Van Med J 32 (4):316 -323, 2025
DOI: 10.5505/vmj.2025.18189

The Relationship Between Resolvin-D1 Level and Vasospasm in Cerebrospinal Fluid in Patients with Aneurysmal Subarachnoid Hemorrhage

Abdulmutalip Karaaslanlı[1], Luay Şerifoğlu[2], Ali Erhan Kayalar[2]

[1]*Van Yüzüncü Yıl University, Neurosurgery, Van, Türkiye*
[2]*Ümraniye Training and Research Hospital, Department of Neurosurgery, Istanbul, Türkiye*

Abstract

Aim: This study explores the role of Resolvin D1 (RvD1) in neuroinflammation and vasospasm following aneurysmal subarachnoid hemorrhage (SAH). The study aims to assess changes in RvD1 levels in cerebrospinal fluid (CSF) after SAH and their relationship with vasospasm, inflammatory markers, and clinical parameters, including Glasgow Coma Scale (GCS) scores.

Materials and Methods: Thirty-nine patients diagnosed with spontaneous aneurysmal hemorrhage between May 2021 and May 2023 were included in the study. This study was planned as a prospective study. RvD1 levels were measured in CSF on days 1 and 3 of bleeding and compared with clinical vasospasm, GCS and CRP values. The rationale for choosing Day 1 and Day 3 for cerebrospinal fluid (CSF) RvD1 measurements is based on the temporal dynamics of early neuroinflammatory response following aneurysmal subarachnoid hemorrhage (SAH). Monitoring these two critical time points provides insight into the early neuroinflammatory trajectory and potential predictive value of RvD1 in relation to vasospasm development.

Results: RvD1 levels were significantly higher on the first day in patients with clinical vasospasm. Similarly, elevated RvD1 levels were observed on subsequent days in patients with clinical vasospasm. Serum CRP levels were also significantly higher on the first days of bleeding in the vasospasm group.

Conclusion: The findings suggest that RvD1, known for its neuroprotective and anti-inflammatory effects, is elevated in patients with clinical vasospasm, highlighting the role of inflammation in vasospasm pathogenesis after SAH. RvD1 could be used as a potential biomarker for predicting clinical vasospasm.

Key words: Aneurysmal subarachnoid hemorrhage; resolvin D1; neuroinflamation; vasospasm; antioxidant.

Introduction

Subarachnoid hemorrhage (SAH) refers to bleeding that occurs in the subarachnoid space of the brain, originating from either arterial or venous vessels. It accounts for approximately 6-8% of all hemorrhagic stroke cases. Trauma is the leading cause of SAH, while spontaneous SAH is most commonly associated with aneurysmal rupture, which constitutes 75-80% of cases. The incidence of aneurysmal SAH is reported to be between 6 and 28 per 100,000 individuals annually. Unfortunately, 10% of patients succumb to the condition within the first few hours of bleeding, and 25% die within the first 24 hours. Within the first three months, the mortality rate reaches 50%, and among the survivors, half experience long-term deficits. Even with successful surgical interventions, many patients face significant challenges in their personal, social, and professional lives, often unable to regain their prior physical performance levels (1,2). SAH is diagnosed by Computed Tomography (CT) and Digital Angiography (DSA). (Image 1,2) The most common complication observed in the clinical follow-up of SAH is vasospasm. Patient follow-up was performed with clinical vasospasm. New onset or increasing severity of headache, changes in consciousness and disorientation are non-localized findings of clinical vasospasm. Focal neurological findings such as cranial nerve palsy and motor deficits may occur. In addition, symptoms may be collected in one of the following two syndromes. Vasospasm is a pathophysiological event with unknown pathology and associated with high mortality and morbidity, and is characterized by reversible narrowing of the vascular diameter at various degrees after arterial wall rupture following SAH. The neurogenic effect of the adrenergic nervous system causes

*Corresponding Author: Abdulmutalip Karaaslanlı , Van Yuzuncu Yil University, Faculty of Medicine, Neurosurgery, Van, Türkiye **Email:** a.karaaslanli2106@gmail.com **Orcid:** Abdulmutalip Karaaslanlı 0009-0005-1046-3484, Luay Şerifoğlu 0000-0003-0253-9950 Ali Erhan Kayalar 0000-0001-5717-5889
Received: 05.06.2025, Accepted: 24.07.2025

