

Original Article

Hematological Parameters in Predicting Return of Spontaneous Circulation Following Cardiac Arrest

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ABSTRACT

Objective: Cardiac arrest is one of the most critical emergencies encountered in the emergency department, requiring immediate intervention due to its high mortality and morbidity. Early prediction of return of spontaneous circulation (ROSC) is crucial for refining resuscitation strategies and improving outcomes. The current study aims to assess the predictive value of hematological parameters and blood gas variables in determining ROSC following cardiac arrest.

Materials and Methods: This study analyzed patients with cardiac arrest or who experienced cardiac arrest during their follow-up in the Emergency Department of Etlik City Hospital between May 1, 2024, and November 30, 2024. Demographic data, as well as initial laboratory values including white blood cell count, lymphocyte, monocyte, neutrophil, platelet count and blood gas parameters, were recorded and analyzed.

Results: Of the 1,015 patients initially screened, 997 patients fulfilled the inclusion criteria and were analyzed in the final dataset. The median lactate level was significantly lower in the ROSC group at 2.64 mmol/L, compared to 4.56 mmol/L in the non-ROSC group ($p < 0.001$). Similarly, the median PLR was notably higher in the ROSC group at 206.7, whereas it was 30.62 in the non-ROSC group ($p < 0.001$). PLR demonstrated very good discriminative ability for ROSC prediction (AUC: 0.823).

Conclusion: PLR, a readily accessible and cost-effective parameter, demonstrated a strong predictive value for ROSC in patients with cardiac arrest. Additional prospective studies are required to verify these results in broader patient groups.

Keywords: Blood gas analysis, cardiac arrest, hematologic parameters, lymphocytes, return of spontaneous circulation

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INTRODUCTION

Cardiac arrest is one of the most critical conditions encountered in emergency departments, requiring immediate intervention due to its high mortality and morbidity. In-hospital cardiac arrest occurs in 1.5 to 2.8 cases per 1,000 hospital admissions. The one-year survival rate of these patients is approximately 7.7%^[1]. Given these poor outcomes, the prompt and effective resuscitation of both in-hospital and out-of-hospital cardiac arrest is of paramount importance. Return of

spontaneous circulation (ROSC) is a key indicator of successful resuscitation^[2].

The early prediction of ROSC plays a critical role in the management of cardiac arrest. This prediction aids in determining the patient's potential outcome, which in turn helps optimize patient care and ensures the efficient use of resources. In cases of prolonged cardiopulmonary resuscitation (CPR), when ROSC cannot be predicted, it contributes to

determining the appropriate timing and standards for the termination of resuscitation [3, 4]. In the literature, clinical and hematological parameters are frequently studied in relation to the prediction of ROSC [5–8]. For example, the UB-ROSC score incorporates demographic characteristics, such as the patient's age, gender, arrest etiology and location, bystander intervention, CPR accessibility, presence of shockable rhythm, and time to reach emergency care [7]. Additionally, blood parameters such as lactate, pH, and NLR (neutrophil-to-lymphocyte ratio) have been shown to have an association with ROSC [9–11], although their prognostic value has not yet been definitively established. Lactate, a consequence of global tissue hypoxia and hypoperfusion, results from anaerobic glycolysis and is widely recognized as a marker of metabolic stress, ischemic injury, fluid resuscitation requirements, and the risk of organ failure [12]. pH reflects changes in the body's acid-base homeostasis and can vary in tissue pathologies such as renal and pulmonary disorders [13]. Low pH levels have been associated with respiratory distress, lactic acid accumulation, metabolic decompensation, and poor prognosis [14–16]. NLR is a simple and cost-effective method that reflects immune and inflammatory responses, tissue damage, and stress, and has been shown to correlate with the severity of many diseases in the literature [17]. PLR, which has been widely studied in conditions ranging from psychiatric disorders to oncology, is a marker of atherosclerosis, inflammation, and platelet activation [18, 19].

This study aims to comprehensively evaluate the predictive value of hematological parameters and blood gas variables in forecasting ROSC following cardiac arrest. The investigation will focus on identifying potential biomarkers that could serve as reliable indicators. Additionally, identifying risk factors associated with ROSC could facilitate more accurate prognostication, allowing healthcare providers to tailor interventions more effectively and optimize treatment strategies for patients experiencing cardiac arrest.

