorumlu Yazar/Corresponding Author: Ezgi BAŞARAN, Department of Obstetrics and Gynecology, Division of Perinatology, Ministry of Health, Ankara Bilkent City Hospital, Ankara, Türkiye
E-mail: ezgi.basrn@gmail.com

Çevrimiçi Erişim/Available online at: https://dergipark.org.tr/tr/pub/jgon

INTRODUCTION

Cerebral venous sinus thrombosis (CVST) is a rare subtype of stroke that accounts for 0.5-1% of all strokes (1). In the general population, the incidence of CVST is on average three times higher in women than in men (2,3).This gender difference has been associated with sex-specific risk factors such as oral contraceptive use, pregnancy, puerperium, or hormone replacement therapy (4). In a prospective international study of crebral vein and dural sinus thrombosis (ISCVT), 20% of patients presented during pregnancy and the puerperium (5). CVST accounts for approximately 2% of pregnancy-related strokes and occurs in up to 0.01% of all pregnancies (6). Pregnancy-related CVST occurs more frequently in the third trimester or in the puerperium (7). Studies have been performed to determine various risk scores to predict the prognosis of patients with cerebral venous and dural sinus thrombosis (8,9).

It is well known that changes in cellular content in peripheral blood are indicative of the inflammatory response in various diseases (10,11). In addition, systemic inflammatory response index (SIRI) and systemic immune inflammation index (SII) have been studied as more complicated inflammatory markers in various diseases and cancers (12-15). Although the effects of inflammation on CVST have not been fully elucidated, conditions such as infections, coagulation factor deficiency, and systemic autoimmune diseases, which are risk factors for CVST, are associated with inflammatory responses (16). This suggests that inflammation plays a role in the etiopathogenesis of CVST (16). The role of inflammation has been confirmed by studies showing markedly elevated inflammatory markers in serum and cerebrospinal fluid (CSF) in CVST (17,18). The SII, based on peripheral lymphocyte, neutrophil, and platelet counts, and the SIRI, based on peripheral lymphocyte, neutrophil, and monocyte, are the new inflammatory indices that reflect in detail the patient's immune and inflammatory state. The role of inflammation in the prognosis of CVST has been proven in a small number of studies. The systemic immune inflammation index was first investigated in CVST patients in a 2020 study by Li et al (17). Although pregnancy and puerperium are known risk factors for CVST, publications on this group of patients are limited to small series (3). Our aim in this study was to investigate the difference of SII and SIRI indices between pregnancy-related CVST patients and healthy pregnant and postpartum women and to evaluate the association between these indices and disease severity and prognosis in the CVST group.

MATERIAL AND METHODS

Study population

We conducted this retrospective cohort study between September 2019 and June 2021 in the Maternal-Fetal Medicine Department of Ankara City Hospital. The study was approved by the Ethics Committee of Ankara City Hospital (Date: No.:E2-21-624). Study was carried out in accordance with the tenets of the Declaration of Helsinki. Written informed consent was obtained from all the participants.

A total of 21 patients with CVST and 80 healthy pregnant and postpartum patients at the same gestational week were included as the control group. Primarily, all patients who were diagnosed with CVST in our hospital between September 2019 and November 2022 or who were referred to our hospital with this diagnosis during prenatal care or the postpartum period were identified. The inclusion criteria were as follows: (1) presence of clinical signs such as headache, visual disturbances, seizures, focal neurological deficits, consciousness disorders, (2) presence of cerebral sinus filling defect on magnetic resonance venography (MRV), (3) acute and subacute patients (less than thirty days from the onset of symptoms). The exclusion criteria were as follows: (1) patients with insufficient clinical data and (2) chronic patients.

Demographic characteristics of the CVST group such as age, presence of known disease, smoking, family history, and disease-related outcomes such as time of onset of symptoms, gestational age or duration of postpartum, current symptoms, laboratory results at admission, presence of preeclampsia, autoimmune disease, or thrombophilia, and imaging findings (location of clot and cerebral infarction or hemorrhage) were extracted. Healthy pregnant and postpartum patients whose gestational age matched that of the CVST group were identified, and a control group was formed with four control subjects for each patient. Disability was graded according to the modified Rankin Scale (mRS, 0=complete recovery, 6=dead)(5).

