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Study on the correlation between postoperative dynamic NLR monitoring levels and clinical prognosis in patients with aneurysmal subarachnoid hemorrhage

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Abstract: This study aimed to investigate the dynamic changes in the neutrophil-to-lymphocyte ratio (NLR) during the early postoperative period in patients with aneurysmal subarachnoid hemorrhage (aSAH) and to assess their predictive value for poor prognosis at discharge. A total of 248 aSAH patients were consecutively enrolled and classified into a favorable-prognosis group (mRS scores 0-2, n=193) and a poor-prognosis group (mRS scores 3–6, n=55) based on their discharge mRS scores. Peripheral blood neutrophil and lymphocyte counts were measured along with NLR calculation on admission day (0 d), 24 hours postoperatively (1 d), 72 hours postoperatively (3 d), and 7 days postoperatively (7 d). Differences in NLR at each time point were compared between the two groups. Univariate and multivariate logistic regression analyses were performed to identify independent predictors of poor prognosis, and a combined predictive model was constructed. The model's discrimination power was evaluated using a receiver operating characteristic (ROC) curve, with internal validation conducted via bootstrap method. The poor-prognosis group exhibited higher age (64 vs. 59 years, P=0.012), a greater proportion of Hunt-Hess grades III–V (63.6% vs. 16.1%, P=0.000), and a higher incidence of intraventricular hemorrhage (56.4% vs. 23.8%, P=0.000). The NLR levels at 24 hours, 72 hours, and 7 days postoperatively were significantly higher in the poor-prognosis group compared to the good-prognosis group, with the most significant intergroup difference observed at 72 hours postoperatively (median: 10.81 vs. 6.33). Multivariate logistic regression identified Hunt-Hess grading III–V (OR=6.313,95% CI: 2.870–13.887, P=0.000), neck width (OR=1.335,95% CI: 1.058–1.686, P=0.015), and 72-hour postoperative NLR (OR=1.103,95% CI: 1.037–1.174, P=0.002) as independent predictors of poor prognosis at discharge. The predictive model constructed based on these three parameters exhibited an area under the ROC curve (AUC) of 0.839 (95% CI not provided, P<0.001), and internal validation using bootstrap calibration demonstrated good model fit. A significant elevation in 72-hour postoperative NLR is an independent risk factor for poor prognosis in aSAH patients, and the combined model incorporating Hunt-Hess grading and tumor neck width demonstrates excellent discriminative power. Dynamic monitoring of early postoperative NLR levels aids in the early identification of high-risk patients.

1. Introduction

Aneurysmal subarachnoid hemorrhage (aSAH) is a cerebrovascular emergency with extremely high mortality and disability rates, accounting for 85% of all spontaneous subarachnoid hemorrhages. Despite advancements in diagnostic and therapeutic techniques in recent years, the prognosis of aSAH patients remains poor, with approximately 40%-70% of survivors exhibiting varying degrees of cognitive dysfunction or long-term neurological deficits. Current clinical prognostic assessments primarily rely on traditional metrics such as the Hunt-Hess scale, Fisher scale, and WFNS scale, yet these methods still have limitations in predicting individualized outcomes [1-2]. In recent years, the role of inflammatory responses in secondary brain injury following aSAH has garnered significant attention. Studies have demonstrated that systemic inflammation intensifies post-aSAH, and the neutrophil/lymphocyte ratio (NLR), as a simple and cost-effective inflammatory biomarker, is closely associated with complications such as cerebral vascular spasm (CVS), delayed cerebral ischemia (DCI), and global cerebral edema (GCE) [3]. Multiple studies have confirmed that elevated NLR levels are significantly correlated with poor prognosis in aSAH patients. Existing research indicates that elevated NLR is strongly associated with early brain injury, DCI, and poor long-term functional outcomes [4-5]. For instance, a retrospective analysis identified NLR>10.92 as an independent predictor of poor prognosis in aSAH patients (AUC = 0.814; sensitivity = 80%; specificity = 71.82%) [6]. Furthermore, inflammatory responses exacerbate secondary brain injury through mechanisms such as disruption of the blood-brain barrier (BBB) and promotion of microthrombus formation, and NLR effectively reflects this pathological process. However, the dynamic trends of NLR changes and the optimal time window for monitoring remain unclear. Currently, the dynamic evolution of postoperative inflammatory responses following a subarachnoid hemorrhage (aSAH) and their mechanisms influencing prognosis have not been fully elucidated. As an indicator of systemic inflammation, the patterns of NLR variation at different postoperative time points and its correlation with clinical outcomes require further investigation. Additionally, existing studies predominantly focus on baseline NLR values at admission, while the value of postoperative dynamic monitoring has not been systematically evaluated.