MATERIALS AND METHODS

Study Design

This study involves a retrospective analysis of individuals aged 18 and above who either presented with cardiac arrest or experienced cardiac arrest during their follow-up in the emergency department for a period of 7 months. Ethical approval for this study was granted by the Ethics Committee of Etlik City Hospital (/2025-BADEK-0238) on February 27, 2025. Due to the retrospective design of the study, informed consent was not required from the patients. The research was carried out in compliance with the principles of the Declaration of Helsinki.

Study Setting

The data for this study were obtained from the Emergency Department of Etlik City Hospital, a prominent tertiary healthcare institution. The hospital is a large-scale medical campus with a total of 4,050 beds, comprising eight specialized hospitals. The Emergency Department handles an average of 2,500 patient visits daily and serves as a central hub for 112 emergency medical services and outpatient emergency care in Ankara.

Study Population and Data Collection

The study consisted of individuals aged 18 and above who either presented with cardiac arrest or experienced cardiac arrest during their follow-up in the Emergency Department at Etlik City Hospital between May 1, 2024, and November 30, 2024. Patients were included regardless of the underlying cause of arrest, provided that resuscitation was attempted. Patients who experienced cardiac arrest secondary to trauma and those with incomplete data were excluded from the study. To identify eligible participants, data were obtained from the Hospital Information Management System (HBYS), which contains electronic medical records. Demographic information (age, sex) and laboratory parameters, including initial hemogram values (white blood cell (WBC), lymphocyte, monocyte, neutrophil, platelet), were recorded. These laboratory values were subsequently transformed into ratios: neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), neutrophil-to-monocyte ratio (NMR), and neutrophil-to-platelet ratio (NPR). Additionally, blood gas parameters, including pH, HCO₃ (bicarbonate), lactate, and base excess, were extracted. ROSC was identified through clinical records documented by attending physicians, with a pulse recovery lasting more than 20 minutes serving as the defining criterion and if ROSC was achieved, the length of stay in the Intensive Care Unit was also recorded. For patients with multiple cardiac arrest episodes during their emergency care, only the laboratory values from the first cardiac arrest were included in the analysis.

Statistical Analysis

Statistical analyses were performed using SPSS 26.0 (IBM Corp., Armonk, New York). The normality of the data was assessed with the Kolmogorov-Smirnov test. Categorical variables were summarized as frequencies (n) and percentages (%), while numerical data were reported as mean±standard deviation for normally distributed variables and as median (minimum–maximum) for non-normally distributed ones. The Independent Samples T-test was applied to compare continuous variables with a normal distribution, whereas the Mann-Whitney U test was used for those not following a normal distribution. The chi-square test was utilized for

the analysis of categorical variables. Univariate analysis was conducted to explore potential risk factors for ROSC, and significant variables identified in this step were incorporated into a multivariate logistic regression model to determine independent predictors of ROSC. The predictive performance of blood parameters for ROSC was assessed using the area under the Receiver Operating Characteristic (ROC) curve (AUC), with optimal cut-off values established through the Youden index. AUC values were categorized as follows: 0.90–1.0 (excellent), 0.80–0.90 (very good), 0.70–0.80 (good), 0.60–0.70 (fair), 0.50–0.60 (poor), and 0.50 (random prediction). A p-value of <0.05 was considered statistically significant.

RESULTS

During the 7 months of the analysis, 1,015 patients who either arrived at the emergency department or experienced cardiac arrest within it were identified. Of these, 997 patients who fulfilled the inclusion criteria were enrolled in the study.

Table 1 displays the demographic data and laboratory findings of these patients. The median age of all patients with cardiac arrest was 74 years, with 54.6% being male. Advanced cardiac

life support in the emergency department resulted in ROSC in 939 patients, while ROSC could not be achieved in 58 patients. No statistically significant differences were found between the ROSC and non-ROSC groups regarding age or sex (p-values: 0.715 and 0.322, respectively). The median WBC count was 11.6 (0.04, 39.21) in the ROSC group and 13.7 (2.8, 36.46) in the non-ROSC group (p=0.012); the median lymphocyte count was 1.05 (0.01, 14.15) in the ROSC group and 1.76 (0.18, 8.75) in the non-ROSC group (p<0.001). There were no statistically significant differences between the ROSC and non-ROSC groups regarding monocytes, neutrophils, or platelets (p-values: 0.670, 0.198, and 0.452, respectively).