In this study, we first performed a descriptive analysis of the CVST group, which consisted of 21 pregnant and postpartum patients we cared for in our hospital. Then, we looked at whether there was a statistical difference in demographic and clinical characteristics and laboratory results between the study and control group and we compared the SII (neutrophilXplatelet/lymphocyte) and SIRI (neutrophilXmonocyte/lymphocyte) values, whose prognostic value has been studied as new inflammatory indices in many subjects (control group, n:80). Furthermore, we analyzed these inflammatory markers within the CVST group and evaluated whether they had an impact on predicting the severity or prognosis of the disease.

Statistical Analysis

All statistical analyzes were performed using SPSS 26 (IBM Inc, Chicago, IL, USA). First, the Shapiro-Wilk test was used to determine

whether the data were normally distributed or not. Because the data were not normally distributed, median and interquartile range values were used to represent related variables, and the Mann-Whitney U test was performed to compare median values between groups. Categorical variables were presented as numbers and percentages. Next, a receiver operating characteristic curve analysis (ROC) was performed to determine the optimal cut-off values for SII and SIRI for predicting pregnancy-related CVST. Then, a ROC analysis was performed to determine the optimal cut-off values for SII and SIRI for predicting adverse outcomes in the study group. The Youden index was used to select appropriate cut-off values for SII and SIRI. P values <0.05 was assumed as statistically significant.

RESULTS

A total of 101 patients were included in this study (n:21 patients in the CVST group and n:80 cases in the control group). The baseline data of the study group are shown in Table 1. Of the 21 patients in the cohort, 18 (85.7%) were pregnant, 3 (14.3%) were postpartum, 3 (14.3%) were suffering in the first trimester, 5 (23.8%) in the second trimester, and 10 (47.6%) in the third trimester. All pregnant patients had a live birth, one of them at 23 weeks' gestation with an Apgar score of 2 at 5 minutes. 4 other patients had a preterm delivery due to preeclampsia and fetal indications.

The most common symptoms were headache (76%) and paresthesias (28.6%). Other less common signs and symptoms were seizures (14.3%), motor weakness (14.3%), dysarthria/aphasia (9.5%), mental status disorders (14.3%), and visual disturbances (4.8%). The diagnosis was confirmed by MR venography in patients who had symptoms and were suspected of having CVST. Thrombi were most commonly located in the transverse sinuses (76.2%) and superior sagittal sinuses (52.4%). Concomitant thrombophilia was found in 81% of patients. Two of the patients who developed CVST had rheumatologic disease and two others had active infection (Covid-19). Two of the patients who developed CVST in the postpartum period delivered after a diagnosis of preeclampsia. In addition, preeclampsia developed in the later weeks of pregnancy in two of the patients who were diagnosed with CVST in the second trimester.

Anticoagulant therapy was initiated in all patients. In addition to anticoagulant treatment, antiepileptic treatment was required in 5 patients, hypertonic solution in 4 patients, and steroid use in

Table 1. Baseline characteristics of pregnancy-related CVST patients

	n:21 (100%)		n:21 (100%)
Pregnant	18(85.7%)	**Clot Location**	
First trimester	3(14.3%)	**Süperior sagital sinus**	11(52.4%)
Second trimester	5(23.8%)	**Sigmoid sinus**	8(38.1%)
Third trimester	10(47.6%)	**Straight sinus**	2(9.5%)
Postpartum	3(14.3%)	**Transverse sinus**	16(76.2%)
Signs and symptoms		**One sinus**	9(42.9%)
Headaches	16(76.2%)	**Two sinus**	8(38.1%)
Paresthesias	6(28.6%)	**More than two**	4(19.0%)
Seizure	3(14.3%)	**Intracranial complications**	
Motor weakness	3(14.3%)	**Intracranial hemorrhage**	1(4.8%)
Visual disturbance	1(4.8%)	**Cerebral infarction**	6(28.6%)
Mental status disorder	3(14.3%)	**Treatment**	
Dysarthria/aphasia	2(9.5%)	**Anticoagulant**	21(100%)
Coma	1(4.8%)	**Antiepileptic**	5(23.8%)
Thrombophilia	17(81.0%)	**Hipertonic solution**	4(19.0%)
Preeclampsia	3(14.3%)	**Steroid**	2(9.5%)
Infection (Covid-19)	2(9.5%)		
mRS score on admission		**Outcome at 3 months**	
1-2	14(66.7%)	**Complete recovery (mRS 0-1)**	17(81.0%)
3-4	5(23.8%)	**Disability (mRS 2-5)**	3(14.3%)
5	2(9.5%)	**Hospital mortality (mRS 6).**	1(4.8%)

Data are given %. mRS, modified Rankin Scale.