Through dynamic NLR monitoring, high-risk populations susceptible to DCI or cerebral edema can be identified to guide clinical interventions; anti-inflammatory therapy, blood pressure management, and neuroprotective strategies can be adjusted based on NLR trends to improve patient functional outcomes; as a routine hematological parameter, NLR is cost-effective and convenient for widespread clinical application. This study holds promise for providing a novel biomarker-based approach for postoperative management of patients with aSAH.

2. Materials and methods

2.1 Research subjects

A retrospective cohort study design was adopted to investigate confirmed cases of aneurysmal subarachnoid hemorrhage (aSAH). Patients should undergo postoperative dynamic monitoring and follow-up.

2.2 Inclusion and Exclusion Criteria

This retrospective study included surgical patients with aSAH (acute subarachnoid hemorrhage) admitted to the Neurointensive Care Unit of the First Affiliated Hospital of Yangtze University between 2020 and 2025. Inclusion criteria: (1) Age ≥30 years; (2) Subarachnoid hemorrhage caused

by aneurysm rupture confirmed by computed tomography angiography (CTA) and/or digital subtraction angiography (DSA); (3) Receiving endovascular embolization or craniotomy within 48 hours of admission. Exclusion criteria: (1) Traumatic subarachnoid hemorrhage or cases of unknown etiology; (2) Pre-existing severe systemic diseases such as hepatic or renal dysfunction, hematologic malignancies; (3) Modified Rankin Scale (mRS) score ≥2 at admission; (4) Failure to complete follow-up. The study was reviewed and approved by the hospital ethics committee. Clinical outcomes were assessed based on mRS scores at 90-day follow-up. Patients with an mRS score of 0–2 were identified.

2.3 Baseline Data Collection

Baseline data of all enrolled patients were collected via the electronic medical record system, covering the following three aspects: demographic characteristics (age [continuous variable, years], gender [male/female], and medical history including hypertension, diabetes, coronary heart disease, hyperlipidemia); clinical characteristics (Hunt-Hess classification at admission: grades I-II, III, IV-V); aneurysm location (anterior/c posterior circulation), Glasgow Coma Scale score (GCS) at admission, and presence of intraventricular hemorrhage; surgical approach (craniotomy for aneurysm clipping [craniotomy group] or endovascular aneurysm embolization [interventional group]), with recorded operative duration and occurrence of immediate postoperative complications.

NLR measurement time points: Peripheral venous blood samples were collected at four time points: preoperatively, 24 hours postoperatively, 72 hours postoperatively, and 7 days postoperatively. All blood samples were obtained on an empty stomach in the morning, and testing was completed within 2 hours after sampling. Testing method: The absolute counts of neutrophils and lymphocytes in peripheral blood were measured using a fully automated hematology analyzer (brand and model specified as applicable). The NLR calculation formula is: Neutrophil count (×109/L) divided by Lymphocyte count (×109/L). Each sample was tested twice, with the mean value reported as the final result. Testing was performed by laboratory technicians who underwent standardized training, and internal quality control was implemented throughout the process.

The primary endpoint was the assessment of neurological functional prognosis at 3 months post-onset using the Modified Rankin Scale (mRS). The mRS score ranges from 0 to 6, where 0 indicates asymptomatic status, 1 indicates presence of symptoms without significant disability, 2 indicates mild disability requiring partial assistance, 3 indicates moderate disability necessitating partial assistance for ambulation, 4 indicates moderate-to-severe disability requiring assistance for walking, 5 indicates severe disability demanding continuous care, and 6 indicates death. Scores of 0–2 were defined as favorable prognosis, while scores of 3–6 were defined as poor prognosis. Three-month follow-up was conducted via a combination of outpatient re-evaluation and telephone follow-up, performed independently by two neurologists trained in scale consistency. In cases of discrepant scores, consensus was sought to determine the final outcome. Follow-up procedures included initial mRS scoring by the attending physician upon discharge and three-month assessments via outpatient visits or telephone calls; for telephone follow-ups, standardized questionnaires were used to systematically evaluate daily activity capacity and self-care abilities to ensure score consistency. Patients deemed lost to follow-up were defined as those who failed three consecutive telephone contacts at different times and did not attend scheduled outpatient visits, with the loss-to-follow-up rate controlled within 0.5%.

2.4 Statistical Analysis Methods

Data analysis and plotting were performed using SPSS 23.0 and GraphPad Prism 6.0. The receiver operating characteristic (ROC) curve of subjects was generated.

