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ORIGINAL ARTICLE **ÖZGÜN ARAŞTIRMA**

MORTALITY SCORES AND VOLUME OF HEMATOMA IN THE EARLY PERIOD OF ACUTE THALAMIC HEMORRHAGE STROKE COULD PREDICT POOR PROGNOSIS

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ABSTRACT

INTRODUCTION: Thalamic hemorrhages constitute 8.3-15 percent of all intracranial hemorrhages. Despite increasing intensive care facilities mortality rates are still high in thalamic hemorrhages. In this study, it was evaluated whether mortality scores, inflammatory parameters and hematoma volume predict poor prognosis in patients hospitalized in the stroke intensive care unit with the diagnosis of acute thalamic hemorrhage.
METHODS: Thirty-two thalamic hemorrhage cases out of 130 cases admitted to our center with the diagnosis of intracranial hemorrhage between January 2017 and April 2020 were included in the study. Admission Acute Physiology and Chronic Health Evaluation II (APACHE II), Simplified Acute Physiology Score II (SAPS II), Sequential Organ Failure Assessment Score (SOFA), total hemorrhage volume and inflammatory parameters were evaluated.
RESULTS: Of the 32 patients, 21 (62%, female: 8) were survivors, and 11 (34%, female: 6) were non-survivors. The mean age of the survivors was 71.38±11.09, and non-survivors was 68.73±10.14. The hemorrhage volume was 16.53±9.63 ml in the non-survivors and 7.01±8.74 ml in the survivors and it was statistically significant. Admission APACHE II, SAPS II, SOFA scores were significantly high in the non-survivors.
DISCUSSION AND CONCLUSION: In this study, it was determined that GCS, APACHE II, SAPS II, SOFA scores and hemorrhage volume could predict poor prognosis in patients followed up with acute thalamic hemorrhage.
Keywords: APACHE II, SAPS II, SOFA, thalamic hemorrhage.

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AKUT TALAMİK HEMORAJİK İNMENİN ERKEN DÖNEMİNDEKİ MORTALİTE SKORLARI VE HEMATOM HACMİ KÖTÜ PROGNOZU ÖNGÖREBİLİR

ÖZ

GİRİŞ ve AMAÇ: Talamik kanamalar tüm kafa içi kanamaların %8,3-15'ini oluşturur. Artan yoğun bakım ünitelerine rağmen talamik kanamalarda ölüm oranları hala yüksektir. Bu çalışmada akut talamik kanama tanısı ile inme yoğun bakım ünitesine yatırılan hastalarda mortalite skorları, inflamatuar parametreler ve hematom hacminin kötü prognozu öngörüp öngörmediği değerlendirildi.

YÖNTEM ve GEREÇLER: Ocak 2017-Nisan 2020 tarihleri arasında merkezimize kafa içi kanama tanısı ile başvuran 130 olgudan 32 talamik kanama olgusu çalışmaya dahil edildi. Başvurudaki Acute Physiology and Chronic Health Evaluation II (APACHE II), Simplified Acute Physiology Score II (SAPS II), Sequential Organ Failure Assessment Score (SOFA), toplam kanama hacmi ve inflamatuar parametreler değerlendirildi

BULGULAR: 32 hastanın 21'i (%62, kadın: 8) sağ kalan ve 11'i (%34, kadın: 6) vefat edendi. Sağ kalanların yaş ortalaması 71.38±11.09, vefat edenlerin yaş ortalaması 68.73±10.14 idi. Vefat edenlerde kanama hacmi 16.53±9.63 ml, sağ kalanlarda 7.01±8.74 ml idi ve istatistiksel olarak anlamlıydı. Başvuru APACHE II, SAPS II, SOFA puanları vefat edelerde anlamlı olarak yüksekti.

TARTIŞMA ve SONUÇ: Bu çalışmada akut talamik kanama ile takip edilen hastalarda GCS, APACHE II, SAPS II, SOFA skorları ve kanama hacminin kötü prognozu öngörebileceği belirlendi.

Anahtar Sözcükler: APACHE II, SAPS II, SOFA, talamik hemoraji.