Table 2. Comparison of demographic and clinical characteristics between the study and control groups

	Control (n = 80)		CVST (n = 21)		p-Value
	Median	Interquartile Range	Median	Interquartile Range	
Age, years	28	6	26	13	0.671
Gravity	2.0	1	2.0	2	0.277
Parity	0.0	1	1.0	2	0.219
Miscarriage	0.0	0	0.0	0	0.843
Birth weight (g)	3400	540	2780	1690	**<.0.001**
Apgar score at first minute	8.0	1	7	1	0.301
Apgar score at fifth minute	9.0	0	9	1	0.302
Hemoglobin (g/dL)	11.8	1.5	12.2	2.9	0.471
White blood cell (10^9/L)	9760	2490	10510	4930	0.688
Neutrophil (10^9/L)	7310	2590	8650	3125	0.098
Monocyte (10^9/L)	480	240	520	265	0.552
Lymphocyte (10^9/L)	1790	730	1860	710	0.525
Platelet (10^9/L)	249000	76000	271000	119000	0.100

p value < 0,05 was considered statistically significant. g, gram; dL, deciliter; L, liter.

Table 3. SII and SIRI for predicting CVST

	Cut-off	AUC	95%CI	p-Value	Sensitivity(%)	Specificity(%)
SII	1251.55	0.695	0.557-0.832	0.006	61.9	78.0
SIRI	2.109	0.644	0.504-0.784	0.043	66.7	63.7

AUC, Area under the curve; CI, confidence interval; SII, systemic immun inflammation index; SIRI, systemic immun inflammatory index

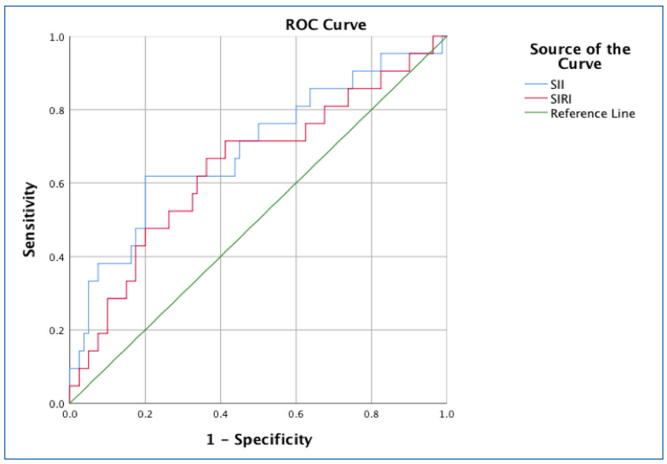

Figure 1. ROC curve of SII and SIRI for predicting the presence of CVST.
CVST, cerebral venous sinus thrombosis; ROC, receiver operating curve; SII, systemic immune inflammation index; SIRI, systemic immune response index.

2 patients. Four patients that presented coma or mental status disorder at the time of admission. Mortality was observed in 1 patient (4.8%), disability (mRS 2-5) was observed in 3 patients (14,3%) after treatment.

Comparison of demographic and clinical characteristics between the study and control groups were shown in Table 2. No statistically significant difference was found between the two group, except for birth weight. Neutrophil, monocyte, lymphocyte and platelet counts were similar between the groups.

After descriptive analysis of the CVST group, we evaluated the ability to discriminate between the patient and healthy groups of SII and SIRI values using the AUC on the ROC curve. SII and SIRI were significantly higher in the CVST group. The discriminatory power of SII based on the area under the ROC curve was 0.695 (95% confidence interval [CI]: 0.557-0.832, p< 0.05) for CVST, and at a cut-off value of 1251.55. The discriminatory power of the SIRI value using the area under the ROC curve was 0.644 (95% CI: 0.504 - 0.784, p< 0.05) for CVST, and using a cut-off value of 2.109. The sensitivity and specificity of predicting CVST using SII was 61.9% and 78.0%, wheras using SIRI was 66.7% and 63.7%, as shown in (Figure 1) (Table 3).