Used for critical value analysis. Qualitative variables were compared using the Pearson chi-square test, continuity correction, or Fisher's exact test. Quantitative variables were compared using the independent samples t-test, corrected t-test, or Mann-Whitney U test. A multivariate logistic regression model was constructed to identify factors associated with 90-day prognosis in patients with aneurysmal subarachnoid hemorrhage. In univariate analysis, covariates with a P-value <0.05 were included in the multivariate logistic regression model. All P-values were considered bilateral, and statistical significance was defined as P <0.05.

3. Results

3.1 Basic Information of the Study Subjects

This study enrolled a total of 248 patients with aneurysmal subarachnoid hemorrhage (aSAH), including 88 males (35.5%) and 160 females (64.5%), with a median age of 61 (range: 53–67) years. At admission, 182 patients (73.4%) had Hunt-Hess grades I–II, and 66 patients (26.6%) had grades III–V; the aneurysms were located in the anterior circulation in 201 cases (81.0%) and in the posterior circulation in 47 cases (19.0%). All patients underwent neutrophil-to-lymphocyte ratio (NLR) measurements at four time points: on admission day (0 d), 24 hours postoperatively (1 d), 72 hours postoperatively (3 d), and 7 days postoperatively (7 d). Based on modified Rankin Scale (mRS) scores at discharge, patients were classified into a favorable-prognosis group (mRS 0–2 points, n = 193,77.8%) and a poor-prognosis group (mRS 3–6 points, n = 55,22.2%). Baseline comparisons between the two groups revealed that the poor-prognosis group had higher age (64 vs. 59 years, P=0.012), a higher proportion of Hunt-Hess grades III–V (63.6% vs. 16.1%, P=0.000), and a higher incidence of intraventricular hemorrhage (56.4% vs. 23.8%, P=0.000). No statistically significant differences were observed between the groups regarding gender, Glasgow Coma Scale (GCS) score, aneurysm location, or aneurysm size (P> 0.05). Details are presented in Table 1.

Table 1 Differences in baseline characteristics and NLR levels among patients with different prognosis

	Overall	Good prognosis (n=193)	Poor prognosis (n=55)	*P*
Gender				
female	160(64.5)	127(65.8)	33(60.0)	0.427
male	88(35.5)	66(34.2)	22(40.0)	
Age	61(53,67)	59(53,66)	64(57,69)	0.012
Hunt-Hess				
I-II	182(73.4)	162(83.9)	20(36.4)	0.000
III-V	66(26.6)	31(16. 1)	35(63.6)	
GCS				
≥ 11	110(44.4)	80(41.5)	30(54.5)	0.085
< 11	138(55.6)	113(58.5)	25(45.5)	
Intraventricular hemorrhage				
No	171(69.0)	147(76.2)	24(43.6)	0.000
Yes	77(31.0)	46(23.8)	31(56.4)	
Aneurysm size	3.45(2.76,4.15)	3.42(2.74,4.05)	3.60(3.03,5.50)	0.077
Location of the aneurysm				
Posterior	47(19.0)	40(20.7)	7(12.7)	0.182
Anterior	201(81.0)	153(79.3)	48(87.3)	

Neutrophils (0 days)	9.86(7.67, 12.67)	9.42(7.46, 12.38)	11.36(8.54, 14.43)	0.008
Lymphocytes (0 days)	0.87(0.63, 1.17)	0.86(0.62, 1. 13)	1.02(0.67, 1.58)	0.117
NLR(0d)	11.38(6.98, 17.39)	11.40(6.83, 16.92)	11.14(8.09, 18.17)	0.820
Neutrophils (1 day)	9.14(7.36, 11.72)	8.92(7.24, 11.23)	10.75(8.21, 13.30)	0.005
Lymphocytes (1 day)	0.88(0.65, 1.17)	0.91(0.67, 1.20)	0.77(0.60, 1.05)	0.079
NLR(1d)	10.74(7.44, 15.30)	10.15(7.15, 13.71)	14.05(9.05, 19.95)	0.001
Neutrophils (3D)	7.67(6.11,9.74)	7.40(5.87,9. 12)	9.71(7.44, 11.65)	0.000
Lymphocytes (3D)	1.10(0.78, 1.48)	1.15(0.89, 1.56)	0.84(0.59, 1. 18)	0.000
NLR(3d)	7.15(4.57, 10. 19)	6.33(4.15,8.79)	10.81(8.68, 14.85)	0.000
Neutrophils (7 days)	7.33(5.73,9.96)	6.93(5.22,9.01)	10.32(7.64, 12.43)	0.000
Lymphocytes (7 days)	1.25(0.95, 1.66)	1.28(1.01, 1.71)	1.10(0.81, 1.35)	0.012
NLR(7d)	5.89(4.12,8.92)	5.52(3.75,7.69)	9.14(5.82, 13.50)	0.000