Blood gas parameters differed significantly between the two groups (p<0.001). The median pH values were 7.38 and 7.28, the median lactate levels were 2.64 and 4.56, and the median base excess values were -3.7 and -9.4, respectively.

Among the laboratory indices, NLR and PLR were significantly greater in the ROSC group, whereas LMR was markedly higher in the non-ROSC group (median NLR: 8.99 vs. 5.57, p=0.006; median PLR: 206.7 vs. 30.62, p<0.001). No significant

Table 1. Demographic and laboratory characteristics of patients with cardiac arrest in the emergency department

	Total patients (n=997)	ROSC group (n=939)	non-ROSC group (n=58)	p
Age (year)*	74 (18,101)	74 (18,101)	75 (20,96)	0.715
Male sex (%)	544 (54.6)	516 (55)	28 (48.3)	0.322
Female sex (%)	453 (45.4)	423 (45)	30 (51.7)	
WBC (x10 ³ / μL)*	11.79 (0.04, 39.21)	11.6 (0.04,39.21)	13.7 (2.8, 36.46)	0.012
Lymphocyte (x10 ³ / μL)*	1.07 (0.01, 14.15)	1.05 (0.01, 14.15)	1.76 (0.18, 8.75)	<0.001
Monocyte (x10 ³ / μL)*	0.62 (0.01, 6.94)	0.63 (0.01, 6.94)	0.6 (0.06, 2.53)	0.670
Neutrophil (x10 ³ / μL)*	9.53 (0.01, 38.23)	9.52 (0.01, 38.23)	10.45 (1.71, 33.93)	0.198
Platelet (x10 ³ / μL)*	221 (11, 769)	222 (11, 769)	207 (27,677)	0.452
NLR*	8.71 (0.05, 435)	8.99 (0.05, 435)	5.57 (0.29, 53.18)	0.006
PLR*	194.18 (0, 35400)	206.7 (0.89, 35400)	30.62 (0, 1054.76)	<0.001
LMR*	1.78 (0.04, 38)	1.75 (0.04, 38)	2.61 (0.28, 33.67)	0.001
NMR*	14.02 (0.67, 336)	13.94 (0.67, 336)	14.88 (3.23, 156.83)	0.603
NPR*	0.04 (0, 0.973)	0.04 (0, 0.973)	0.05 (0.008, 0.501)	0.089
pH*	7.38 (6.57, 7.69)	7.38 (6.69, 7.69)	7.28 (6.57, 7.53)	<0.001
HCO ₃ (mEq/L)**	21.04±6.47	21.27±6.39	17.43±6.69	<0.001
Lactate (mmol/L)*	2.72 (0.32, 22.11)	2.64 (0.32, 22.11)	4.56 (0.89, 21.71)	<0.001
Base excess (mEq/L)*	-3.9 (-31.9, 16.7)	-3.7 (-30, 16.7)	-9.4 (-31.9, 10)	<0.001

* median (min, max) ** arithmetic mean±standard deviation; ROSC: Return of spontaneous circulation; WBC: White blood cell; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; LMR: Lymphocyte-to-monocyte ratio; NMR: Neutrophil-to-monocyte ratio; NPR: Neutrophil-to-platelet ratio; HCO₃: Bicarbonate.

differences were observed in NMR and NPR values (median NMR: 13.94 vs. 14.98, $p=0.603$; median NPR: 0.04 vs. 0.05, $p=0.089$, respectively).

Table 2 summarizes the findings from the univariate and multivariate analyses performed to determine potential predictors of ROSC in patients who experienced cardiac arrest.

In univariate analysis, we observed that a one-unit increase in WBC count was linked to a 4% reduction in the likelihood of ROSC. Similarly, each unit increase in lymphocyte count was associated with a 24% lower chance of achieving ROSC. Conversely, a rise in NLR was correlated with a 2.9% greater probability of ROSC, while an increase in PLR was linked to a 0.6% higher likelihood of ROSC. On the other hand, a higher LMR was associated with an 8.3% decrease in the probability of ROSC. No significant relationship was found between NMR, NPR, and ROSC.

Regarding blood gas parameters, a rise in pH levels was strongly associated with a 60-fold increase in the probability of achieving ROSC, highlighting the importance of pH balance in resuscitation outcomes. Additionally, a one-unit increase in HCO_3 was linked to a 9.9% higher likelihood of ROSC. Elevated

lactate levels, however, were associated with an 18% decrease in the probability of ROSC. Lastly, each unit increase in base excess corresponded to a 0.9% higher chance of achieving ROSC.