The ability of SII and SIRI scores to discriminate disease severity and prognosis within the CVST group was also assessed. Those who had an mRS score of 0-1 at diagnosis were classified as having mild disease, while those with a score of 2 or more were considered to have severe disease. It was found that the SII and SIRI indices were higher in the group with severe disease, but the results were not

Table 4. SII and SIRI for assessing disease severity in the CVST group

	Cut-off	AUC	95%CI	p-Value	Sensitivity(%)	Specificity(%)
SII	1174.04	0.731	0.511-0.951	0.082	76.9	62.5
SIRI	2.169	0.635	0.386-0.883	0.311	69.2	62.5

AUC, Area under the curve; CI, confidence interval; SII, systemic immun inflammation index; SIRI, systemic immun inflammatory index

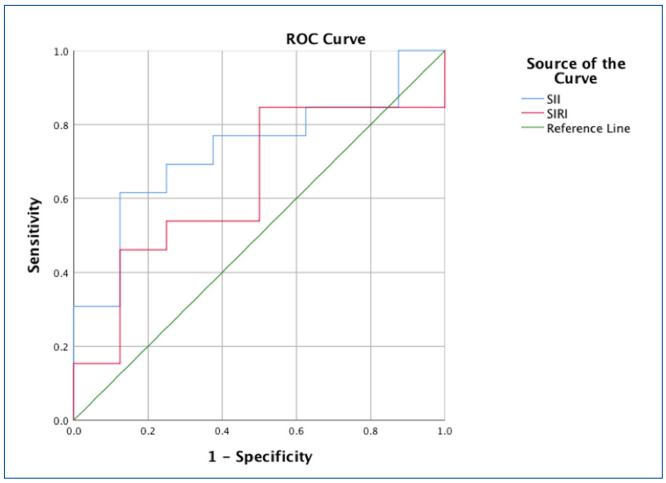

Figure 2. ROC curve of SII and SIRI in assessing disease severity in the CVST group.

CVST, cerebral venous sinus thrombosis; ROC, receiver operating curve; SII, systemic immune inflammation index; SIRI, systemic immune response index.

statistically significant. The discriminating power of the SII and SIRI based on the area under the ROC curve was 0.731 (95% confidence interval [CI]: 0.511 - 0.951, p>0.05) and 0.635 (95% CI: 0.386 - 0.883, p>0.05) for severe disease. When SII is used to estimate the severity of the disease, if the cut-off value is accepted as 1174.04, the sensitivity was 76.9% and the specificity was 62.5%, when we use SIRI and accepted cut-off value of 2.169, the sensitivity was 69.2% and the specificity was 62.5%, as shown in (Figure 2) (Table 4).

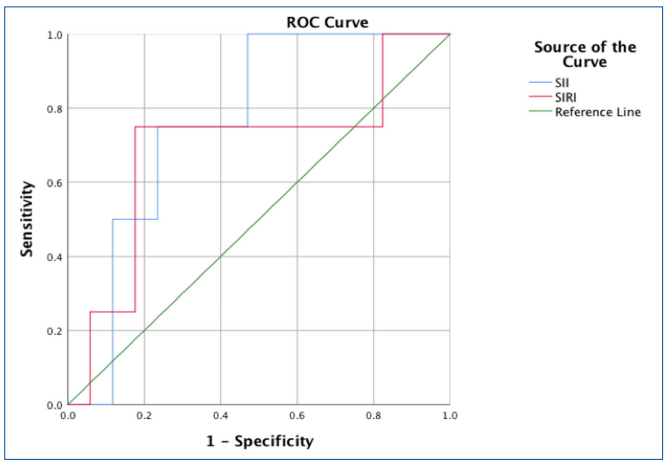

Figure 3. ROC curve of SII and SIRI in assessing prognosis in the CVST group.

CVST, cerebral venous sinus thrombosis; ROC, receiver operating curve; SII, systemic immune inflammation index; SIRI, systemic immune response index.