Content of this journal is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

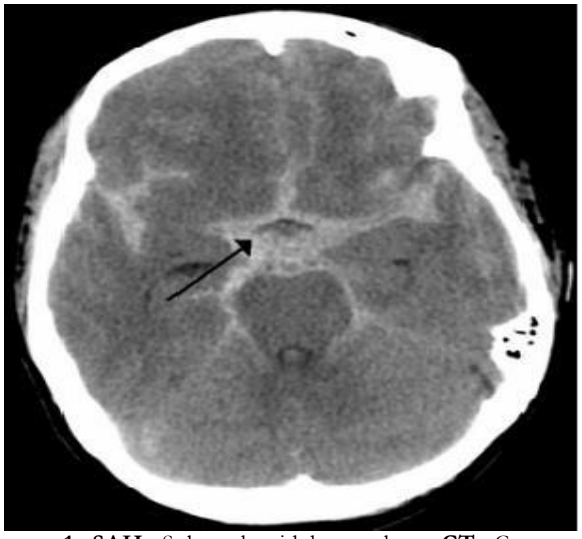

Image 1: SAH: Subarachnoid hemorrhage **CT:** Computed tomography

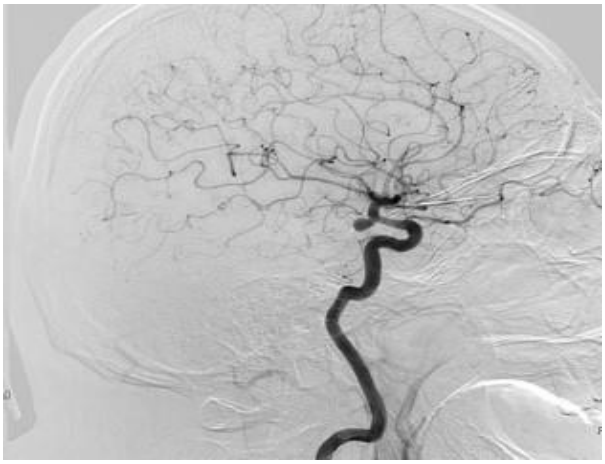

Image 2: Digital Subtraction Angiography (DSA)

chemical reactions in the arterial wall due to the increase in the rate of certain substances in the bloodstream and the resulting myogenic response (3). In the first phase of acute vasospasm, serotonin secreted from platelets causes vasoconstriction in circulating arteries even at low concentrations, creating a myogenic response in the vascular wall (4). In addition, increased sympathetic nervous activity due to factors such as stress and fear may contribute to increased myogenic response in the arterial wall and worsening vasospasm (3,5). The effect of serotonin decreases after approximately 24-36 hours. However, vasospasm occurs through spasmogenic proteins and hemoglobin degradation products released from erythrocytes and causes a decrease in cerebral perfusion. In recent years, a substance called endothelin-I in the hypothalamus stimulates blood elements, resulting in increased production of thrombin, oxyhemoglobin and platelets, followed by very strong vasoconstriction in cerebral vessels (3,4,5).

Neuroinflammation in SAH is a chemical process driven by various cellular and molecular factors. Elevated levels of proinflammatory cytokines, such as IL-1ß, IL-6, and TNF, along with adhesion molecules like P-selectin and S-selectin, are observed in the blood and cerebrospinal fluid. Additionally, activation of the complement system and accelerated erythrocyte lysis contribute to the inflammatory response. The release of spasmogenic substances, including ET-1, increases, while the production of free radicals leads to toxic effects on nerve cells. These processes can result in neuronal dysfunction, apoptosis, and a heightened inflammatory response. This cascade is associated with hyperthermia, vascular spasm, early brain injury, and unfavorable neurological outcomes (6,7). Essential polyunsaturated fatty acids (PUFAs) are required for cell membranes and intracellular structures and are not synthesized in mammalian cells, so they must be obtained from the diet. They are divided into two important groups: Omega-3 and Omega-6 PUFAs. Long-chain polyunsaturated fatty acids DHA (docosahexaenoic acid) and its metabolites are necessary for the development of the nervous system and are produced from omega-3 PUFA. DHA inhibits the production of important inflammatory cytokines such as TNF, IL-1 and IL-6, promotes synaptogenesis and neurogenesis, stimulates gene expression and neuronal activity, and has a neuroprotective effect (2,8). Resolvin D1(RvD1) is a derivative of the omega-3 fatty acid DHA and is a powerful anti-inflammatory product effective in resolving inflammation. RvD1, through its receptors on macrophages, stimulates phagocytosis, increases clearance, reduces expression of membrane surface proteins, limits neutrophil infiltration, and stimulates the M2 phenotype of monocytes/macrophages and microglial cells. With these properties, it may be beneficial on neuroinflammation and vasospasm, especially in patients with aneurysmal SAH. Therefore, the primary aim of this study is to examine the change in RvD1 levels in the cerebrospinal fluid(CSF) of aneurysmal SAH patients over days and to reveal its relationship with vasospasm. It is also planned to examine the change in RvD1 levels and its relationship with C-reactive protein (CRP), a marker of inflammation (9,10)