3.2 Univariate analysis of poor prognosis

Using poor prognosis at discharge (mRS scores of 3–6) as the dependent variable, a univariate analysis was performed on clinical and laboratory parameters (quantitative data analyzed using the Mann-Whitney U test; categorical data using the χ^2 test). The results demonstrated that age (P=0.012), Hunt-Hess grading III–V (P=0.000), and intraventricular hemorrhage (P=0.000) were significantly associated with poor prognosis.

Dynamic changes in NLR: The NLR levels in the poor-prognosis group were significantly higher than those in the good-prognosis group at 24 hours postoperatively (day 1),72 hours postoperatively (day 3) (see Figure 1), and 7 days postoperatively (day 7; P-values were 0.001, <0.001, and <0.001, respectively), with the most significant intergroup difference observed at 72 hours postoperatively (good-prognosis group: 6.33 vs. poor-prognosis group: 10.81). No significant difference in NLR was observed between the two groups on admission day (day 0; P=0.820). Additionally, neutrophil counts at all postoperative time points (day 1, day 3, day 7) were associated with poor prognosis (P<0.01), while lymphocyte counts showed statistically significant differences at days 3 and 7 postoperatively (P<0.05).

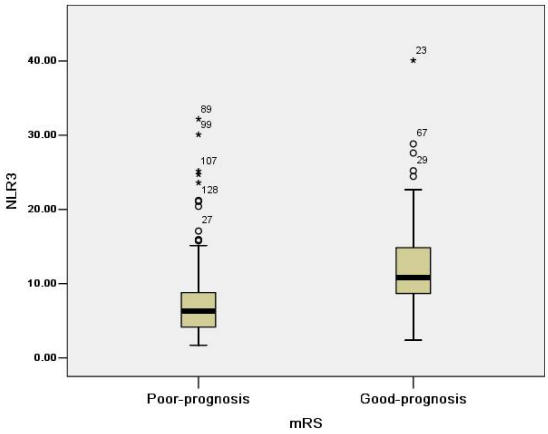


Figure 1 Comparison of NLR levels on day 3 postoperatively among patients with different prognosis

3.3 Construction of a Multivariate Logistic Regression Model

Variables with P <0.1 in univariate analysis (age, Hunt-Hess grading, intraventricular hemorrhage, tumor neck diameter, postoperative 24-hour NLR, postoperative 72-hour NLR, and postoperative 7-day NLR) were included in the multivariate logistic regression model, and

independent predictors were identified using forward stepwise regression. Hunt-Hess grades III–V (OR = 6.313; 95% CI: 2.870–13.887; P=0.000), tumor neck width (OR = 1.335; 95% CI: 1.058–1.686; P=0.015), and postoperative 72-hour NLR (OR = 1.103; 95% CI: 1.037–1.174; P=0.002) were identified as independent predictors of poor prognosis at discharge. The results are presented in Table 2.

Table 2 Multivariate logistic regression model

	B	S.E.	Wald	Sig.	Exp(B)	Lower	Upper
Hunt-Hess	1.843	0.402	20.992	0.000	6.313	2.870	13.887
Aneurysm size	0.289	0.119	5.921	0.015	1.335	1.058	1.686
NLR3	0.098	0.032	9.567	0.002	1.103	1.037	1.174

A prognostic prediction model was constructed based on the aforementioned independent predictors (HH grading, tumor neck diameter, and postoperative NLR at 72 hours). The area under the ROC curve for predicting poor prognosis at discharge was 0.839 (95% CI to be provided; P <0.001), indicating excellent discriminative power of the model. See Figure 2 for details.