The mRS scores at the third month of treatment were used to assess prognosis. Those with an mRS score of 0-1 were classified as having a good prognosis, and those with an mRS score of 2 or more were classified as having a poor prognosis. It was found that the SII and SIRI indices were higher in the poor prognosis group, but the results were not statistically significant. The discriminatory power of the SII and SIRI using the area under the ROC curve was 0.765 (95% confidence interval [CI]: 0.548 - 0.981, p>0.05) and 0.691 (95% CI: 0.366 - 0.1000, p>0.05) for poor prognosis. When SII is used to estimate poor prognosis, if the cut-off value is accepted as 1577.07, the sensitivity was 75.0% and the specificity was 71.6%, when we use SIRI and accepted cut-off value of 2.684, the sensitivity was 75.0% and the specificity was 71.6%, as shown in (Figure 3) (Table 5).

DISCUSSION

CVST can be life-threatening, and morbidity and mortality increase significantly, especially when diagnosis and treatment are delayed. Prompt diagnosis and treatment is one of the most important factors that reduce morbidity and mortality and improve outcomes. Due to the difficulty in diagnosis and the importance of early diagnosis and treatment, cost-effective and easily accessible methods are becoming increasingly important.

In our study, we basically investigated whether there was a difference between SII and SIRI indices between pregnancy-related CVST patients and healthy pregnant and postpartum women. Our main finding was that SII and SIRI scores were significantly higher in the CVST group at the time of hospital admission. We also examined the effect of SII and SIRI indices in predicting the severity of the disease and prognosis in the group with CVST patients, and

Table 5. SII and SIRI for assessing prognosis in the CVST group

	Cut-off	AUC	95%CI	P value	Sensitivity(%)	Specificity(%)
SII	1577.07	0.765	0.548-0.981	0.107	75.0	71.6
SIRI	2.684	0.691	0.366-0.1000	0.244	75.0	71.6

AUC, Area under the curve; CI, confidence interval; SII, systemic immun inflammation index; SIRI, systemic immun inflammatory index

although the scores were higher in patients with severe and poor prognosis, we could not obtain a statistically significant result.

CVST is a rare form of stroke, and diagnosis can be challenging due to nonspecific findings (3). Although the etiopathogenesis of CVST is not fully understood, it is thought that the disease is multifactorial and thrombo-inflammatory processes play the most important role (18). In addition to draining blood, the cerebral sinuses are essential for CSF transport. Occlusion of the cerebral sinuses blocks CSF transport, resulting in intracranial hypertension. In the second mechanism, occlusion of a cortical vessel blocks blood flow from brain tissue, resulting in increased vasculer pressure and disruption of the blood-brain barrier (19). This process can lead to brain tissue damage. Headache is the most common symptom, but it does not occur in a minority of patients, while almost half of them experience seizures in the acute phase. Patients may present with various combinations of symptoms (20). Bentley et al. reported that most patients are misdiagnosed and that in 40% of patients admitted to the hospital, the diagnosis is delayed for days (21). Patients with pregnancy-related CVST are more likely to have a delayed or missed diagnosis than other CVST patients. Symptoms and signs of preeclampsia and eclampsia, as well as headache used are magnetic resonance imaging (MRI) with MR-venography, computed tomography (CT)-venography, and catheter angiography, but MRI with MR-venography being the most commonly preferred method (7). Moreover, MRI is not always positive for the diagnosis of CVST in the acute phase. For this reason, new parameters that facilitate diagnosis are gaining importance.

Inflammation, infection, hypercoagulability, and stasis are well-defined risk factors in the etiopathogenesis of CVST (22,23). Although the mechanism of CVST is still not fully understood, previous evidence suggests that it is a multifactorial disease in which thromboinflammatory processes play an important role (24).