Materials and Methods

This study included patients diagnosed with aneurysmal SAH who were hospitalized in the Ümraniye Education and Research Hospital,

Neurosurgery Clinic between 2022 and 2023. All participants and/or their first-degree relatives were informed about the study, and written informed consent was obtained before inclusion. Ethics committee approval was obtained for the study on April 25, 2022, with protocol number 9869.

Inclusion criteria:

1. Patients with a confirmed diagnosis of aneurysmal SAH based on imaging techniques.
2. Individuals who provided written consent after being informed about the study.

Exclusion criteria:

1. Patients with a history of alcohol or substance use disorder.
2. Presence of chronic inflammatory diseases or a history of active cancer (e.g. chronic lung disease, kidney disease, chronic hepatitis, thyroid disease, rheumatoid arthritis).
3. Diagnoses of mental retardation, dementia, or psychiatric disorders secondary to a general medical condition.
4. Presence of ongoing infections or allergies.
5. Traumatic subarachnoid hemorrhage.

A total of 39 patients (20 female and 19 male) who met the inclusion and exclusion criteria were enrolled in the study. Detailed anamneses were obtained for all participants, neurological examinations were conducted, and brain computed tomography (CT) scans followed by cerebral angiography were performed to confirm the diagnosis. At the time of admission, patients were classified using the Fisher, Hunt-Hess, and World Federation of Neurosurgical Societies (WFNS) grading systems. During clinical follow-up, patients were divided into two groups randomly based on the presence or absence of clinical vasospasm, which was determined by a decrease in Glasgow Coma Scale (GCS) scores. Of the total participants, 21 patients were identified as having clinical vasospasm, while 18 patients did not exhibit vasospasm. Cerebrospinal fluid (CSF) samples were collected from the patients on the 1st and 3rd days following the onset of bleeding. A total of 5 cc of CSF was drawn into 10 cc sterile yellow-capped CSF tubes. The samples were then transported to the Science Laboratory under +4°C conditions and stored in a deep freezer at -80°C. Resolvin D1 (RvD1) levels were analyzed from these samples using the Human Resolvin D1 ELISA Kit (Human RvD1 ELISA kit, SUNRED, 201-12-9313). The CSF samples were processed in accordance with the colorimetric measurement principle for the RvD1 parameter, following the manufacturer's instructions. Additionally, laboratory test results of the patients after discharge were reviewed retrospectively. Statistical analyses were performed based on the data obtained from the study.

Statistical analysis: For continuous variables, the mean and standard deviation were reported if the data followed a distribution close to normal, while the median and quartiles were presented for data that did not. Categorical variables were expressed as numbers and percentages. The Shapiro-Wilk test was applied to assess whether continuous variables were distributed close to normal. Wilcoxon and Friedman test were employed to evaluate differences over time. The relationship between two continuous variables was assessed using the Pearson correlation test for normally distributed variables and the Spearman correlation test for non-normally distributed variables. The association between vasospasm and resolvin D1 levels was presented as odds ratios with 95% confidence intervals. A p-value of <0.05 was considered statistically significant. Statistical analyses were performed using R software version 4.2.2.