Multivariate analysis was subsequently performed; however, HCO_3 was excluded due to multicollinearity problem. In our final model, only PLR and lactate remained as independent predictors of ROSC. A decrease of 1 unit in lactate levels correlated with a 14% higher probability of ROSC. Likewise, each 1-unit rise in PLR was linked to a 0.5% increase in the likelihood of ROSC.

Table 3 displays the outcomes of the receiver operating characteristic (ROC) analysis, and Figure 1 demonstrates the ROC curves for hematological and blood gas parameters in predicting ROSC. PLR demonstrated very good discriminative ability (AUC: 0.823, $p<0.001$) with an optimal cut-off value of 70.52, yielding a sensitivity of 84% and specificity of 69%. Lactate exhibited good predictive value ($p<0.001$) with cut-off of 3.29 mmol/L, demonstrating a sensitivity of 65% and specificity of 78%. Lymphocyte count, NLR, LMR, pH, HCO_3 , and base excess demonstrated fair predictive value (AUC values: 0.680, 0.608, 0.634, 0.683, 0.663, and 0.691, respectively).

Table 2. Univariate and multivariate logistic regression analysis of factors predicting ROSC in cardiac arrest patients

	B	SE	p	OR	95% CI	B	SE	p	OR	95% CI
	Univariate Logistic Regression Analysis					Multivariate Logistic Regression Analysis				
Age (year)	0.008	0.009	0.381	1.008	0.991-1.025					
Male sex (%)	0.268	0.271	0.323	1.307	0.769-2.222					
WBC ($\times 10^3/\mu\text{L}$)	-0.039	0.017	0.027	0.962	0.930-0.996	0.004	0.027	0.855	1.004	0.953-1.058
Lymphocyte ($\times 10^3/\mu\text{L}$)	-0.276	0.060	<0.001	0.759	0.675-0.854	0.089	0.109	0.418	1.093	0.882-1.354
Monocyte ($\times 10^3/\mu\text{L}$)	-0.191	0.219	0.383	0.826	0.537-1.270					
Neutrophil ($\times 10^3/\mu\text{L}$)	-0.021	0.020	0.275	0.979	0.942-1.017					
Platelet ($\times 10^3/\mu\text{L}$)	0	0.001	0.700	1	0.998-1.003					
NLR	0.028	0.014	0.05	1.029	1-1.058	-0.021	0.020	0.286	0.979	0.942-1.018
PLR	0.006	0.001	<0.001	1.006	1.003-1.008	0.005	0.001	<0.001	1.005	1.003-1.008
LMR	-0.086	0.022	<0.001	0.917	0.879-0.958	-0.039	0.030	0.189	0.962	0.908-1.019
NMR	-0.001	0.005	0.853	0.999	0.990-1.008					
NPR	-1.846	1.390	0.184	0.158	0.010-2.408					
pH	4.096	0.733	<0.001	60.075	14.276-252.801	0.188	1.367	0.890	1.207	0.083-17.598
HCO_3 (mEq/L)	0.094	0.022	<0.001	1.099	1.053-1.147					
Lactate (mmol/L)	-0.201	0.031	<0.001	0.818	0.770-0.869	-0.150	0.052	0.004	0.860	0.778-0.952
Base excess (mEq/L)	0.086	0.016	<0.001	1.090	1.056-1.125	0.020	0.029	0.499	1.020	0.964-1.079

WBC: White blood cell; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; LMR: Lymphocyte-to-monocyte ratio; NMR: Neutrophil-to-monocyte ratio; NPR: Neutrophil-to-platelet ratio; HCO_3 : Bicarbonate.