INTRODUCTION

The thalamus modulates connections from the cortex, basal ganglia, brain stem, cerebellum and spinal cord, in their nuclei and transmits them to the cortex. In thalamic hemorrhages, symptoms such as paresis, hypoesthesia, aphasia, gaze paresis, amnesia and impaired consciousness occur depending on the affected area (1,2). Mortality varies between 14-52% and constitute 8.3-15% of all intracranial hemorrhages (2,3). Several studies have shown that Glasgow Coma Score (GCS), hemorrhage diameter, hemorrhage volume, location of hemorrhage, presence of intraventricular hemorrhage, and development of hydrocephalus secondary to hemorrhage affect prognosis (1,3,4). Despite increasing neurology intensive care examination and treatment opportunities, mortality rates are still high (4). Determining simple and practical evaluation criteria in the early period of thalamic hemorrhages can predict the prognosis. This may enable new approaches in the follow-up and treatment periods of the disease and reduce high mortality rates, thus providing a good prognosis.

In this study, it was evaluated whether mortality scores, inflammatory parameters and hematoma volume predict poor prognosis in patients hospitalized in the stroke intensive care unit with the diagnosis of acute thalamic hemorrhage.

METHODS

In order to perform the study, ethical approval was obtained from Necmettin Erbakan University Ethical Committee (Number: 2021/3276, Date: 4 Jun 2021). The study was conducted in accordance with the ethical standards of the Declaration of Helsinki. Patients who applied to our center with the diagnosis of intracranial hemorrhage and were followed up in the stroke intensive care unit between January 2017 and April 2020 were screened retrospectively. Thirty-two thalamic hemorrhage cases out of a total of 130 cases were included in the study. Demographic information, comorbidities, medication, admission laboratory parameters, admission CT images and admission GCS (5), mRS (6), Acute Physiology and Chronic Health Evaluation II (APACHE II) (7), Simplified Acute Physiology Score II (SAPS II) (8), and Sequential Organ Failure Assessment Score (SOFA) (9) was obtained via the hospital information operating system. Cranial CT images obtained at the entrance to the hospital were used to measure the hemorrhage volume of the cases. Total hemorrhage volume was measured using a computer program (syngo.via, SIEMENS).

Statistical Analysis: For statistical analysis, mean, median, quartile and standard deviation (SD) were used in the descriptive statistics of the data with the SPSS 25.0 (Statistical Package for the Social

Sciences) program. Kurtosis, skewness values and Kolmogorov-Smirnov test were used for the normality distribution of the variables. Student's t test was used for normally distributed independent variables and Man Whitney-U test was used for non-normally distributed independent variables. Chi-square analyzes were performed for categorical data. ROC analysis was used to calculate the optimal threshold value of the obtained data. The confidence interval was accepted as 95%. In the comparison of the groups, values below 0.05 were considered significant.

RESULTS

32 cases with acute thalamic hemorrhage were included in the study. Of the 32 patients, 21 (65.62%, female= 8) were survivors, and 11 (34.37%, female= 6) were non-survivors. The mean age of the survivors was 71.38±11.09, and the mean age of the non-survivors was 68.73±10.14. There were no statistically significant difference between survivors and non-survivors patients in terms of demographic characteristics, comorbidities, medication and laboratory values. Neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) values were not significantly different between the two groups. The hemorrhage volume was 16.53±9.63 ml in the non-survivors and 7.01±8.74 ml in the survivors, and it was statistically significant. Admission APACHE II, SAPS II, SOFA, GCS scores were significantly high in the non-survivors. (Table).

While the value under the ROC curve showing the relationship between the hemorrhage volume and mortality was 0.823 and the cut-off value was >9.02 ml, the sensitivity= 0.812, the specificity= 0.762 (Figure 1). The areas under the ROC curve of APACHE II, SAPS II and SOFA scores were found to be significant in non-survivors (Figure 2).

Table. Comparisons between the survivors and non-survivors groups.