Results

A total of 39 patients were included in the study. Postoperatively, these patients who had spontaneous aneurysmal subarachnoid hemorrhage were followed up by the intensive care and neurosurgery clinics of our hospital. The average age of the patients was recorded as 52.6 and consisted of a total of 39 patients, 19 men and 20 women. The youngest SAH patient was 24 years old and the oldest SAH patient was 83 years old. During the 10-day clinical follow-up of the patients, blood samples were taken regularly and sent to the laboratory. In this study, 39 patients with spontaneous aneurysmal subarachnoid hemorrhage were followed up and their functional status was evaluated according to the Modified Rankin Scale. While the average CRP level of the patients was 17.5, the average GCS was recorded as 13.2 in the 10-day clinical follow-up. During clinical follow-up, vasospasm was detected in 21 patients, and 16 patients had to be reintubated due to GCS regression due to vasospasm. Additionally, 9 patients died during the follow-up period. Of the 39 patients who underwent surgery, 23 were discharged after receiving a score of 0 or 1 on the Modified Rankin Scale. The remaining patients received different levels

Table 1: Demographic and first predictive values of the specifications

Variables	Summary of statistical values
Age, year	Mean and SD 52.6±13.0
	Median and quarters 52 (44.5 – 61)
	Minimum and maximum 24 – 83
Gender, % and n	Man 48.7% (19), Woman 51.3%
CRP	Mean and SD 17.5±31.4
	Median and quarters 5.81 (3.24 – 15.2)
	Minimum and maximum 0.3 – 182
GCS	Mean and SD 13.2±3.57
	Median and quarters 15 (14 – 15)
	Minimum and maximum 3 – 15
Vasospasm % and (n)	53.8 (21)
Death % and (n)	23.1 (9)
Intubation % and (n)	41 (16)
Sedation % and (n)	7.7 (3)
Modified rankin grade % and (n)	Grade 0; 51.3 (20)
	Grade 1; 7.7 (3)
	Grade 2; 7.7 (3)
	Grade 3; 2.6 (1)
	Grade 4; 2.6 (1)
	Grade 5; 5.1 (2)
	Grade 6; 23.1 (9)

GCS: Glasgow Coma Scale, **CRP:** C-reactive protein

Table 2: Resolvin D1 values of first and third day, SD: Standard deviation.

Variables	Statistic summary
Resolvin D1, 1st day	Mean and SD 1214 ng/L ± 970 ng/L
	Median and quarters 966 ng/L (886 ng/L – 1070 ng/L)
	Minimum and maximum 487 ng/L – 5086 ng/L
Resolvin D1, 3rd day	Mean and SD 1071 ng/L ±511 ng/L
	Median and quarters 961 ng/L (914 ng/L – 1042 ng/L)
	Minimum and maximum 725 ng/L - 3771 ng/L

of care (Table-1). RvD1 levels were measured in the CSF of the patients included in the study population on the first day of hospitalization. The average of RvD1 levels measured on the first day was recorded as 1214±970 ng/L, and on the third day this value was measured as 1071±511 ng/L. As a result of the analysis performed with the Shapiro-Wilks test, it was determined that the RvD1 levels measured on both the first day and the third day were not statistically normally distributed. The median and quarter values of RvD1 levels measured on the first day and third day were 966 (886-1070) ng/L and 961 (914-1042) ng/L, respectively(Table-2). The difference between RvD1 levels on the first day and the third day was tested with the Wilcoxon signed rank test, but it was observed that there was no significant difference between the two measurements (W = 267, p value 0.963). CRP levels of the patients in the study were measured every day from the first day to the tenth day, and the average and median values according to the days are calculated. According to the Shapiro-Wilk test results, all CRP levels were not distributed normally and the p value was found to be <0.05. Friedman analysis revealed a significant difference in CRP levels according to days (X^2=47.8, p<0.001). Accordingly, CRP levels increased from the first day to the fourth day, reached the peak level on the fourth day, and then gradually decreased until the tenth day (Figure-1).