Table 3. Diagnostic performance of laboratory parameters for predicting ROSC

	AUC	95% CI	Optimal Cut-off point	p	Sensitivity	Specificity
WBC ($\times 10^3/\mu\text{L}$)	0.598	0.530-0.667	7.76	0.012	0.24	0.83
Lymphocyte ($\times 10^3/\mu\text{L}$)	0.680	0.605-0.755	1.71	<0.001	0.75	0.55
NLR	0.608	0.534-0.682	7.76	0.006	0.57	0.66
PLR	0.823	0.757-0.889	70.52	<0.001	0.84	0.69
LMR	0.634	0.552-0.716	2.17	0.001	0.62	0.62
NMR	0.521	0.443-0.599	14.20	0.598	0.52	0.59
NPR	0.566	0.487-0.645	0.047	0.040	0.56	0.60
pH	0.683	0.607-0.759	7.30	<0.001	0.71	0.59
HCO_3 (mEq/L)	0.663	0.589-0.737	14.3	<0.001	0.86	0.41
Lactate (mmol/L)	0.737	0.673-0.802	3.29	<0.001	0.65	0.78
Base excess (mEq/L)	0.691	0.618-0.764	-10.6	<0.001	0.81	0.48
PLR+lactate	0.845	0.792-0.898	-	<0.001	-	-

WBC: White blood cell; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; LMR: Lymphocyte-to-monocyte ratio; NMR: Neutrophil-to-monocyte ratio; NPR: Neutrophil-to-platelet ratio; HCO_3 : Bicarbonate.

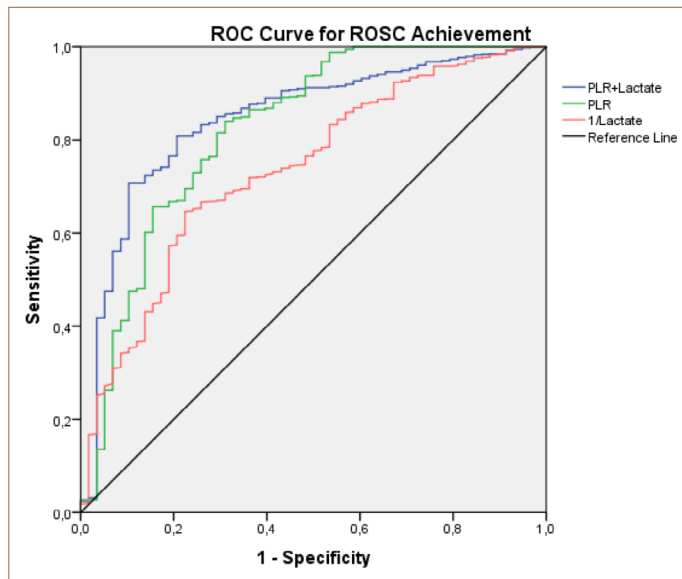


Figure 1. ROC Curve of laboratory parameters for ROSC achievement.

ROSC: Return of spontaneous circulation; PLR: Platelet-to-lymphocyte ratio; ROC: Receiver Operating Characteristic.

In contrast, WBC, NMR, and NPR exhibited poor predictive performance (AUC values: 0.598, 0.521, and 0.566, respectively). The combined use of PLR and lactate further improved the predictive performance ($p < 0.001$). Among all parameters, HCO_3 had the highest sensitivity (86%) for predicting ROSC, while WBC demonstrated the highest specificity (83%).

DISCUSSION

In our study, the best parameters for predicting ROSC in patients who experienced cardiac arrest in the emergency department were found to be PLR and lactate. A PLR of 70.52 or higher predicted ROSC with 84% sensitivity and 69% specificity, with an AUC of 0.82. The AUC for lactate was 0.74. Our findings are consistent with some reports in the literature.

A retrospective study conducted in 2019 on 216 cardiac arrest patients also identified PLR and NLR as the best predictors of ROSC, although their discriminative power was relatively lower (AUC: 0.61 and 0.65) [20]. However, in another retrospective study analyzing 346 out-of-hospital cardiac arrest cases, NLR was found to be associated with poor outcomes, whereas PLR showed no significant relationship [21]. Additionally, a retrospective study involving 67 patients evaluated the predictive power of blood gas parameters for ROSC in in-hospital cardiac arrest patients. That study found that only bicarbonate was a significant predictor (AUC: 0.67), whereas lactate was not statistically significant [22]. Furthermore, a prospective study involving 136 out-of-hospital cardiac arrest patients identified pCO_2 as the only independent predictor of ROSC, with an AUC of 0.68, making it the best-performing blood gas parameter for ROSC prediction in that cohort [23].