Many thrombotic and inflammatory markers have been studied in assessing disease severity and predicting prognosis in patients (18). In a 2014 study, it was shown that high D-dimer levels can be an important biomarker for CVST, while the positive predictive value of an elevated D-dimer-fibrinogen combination is even higher (25). Neutrophil-to-lymphocyte ratio (NLR) has been identified as an important inflammatory marker in cerebral arterial ischemia, but its role in CVST is not clear. Although there are conflicting results in the literature, a 2022 review by Ding et al. found that NLR is significantly elevated in patients with CVST (26). In addition to the known inflammatory effect of neutrophils; it has also been shown in studies that it is a tissue factor that provokes thrombus formation (27). In another recent study, high NLR and platelet-to-lymphocyte ratio (PLR) levels were found to be associated with the presence of CVST (28). In previous studies, SII has been shown to be more reliable than other leukocyte-based indicators of inflammation, including PLR and lymphocyte-to-monocyte ratio (LMR) (28). SIRI has also received more attention after some studies showed that it is able to predict the progression of diseases such as cancer, cardiovascular disease, and ischemic stroke (29-31). Moreover, the association between high SIRI levels and mortality in stroke patients has been previously demonstrated (32). All these studies show us that biomarkers indicating thromboinflammatory state and their combinations occupy an important place in the diagnosis of CVST.

Our results show that SII and SIRI indices, which are easily accessible and can be combined with some thromboinflammatory parameters, can be used to predict pregnancy-related CVST. But, of course, these indices alone cannot be used to tell whether CVST is present or not. They can be used as a diagnostic aid in patients with clinical suspicion. The small number of CVST patients may be the reason why we could not obtain statistically significant results in terms of disease severity and prognosis, and this relationship can be demonstrated by studies with a larger number of patients.

Informed Consent: Written informed consent was obtained from all the participants.

Author Contributions: EB: Manuscript writing, Data collection, Literature search. AT: Project development, Reviewing, Editing, Data analysis. NF: Data collection, Literature search. ZA: Data collection, Data analysis, Literature search. HŞ: Patient selection, Data collection. ÖK: Data analysis, Literature search, Reviewing. NNÖ: Patient selection, Reviewing, Editing. DŞ: Project development, Visualization, Reviewing, Editing

Conflict of interest: The authors declare that they have no conflict of interest.

REFERENCES

1. Bousser MG, Ferro JM. Cerebral venous thrombosis: an update. Lancet Neurol. 2007;6(2):162-70.
2. Piazza G. Cerebral venous thrombosis. Circulation. 2012;125(13):1704–9.
3. Coutinho JM, Ferro JM, Canhao P, Barinagarrementeria F, Cantu C, Bousser MG, et al. Cerebral venous and sinus thrombosis in women. Stroke. 2009;40(7):2356–61.
4. Stam J. Thrombosis of the cerebral veins and sinuses. N Engl J Med. 2005;352(17):1791-98.
5. Ferro JM, Canhao P, Stam J, Bousser MG, Barinagarrementeria F. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). Stroke. 2004;35(3):664–70.
6. James AH, Bushnell CD, Jamison MG, Myers ER. Incidence and risk factors for stroke in pregnancy and the puerperium. Obstet Gynaecol. 2005;106(3):509–16.
7. Saposnik G, Barinagarrementeria F, Brown Jr 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(4):1158–92.
8. Ferro JM, Bacelar-Nicolau H, Rodrigues T, Bacelar-Nicolau L, Canhao P, Crassard I, et al. Risk score to predict the outcome of patients with cerebral vein and dural sinus thrombosis. Cerebrovasc Dis. 2009;28(1):39–44.
9. Barboza MA, Chiquete E, Arauz A, Merlos-Benitez M, Quiroz-Compean A, Barinagarrementeria F, et al. A practical score for prediction of outcome after cerebral venous thrombosis. Front Neurol. 2018;9:882.