Figure 1: Mean CRP values of ten days, CRP: C-reactive protein

GCS levels of the patients in the study were measured every day from the first day to the tenth day, and their average values according to the days are shown. According to the Shapiro-Wilk test results, all GCS levels were not distributed normally and the p value was not <0.05. Friedman analysis showed that there was no significant difference in GCS levels according to days (X^2 = 11.7, p = 0.233). When the patient population was followed, death occurred in 9 patients (23.1%). No difference was determined between the age, gender, CRP levels at hospital admission, first and 3rd day RvD1 levels and basal GCS scores of the deceased and surviving patients. Additionally, no significant relationship was detected between death and vasospasm. According to Spearman correlation analysis, no significant relationship could be detected between RvD1, age and basal CRP levels and modified Rankin scores on the 1st and 3rd days. However, a significant negative relationship was detected between the baseline GCS score and modified Rankin scores. When the patient population was followed, vasospasm was observed in 21 patients (53.8%). No significant difference was determined between the age, gender, CRP levels at hospital admission and follow-up, and RvD1 levels on the 1st and 3rd days of the patients who did and did not develop vasospasm. However, the baseline GCS score was found to be statistically significantly higher in patients who did not develop vasospasm. In the study, a generalized mixed linear model was applied to show the possibility of vasospasm using repeated measurements of RvD1 levels. In this model, the response variable was determined as the presence/absence of vasospasm, and RvD1 levels and day (day 1, day 3) were taken as independent variables. Random intercept and slope values were estimated for RvD1 levels. As a result, a negative relationship was found between RvD1 levels and the risk of vasospasm, and this relationship was found to be statistically significant (odds ratio 0.95, 95% confidence interval 0.92-0.99, p=0.016) (Figure-2). According to the results of the Spearman correlation analysis performed in the study, different levels of relationship were determined between RvD1 levels and basal variables. Accordingly, no significant relationship was detected between day RvD1 level and age, basal CRP and basal GCS. No significant relationship was observed between day 3 RvD1 level and basal CRP and basal GCS, but a borderline positive relationship was detected between age and day 3 RvD1 levels.

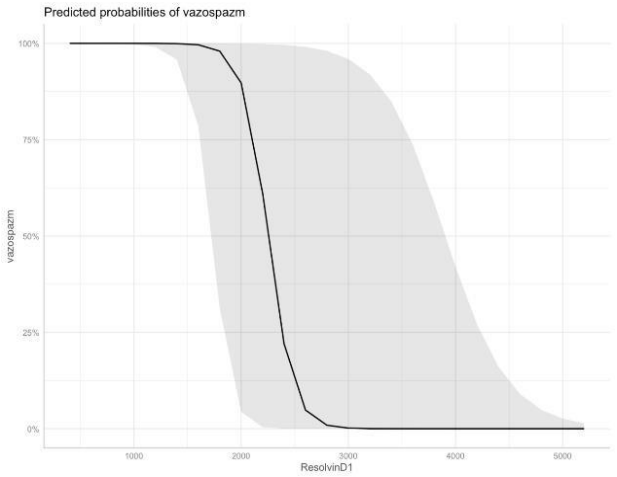

Figure 2: Correlation of vasospasm and Resolvin D1

Discussion

Neuroinflammation plays a critical role in the pathogenesis of SAH. Recent research has highlighted the presence of an inflammatory response characterized by elevated cytokine levels following SAH, demonstrating its impact on early brain injury, vasospasm, and delayed brain damage. The inflammatory response involves various cellular and molecular components, including the activation of glial cells and the release of cytokines (11). Studies have explored the connection between inflammatory pathways and poor neurological outcomes after SAH (12). Within hours of SAH onset, pro-inflammatory cytokines such as IL-1ß, IL-6, and TNF, along with adhesion molecules like P-selectin and S-selectin, can reach high concentrations in the serum and cerebrospinal fluid (CSF), reflecting the severity of the inflammatory response (13,14,15). Additionally, the complement system is activated, erythrocyte lysis accelerates, and the release of spasmogenic substances such as ET-1 increases, further emphasizing the intensity of inflammation (16,17). The activation of inflammatory cells, particularly microglia and astrocytes, leads to an upregulation of cell adhesion molecules, facilitating the infiltration of macrophages and neutrophils from the circulation into the subarachnoid space. Chronic or excessive production of pro-inflammatory molecules exerts toxic effects on neurons, disrupting neurotransmitter mechanisms and the neuroendocrine system, impairing synaptic plasticity, and ultimately causing neuronal dysfunction and apoptosis (11,12,17). A study by Kendirlioğlu et al. (2018) investigated the progression of serum RvD1 levels in patients with aneurysmal SAH over time and its potential relationship with vasospasm and inflammatory