	Survivors ***N*=21**	**Non-survivors** ***N*=11**	**P value**
Gender			
Female [n (%)]	8 (38)	6 (54)	0,373
Age (years)	71,38±11,09	68,73±10,14	0,514
Male	69,69±10,34	64,80±10,66	0,732
Female	74,13±12,42	72,00±9,29	0,386
Comorbidities			
Diabetes mellitus [n (%)]	5 (23)	4 (36)	0,681
Hypertension [n (%)]	16 (76)	9 (81)	0,715
Cerebrovascular Disease history [n (%)]	5 (23)	3 (27)	0,830
Medication history			
Anti-aggregant [n (%)]	7 (33)	4 (36)	0,864
Anti-coagulant [n (%)]	2 (9)	2 (18)	0,482
Anti-hypertensive [n (%)]	13 (62)	8 (73)	0,540
Laboratory			
White blood cell (*10^9/L)	9,58±3,93	11,29±6,65	0,365
Neutrophils (*10^9/L)	7,30±3,70	8,88±6,55	0,388
Lymphocyte count (*10^9/L)	1,62±0,60	1,58±0,62	0,880
Hemoglobin (g/L)	14,67±2,05	13,20±2,98	0,112
Platelet count (*10^9/L)	237,5±87,0	264,0±104,8	0,453
Serum urea [median (IQR)]	35,1[28,5-36,5]	44[33,1-93,3]	0,074
Serum creatinine (mmol/L) [median (IQR)]	0,9[0,7-1]	0,9[0,7-2,2]	0,119
Serum Glucose (mg/dL)	151,19±87,71	214,36±139,49	0,126
Serum Albumin (g/L)	36,75±3,77	34,00±6,00	0,486
C-reactive protein (mg/L) [median (IQR)]	4,7[0,8-15,8]	11,7[2,9-29,5]	0,140
NLR	3,96[3,00-5,74]	4,76[2,25-9,07]	0,736
PLR	151,3[109,7-191,0]	145,0[108,5-278,4]	0,796
Hemorrhage Volume (ml)	7,01±8,74	16,53±9,63	**0,008**
Presence of IVH [n (%)]	11(%52,4)	6(%54,5)	0,907
Disease severity scores			
GCS on admission [median (IQR)]	14[12-15]	7[3-12]	**0,006**
SAPS II on admission [median (IQR)]	33,5[28,5-38,5]	42[35-68]	**0,023**
APACHE II on admission [median (IQR)]	11[8,5-13]	17[9-22]	**0,047**
SOFA on admission [median (IQR)]	2,5[1-4]	6[4-7]	**0,016**

APACHE II: Acute Physiology and Chronic Health Evaluation II, GCS: Glasgow Coma Score, IVH: intraventricular hemorrhage NLR: neutrophils lymphocytes ratio, SAPS II: Simplified Acute Physiology Score II, SOFA: Sequential Organ Failure Assessment Score, PLR: Platelets to lymphocyte ratio.

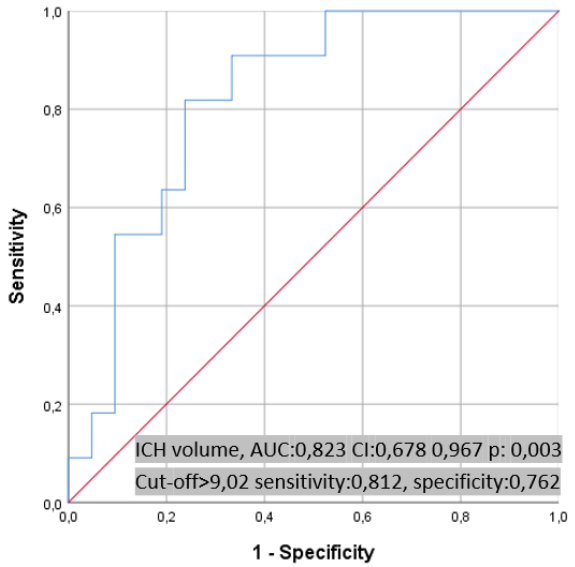

Figure 1. The ROC curve shows the relationship between hemorrhage volume and mortality.

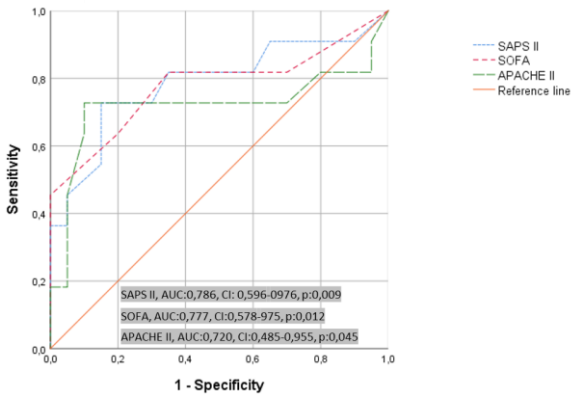

Figure 2. The ROC analysis of admission APACHE II, SAPS II and SOFA scores.

DISCUSSION AND CONCLUSION

In this study, it was determined that GCS, APACHE II, SAPS II, SOFA scores and hemorrhage volume could predict poor prognosis in patients followed up with acute thalamic hemorrhage.