The superior predictive value of PLR compared to lactate in our study suggests that systemic inflammation, endothelial dysfunction, and thrombogenic activity may be key determinants in the restoration of ROSC. PLR elevation,

indicative of increased platelet activity and relative lymphopenia, reflects a heightened thrombotic state and potential immune dysregulation, both of which are critical in the post-arrest period. The ischemia-reperfusion process in ROSC after cardiac arrest is a catastrophic sequence of events involving apoptotic and programmed cell death, driven by inflammatory mediators that contribute to tissue degradation. This inflammatory cascade leads to endothelial dysfunction, microvascular impairment, and altered perfusion dynamics, ultimately impacting cardiac function and resuscitation outcomes [24]. In line with these pathophysiological mechanisms, PLR has been identified in the literature as a predictor of mortality, particularly in cardiovascular diseases. A prospective study conducted in 2014 on 2,518 patients with ST-elevation myocardial infarction (STEMI) found that PLR, with a cutoff value of 162.31 and an AUC of 0.60, could serve as an indicator of both in-hospital and long-term mortality [25]. Similarly, a 2019 retrospective study on 96 patients with aortic dissection reported that PLR levels were significantly higher in non-survivors compared to survivors (mean values of 279.3 vs. 182.3, respectively, $p < 0.001$). With a cutoff value of 195.8 and an AUC of 0.75, PLR was determined to be an independent predictor of in-hospital mortality [26]. These findings further support the role of PLR as a more integrative biomarker of the complex hemodynamic responses following cardiac arrest.

In our study, lactate was identified as the second-best predictor of ROSC after PLR, with a cutoff value of 3.29, a specificity of 78%, and a sensitivity of 65% in patients who experienced cardiac arrest in the emergency department. However, the prognostic value of lactate in cardiac arrest patients remains a topic of debate. For instance, a retrospective study conducted in Tokyo in 2016 on 372 out-of-hospital cardiac arrest (OHCA) patients who achieved ROSC found no significant difference in lactate levels between those with good and poor neurological outcomes (82 ± 49 vs. 96 ± 41 mg/dL, $p = \text{NS}$) [27]. Similarly, a 2024 prospective study in France on 60 OHCA patients reported no significant difference in initial lactate levels at emergency department admission between those who achieved ROSC and those who did not (6.4 vs. 6.2 mmol/L) [28]. A study conducted in Türkiye on 140 OHCA patients also found no significant difference in lactate levels between those who achieved ROSC and those who did not (9.1 ± 3.2 mmol/L vs. 9.8 ± 2.9 mmol/L, $p = 0.1$). Conversely, a prospective multicenter study involving 3,674 OHCA patients concluded that elevated lactate levels were associated with an increased risk of 1-month mortality [29]. The variability in the literature regarding the prognostic value of lactate may be attributed to factors such as the duration of resuscitation, preexisting comorbidities, and individual metabolic responses to ischemia [12]. Therefore, its role in predicting ROSC remains inconclusive.

These findings underscore the potential of PLR as a valuable predictor of ROSC, though results may vary across different patient populations. Additional large-scale prospective studies are needed to better understand the prognostic significance of PLR and lactate in this context.

CONCLUSION

PLR, a readily accessible and cost-effective parameter derived from the routine hemogram, has demonstrated strong predictive value for ROSC in patients with cardiac arrest. Given its simplicity and availability in the emergency department setting, PLR presents as a promising marker. Future studies involving larger and more heterogeneous populations are needed to validate these findings.

There are several limitations to our study. First, due to its retrospective design, the accuracy of the data could have been affected by missing or incorrectly entered information, which may influence the reliability of our findings. Additionally, since the study was conducted in a single center, the results may not be generalizable to broader populations, limiting the external validity. Furthermore, we did not assess hospital outcomes, as we were unable to differentiate between those who died, were discharged, or experienced favorable versus poor neurological outcomes.

DECLARATIONS

Ethics Committee Approval: The Etlik City Hospital Ethics Committee granted approval for this study (date: 27.02.2025, number: 2025-BADEK-0238).

Author Contributions: Concept – OFT; Design – SG; Supervision – SG; Resource – OFT; Materials – SG; Data collection and/or processing – OFT; Analysis and/or interpretation – SG; Literature review – SG; Writing – SG; Critical Review – OFT.

Conflict of Interest: None declared.

Use of AI for Writing Assistance: The authors declared that no artificial intelligence (AI)-assisted technologies, including Large Language Models (LLMs), chatbots, image generators, or tools such as ChatGPT, were utilized in this study.

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