10. Macrez R, Ali C, Toutirais O, Le Mauff B, Defer G, Dirnagl U, et al. Stroke and the immune system: from pathophysiology to new therapeutic strategies. Lancet Neurol. 2011;10(5):471-80.
11. Tao C, Wang J, Hu X, Ma J, Li H, You C. Clinical value of neutrophil to lymphocyte and platelet to lymphocyte ratio after aneurysmal subarachnoid hemorrhage. Neurocrit Care. 2017;26(3):393-401.
12. Wang BL, Tian L, Gao XH, Ma XL, Wu J, Zhang CY, et al. Dynamic change of the systemic immune inflammation index predicts the prognosis of patients with hepatocellular carcinoma after curative resection. Clin Chem Lab Med. 2016;54(12):1963–69.
13. Dolan RD, McSorley ST, Park JH, Watt DG, Roxburgh CS, Horgan PG, et al. The prognostic value of systemic inflammation in patients undergoing surgery for colon cancer: comparison of composite ratios and cumulative scores. Br J Cancer. 2018;119(1):40–51.
14. Huang H, Liu Q, Zhu L, Zhang Y, Lu X, Wu Y, et al. Prognostic Value of Preoperative Systemic Immune-Inflammation Index in Patients with Cervical Cancer. Sci Rep. 2019;9(1):3284.
15. Wei L, Xie H, Yan P. Prognostic value of the systemic inflammation response index in human malignancy: A meta-analysis. Medicine (Baltimore). 2020;99(50):e23486.
16. Silvis SM, de Sousa DA, Ferro JM, Coutinho JM. Cerebral Venous Thrombosis. Nat Rev Neurol. 2017;13(9):555–65.
17. Li S, Liu K, Gao Y, Zhao L, Zhang R, Fang H, et al. Prognostic value of systemic immune–inflammation index in acute/subacute patients with cerebral venous sinus thrombosis. Stroke Vasc Neurol. 2020;5(4):368-73
18. Wang L, Duan J, Bian T, Meng R, Wu L, Zhang Z, et al. Inflammation Is Correlated With Severity and Outcome of Cerebral Venous Thrombosis. J Neuroinflamm. 2018;15(1):329.
19. Ungersbock K, Heimann A, Kempski O. Cerebral blood flow alterations in a rat model of cerebral sinus thrombosis. Stroke. 1993;24:563-70.
20. Coutinho JM. Cerebral venous thrombosis. J Thromb Haemost. 2015;13(1):238–44.
21. Bentley JN, Figueroa RE, Vender JR. From presentation to follow-up: diagnosis and treatment of cerebral venous thrombosis. Neurosurg Focus. 2009;27(5):E4.
22. Siddiqi SA, Nishat S, Kanwar D, Ali F, Azeemuddin M, Wasay M. Cerebral venous sinus thrombosis: association with primary varicella zoster virus infection. J Stroke Cerebrovasc Dis. 2012;21(8):917.e1–917.e49174.
23. Goeijenbier M, van Wissen M, van de Weg C, Jong E, Gerdes VE, Meijers JC, et al. Review: viral infections and mechanisms of thrombosis and bleeding. J Med Virol. 2012;84:1680–96.
24. Ferro JM, Canhão P. Cerebral venous sinus thrombosis: update on diagnosis and management. Curr Cardiol Rep. 2014;16(9):523.
25. Meng R, Wang X, Hussain M, Dornbos D 3rd, Meng L, Liu Y, et al. Evaluation of plasma D-dimer plus fibrinogen in predicting acute CVST. Int J Stroke. 2014;9:166-73.
26. Ding J, Song B, Xie X, Li X, Chen Z, Wang Z, et al. Inflammation in Cerebral Venous Thrombosis. Front Immunol. 2022;13:833490.
27. Darbousset R, Thomas GM, Mezouar S, Frere C, Bonier R, Mackman N, et al. Tissue factor-positive neutrophils bind to injured endothelial wall and initiate thrombus formation. Blood. 2012;120:2133–43.
28. Akboga YE, Bektas H, Anlar O. Usefulness of platelet to lymphocyte and neutrophil to lymphocyte ratios in predicting the presence of cerebral venous sinus thrombosis and in-hospital major adverse cerebral events. J Neurol Sci. 2017;380:226–9.
29. Pacheco-Barcia V, Mondejar SR, France T, Asselah J, Donnay O, Zogopoulos G, et al. A systemic inflammation response index (SIRI) correlates with survival and predicts oncological outcome for mFOLFIRINOX therapy in metastatic pancreatic cancer. Pancreatology. 2020;20(2):254–64.
30. Ferrara D, Montecucco F, Dallegri F, Carbone F. Impact of different ectopic fat depots on cardiovascular and metabolic diseases. J Cell Physiol. 2019;234(12):21630–41.
31. Zhou Y, Zhang Y, Cui M, Zhang Y, Shang X. Prognostic value of the systemic inflammation response index in patients with acute ischemic stroke. Brain Behav. 2022;12(6):e2619.
32. Zhang Y, Xing Z, Zhou K, Jiang S. The Predictive Role of Systemic Inflammation Response Index (SIRI) in the Prognosis of Stroke Patients. Clin Interv Aging. 2021;16:1997-2007.