Although the GCS score was previously used to predict prognosis in traumatic brain injuries (10), it has also been used in the evaluation of stroke-related impaired consciousness and mortality (11). In studies conducted in cases with thalamic hemorrhage, GCS scores were found to be lower in non-survivors (2,4,12). Consistent with other studies, GCS scores were found to be lower in non-survivors in our study and were statistically significant. APACHE II and SAPS II scores predict mortality by taking age, disease histories, vital conditions, infection parameters, kidney function parameters and lung conditions as criteria, regardless of hospitalization diagnosis of the patients in the intensive care unit (7,8). Moon et al. found APACHE II score (AUC= 0.805) to be a better predictor of mortality in patients with acute hemorrhagic stroke than SAPS II score (AUC= 0.783) (13). In our study, both SAPS II (AUC= 0.786) and APACHE II (AUC= 0.720) scores were higher in non-survivor patients, and SAPS II score had a greater predictive advantage. SOFA score, which was previously used to evaluate organ failure due to sepsis, has been using to evaluate organ failure in cases without sepsis over time. The SOFA score evaluates six systems including respiratory, kidney, cardiovascular, coagulation, liver, and concussions. Although it is used for morbidity prediction rather than mortality prediction, it has also been shown to be associated with mortality (9). However, the prediction of mortality is not as strong as SAPS II or APACHE II. In our study, the SOFA score was significantly higher in non-survivors (14). According to our literature review, this is the first study in which the APACHE II, SAPS II and SOFA scores were shown to be significantly higher in non-survivors patients with acute thalamic hemorrhage.

Neutrophils are the first cells to reach brain tissue from peripheral blood after cerebral hemorrhage. It aggravates the injury by developing secondary brain damage through pathways such as cytotoxic mediators triggered by neutrophils, proinflammatory cytokines such as TNF-a and IL-1b, and increased matrix metalloproteinase (15). In the first days following a cerebral hemorrhage, increasing catecholamine and steroid levels as a result of hyperactivation of the hypothalamo-pituitary-adrenal axis and the sympathetic nervous system causes apoptosis and functional dysfunction of lymphocytes in the peripheral blood (16). Immune deficiency due to decreased lymphocyte count and dysfunction has been associated with a poor prognosis in patients with cerebral hemorrhage (17). Platelets, on the other hand, play a critical role in immunomodulatory and inflammatory processes by interacting with various cells, including neutrophils, T lymphocytes and macrophages, which contribute to the initiation or exacerbation of the inflammatory process by inducing the

release of inflammatory cytokines (18). The ratio of increased neutrophil and platelet counts and decreased lymphocyte count following cerebral hemorrhage is an indicator of inflammatory response and has been associated with a poor prognosis (19,20). In our literature review, we could not find any study on PLR and NLR in thalamic hemorrhage cases. In our study, however, no significant difference was found between non-survivors and survivors patients in terms of NLR and PLR ratios.

Although in previous studies, a hemorrhage volume of >30 ml in intracranial hemorrhages, regardless of the bleeding site, was considered as a poor prognosis criterion (21), also smaller volumes of thalamic hemorrhages have been associated with poor prognosis (3,4,22). In our study, the hemorrhage volume was significantly higher in non-survivors, and the sensitivity was found to be 0.812 and the specificity 0.762 at a cut-off value >9.02 ml.

The determination of easy and practical evaluation criteria that predict the prognosis in the early stages of diseases allows new approaches in the follow-up and treatment of diseases. In this context, we think that these data will contribute to early follow-up and treatment approaches in terms of reducing the still high mortality rates in patients with acute thalamic hemorrhage despite the developing and increasing intensive care facilities.

The main limitations of our study are its retrospective nature and the limited number of cases followed in a single center. Despite all this, the results of our study are in agreement with the general literature and also provide information that mortality scores and hemorrhage volume in the early period of acute thalamic hemorrhages may predict poor prognosis.

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Ethics

Ethics Committee Approval: The study was approved by Necmettin Erbakan University Ethical Committee (Number: 2021/3276, Date: 04.06.2021).

Informed Consent: The authors declared that it was not considered necessary to get consent from the patients because the study was a retrospective data analysis.

Authorship Contributions: Surgical and Medical Practices: HHK, AB, FT. Concept: HHK, AB, FT. Design: HHK, AB, FT. Data Collection or Processing: HHK, AB, FT. Analysis or Interpretation: HHK, AB, FT. Literature Search: HHK, AB, FT. Writing: HHK, AB, FT.

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