markers such as CRP, neutrophils, and albumin [18]. The study observed a progressive increase in serum CRP levels from Day 1 to Day 4, followed by a gradual decline from Day 4 to Days 9 and 14. Serum albumin levels, measured on Day 1, were significantly lower in the patient group compared to the control group and showed a further decline over time. The elevation of RvD1 levels detected on Day 1 in patients with radiological vasospasm suggests that RvD1 may serve as an indicator of vasospasm and, consequently, a marker of disease severity. Liu et al. demonstrated that RvD1 exhibits potent anti-inflammatory properties by interacting with the lipoxin A4 receptor/formyl peptide receptor 2 (ALX/FPR2) in various diseases (19). However, its role in the central nervous system (CNS) remains poorly understood. Their study aimed to investigate the potential functions of the RvD1-ALX/FPR2 interaction in the brain following SAH. The findings suggested that this interaction may have dual roles in the CNS, as inhibiting hemoglobin (Hb) promoted microglial pro-inflammatory polarization, while ameliorating Hb reduced neuronal oxidative damage and cell death. These results highlight ALX/FPR2 as a promising therapeutic target and RvD1 as a potential treatment for SAH and other inflammation-related brain disorders. Wei et al. concluded that RvD1 reduced inflammation-mediated blood-brain barrier disruption and improved neurological outcomes in a rat model of SAH [20]. This protective effect was partially mediated through the FPR2/A20 pathway and the inhibition of NLRP3 inflammasome activation. These findings suggest that RvD1 could serve as a novel therapeutic agent, with FPR2 as a potential pharmacological target for SAH treatment. Liu Guang Jie et al. emphasized that excessive inflammation is a key contributor to early brain injury (EBI) and is associated with poor outcomes following SAH (21). Their results indicated that RvD1 exerts significant anti-inflammatory effects and alleviates EBI, suggesting its potential as a therapeutic option for SAH-induced injury. Yu et al. found that serum RvD1 levels were significantly lower in patients with aneurysmal SAH (aSAH) and were strongly correlated with the severity of the condition. Furthermore, RvD1 levels were associated with extended Glasgow Outcome Scale (GOSE) scores and poor prognosis six months after aSAH (22). These findings support the idea that serum RvD1 could serve as a valuable prognostic biomarker for risk stratification and outcome prediction in aSAH patients.

Study limitations: This study was conducted with a relatively small patient population from a single center, which may limit the generalizability of the findings. In addition, the absence of radiological vasospasm evaluation and long-term follow-up data restricts the ability to fully determine the prognostic value of RvD1 levels.

Conclusion

When patients with a decrease in GCS scores were compared to those without, it was observed that patients with clinical vasospasm exhibited both a reduction in GCS and an increase in CRP levels. Additionally, RvD1 levels were found to be elevated on the 1st and 3rd days following the onset of bleeding in these patients. These findings suggest that inflammatory mechanisms play a significant role in the etiopathogenesis of clinical vasospasm in individuals with aneurysmal SAH. Furthermore, it is proposed that RvD1 could serve as a potential biomarker for predicting the risk of clinical vasospasm in this patient population. Based on these observations, further research is needed to explore the role of RvD1, alongside inflammatory cytokines, in the development of neuroinflammation and clinical vasospasm following aSAH through larger, population-based studies. Specifically, when comparing the group with radiological vasospasm to the group without vasospasm, and considering that vasospasm is thought to begin around day 3, the elevated RvD1 levels observed on day 1 in the vasospasm group may serve as an important early indicator of the potential development of vasospasm.

Ethical considerations:

- **Human subjects:** Informed consent was obtained or waived for all participants in this study. Ethics committee approval was obtained for the study from Ümraniye Training and Research Hospital with the date 25/04/2022 and protocol number 9869.
- **Animal subjects:** This study did not involve animal subjects or tissue, as confirmed by all authors.

Conflicts of interest:

- **Payment/services information:** The authors declare that no financial support was received from any organization for the submitted work.
- **Financial relationships:** The authors report no financial relationships with any organizations that could have an interest in the submitted work, either at present or within the past three years.

- **Other relationships:** The authors confirm that there are no other relationships or activities that could have influenced the submitted work.

References

1. Kocaeli H, Kofralı E. SAK: Anevrizmalar. Nörobilimde Bugün 2003;1:1-6.
2. Chou SH, Feske SK, Atherton J, Konigsberg RG, DeSantis SM, Mariani CL, et al. Early elevation of serum tumor necrosis factor-α is associated with poor outcome in subarachnoid hemorrhage. J Investig Med 2012; 60(7): 1054-1058.
3. Clozel M, Watanebe H. BQ-123, a peptidic endothelin -a receptor antagonist, prevents the early cerebral vasospazm following subarachnoid hemorrhage after intracisternal but not intravenous injection. Life Sciences 1993;52:825-834.
4. Hurst RW, Schnee C, Raps EC, Farber R, Flamm ES: Role of transcranial doppler in neuroradiological treatment of intracranial vasospasm Stroke 1993;24:299-303.
5. Peerles SJ. Pre-postoperative managment of cerebral aneurysms. Clin Neurosurg 1979; 11:407-412.
6. Greenhalgh AD, Brough D, Robinson EM, Girard S, Rothwell NJ, Allan SM: Interleukin-1 receptor antagonist is beneficial after subarachnoid haemorrhage in rat by blocking haemdriven inflammatory pathology. Dis Model Mech 2012;5:823-833.
7. Macdonald RL. Delayed neurological deterioration after subarachnoid haemorrhage. Nat Rev Neurol 2014;10:44-58.
8. Pluta RM, Hansen-Schwartz J, Dreier J, Vajkoczy P, Macdonald RL, Nishizawa S. Cerebral vasospasm following subarachnoid hemorrhage: Time for a new world of thought. Neurol Res 2009; 31:151-158.
9. Colby GP, Coon AL, Tamargo RJ. Surgical management of aneurysmal subarachnoid hemorrhage. Neurosurg Clin N Am 2010; 21:247-261
10. Wolpert SM, Serbinenko FA: Balloon catheterization and occlusion of major cerebral vessels. AJNR Am J Neuroradiol 2000;21:1359-1360.
11. Jung CS, Iuliano BA, Harvey-White J, Espey MG, Oldfield EH, Pluta RM. Association between cerebrospinal fluid levels of asymmetric dimethyl-L-arginine, an endogenous inhibitor of endothelial nitric oxide synthase, and cerebral vasospasm in a primate model of subarachnoid hemorrhage. J Neurosurg 2004;101:836-842.
12. Suzuki Y, Osuka K, Noda A, Tanazawa T: Takayasu M, Shibuya M, Yoshida J. Nitric oxide metabolites in the cisternal cerebral spinal fluid of patients with subarachnoid hemorrhage. Neurosurgery 1997;41:807-811.
13. Provencio JJ, Vora N: Subarachnoid hemorrhage and inflammation: bench to bedside and back. Semin Neurol 2005; 25:435-444.
14. Hendryk S, Jarzab B, Josko J: Increase of the IL 1 beta and IL 6 levels in CSF in patients with vasospasm following aneurysmal SAH. Neuro Endocrinol Lett 2004;25:141-147.
15. Dumont AS, Dumont RJ, Chow MM, Kassell NF, Lee KS, Zuccarello M, et al. Cerebral vasospasm after subarachnoid hemorrhage: putative role of inflammation. Neurosurgery 2003; 53(1): 123-133.
16. Rollins S, Perkins E, Mandybur G, Zhang JH: Oxyhemoglobin produces necrosis, not apoptosis, in astrocytes. Brain Res 2002; 945:41-49.
17. Hong S, Lu Y, Yang R, Gotlinger KH, Petasis NA, Serhan CN. Resolvin D1, protectin D1, and related docosahexaenoic acid derived products: Analysis via electrospray/low energy tandem mass spectrometry based on spectra and fragmentation mechanisms. J Am Soc Mass Spectrom 2007;18:128-144.
18. Kendirlioglu, BC, Aydogmus E, Hicdonmez T: Comparison of Resolvin D1 Levels in Patients with Aneurysmal Subarachnoid Haemorrhage with Those in Healthy Controls. South Clin Ist Euras 2021; 32:273-279.
19. Liu GJ, Tao T, Wang H, Zhang XS, Chen XQ, Zhou ML. Functions of resolvin D1-ALX/FPR2 receptor interaction in the hemoglobin-induced microglial inflammatory response and neuronal injury. J Neuroinflammation 2020; 14(1): 239.
20. Wei C, Guo S, Liu W, Zhang Y, Wang J, Li H, et al. Resolvin D1 ameliorates inflammation-mediated blood-brain barrier disruption after subarachnoid hemorrhage in rats by modulating A20 and NLRP3 inflammasome. Front Pharmacol 2021; 3(1): 610-734.

21. Liu GJ, Tao T, Zhang XS, Zhou ML, Chen XQ, Wang J, et al. Resolvin D1 attenuates innate immune reactions in experimental subarachnoid hemorrhage rat model. Mol Neurobiol 2021; 58(4): 1963-1977.

22. Yu D, Jiang F, Xu W, Zhang Y, Wang J, Li H, et al. Declined serum Resolvin D1 levels to predict severity and prognosis of human aneurysmal subarachnoid hemorrhage: A prospective cohort study. Neuropsychiatr Dis Treat 2023; 27(1): 1463-1476