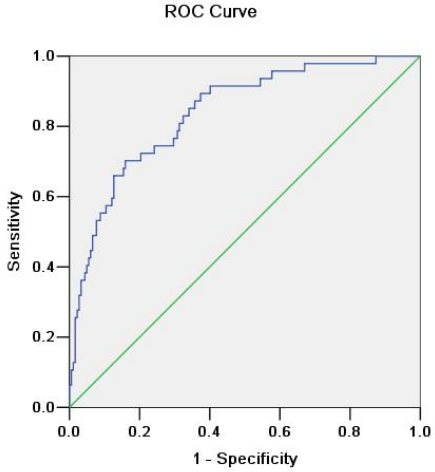


Figure 2 ROC curve of the prediction model

4. Discussion

4.1 Dynamic Changes and Clinical Significance of NLR After aSAH Surgery

This study conducted dynamic monitoring of NLR at three time points (24 hours postoperatively [1 day], 72 hours postoperatively [3 days], and 7 days postoperatively [7 days]) in patients with aSAH and revealed significant differences in the trajectory of NLR changes between the two groups. In the group with favorable prognosis, postoperative NLR exhibited a sustained downward trend: the median value decreased from 10.15 at 24 hours to 6.33 at 72 hours, further declining to 5.52 at 7 days. In contrast, the group with poor prognosis showed a marked increase in postoperative NLR at 24 hours compared to baseline levels (median 11.14 at 0 days), reaching 14.05, followed by a gradual decline (10.81 at 72 hours and 9.14 at 7 days); however, NLR values at all time points remained significantly higher than those in the favorable-prognosis group (all P-values <0.01). Notably, the decline in NLR from 24 to 72 hours was less pronounced in the poor-prognosis group, suggesting a slower resolution of inflammatory responses. These findings indicate that abnormal elevation or persistent high NLR levels in the early postoperative period may reflect an excessive or dysregulated inflammatory response, contributing to exacerbation of secondary brain injury [7–9].

Further analysis revealed that the NLR levels in patients with intraventricular hemorrhage were significantly higher than those without such hemorrhage (data not shown), suggesting that the inflammatory cascade triggered by local bleeding may be a major contributor to elevated NLR levels. Following neutrophil activation, these cells release damaging mediators such as matrix metalloproteinases and reactive oxygen species, which compromise the blood-brain barrier and vascular endothelial integrity; whereas lymphopenia reflects a stress-induced immunosuppressive state. As a ratio of these two parameters, NLR comprehensively reflects the degree of imbalance between pro-inflammatory and anti-inflammatory mechanisms, and dynamic monitoring of NLR trends aids in early identification of high-risk patients with dysregulated inflammatory responses [10–13].

4.2 The predictive value of NLR for the prognosis of aSAH

Univariate and multivariate logistic regression analyses demonstrated that the NLR at 72 hours postoperatively was an independent predictor of poor prognosis at discharge (OR = 1.103,95% CI: 1.037–1.174, P = 0.002), with its association strength second only to the Hunt-Hess grading system (OR = 6.313).

ROC curve analysis confirmed that the combined predictive model constructed based on Hunt-Hess grading, tumor neck status, and postoperative 72-hour NLR exhibited an area under the curve (AUC) of 0.839 (P <0.001) for predicting poor prognosis at discharge, indicating excellent discriminative power. Compared with other time points, postoperative 72-hour NLR demonstrated superior predictive performance due to the following reasons: postoperative 24-hour NLR exhibits significant individual variability owing to dual influences from preoperative conditions (e.g., pre-existing inflammatory responses at admission) and surgical trauma; postoperative 7-day NLR is susceptible to interference from clinical interventions (e.g., anti-inflammatory agents or glucocorticoids); whereas postoperative 72 hours coincides with the peak inflammatory phase of secondary brain injury, providing a more reliable reflection of the body's intrinsic immune response intensity to hemorrhage and surgical trauma [14–16].

Furthermore, this study identified for the first time that tumor neck width is also an independent risk factor for poor prognosis (OR = 1.335; 95% CI: 1.058 – 1.686; P=0.015). A wider tumor neck may indicate more complex aneurysm morphology, greater challenges in vascular reconstruction, or associations with hemodynamic disturbances and increased thrombosis risk, thereby adversely affecting prognosis. The combination of NLR with clinical anatomical parameters (HH grading and tumor neck width) significantly improves the accuracy of prognostic prediction, suggesting that NLR can serve as a valuable supplement to conventional prognostic assessment systems.

4.3 Comparison with Previous Studies and Innovations

The findings of this study are largely consistent with previous domestic and international research. Previous studies have demonstrated that elevated NLR levels in the early postoperative period are associated with increased risk of delayed cerebral ischemia and poor prognosis in patients with aSAH; however, most studies focused solely on single time points (e.g., admission or 24 hours postoperatively) without systematic analysis of NLR dynamics. The innovations of this study include: first, establishing three time points (24 hours, 72 hours, and 7 days postoperatively) to comprehensively delineate the dynamic changes in NLR following aSAH, and for the first time comparing differences in NLR variation patterns across different prognostic groups; second, identifying that the decline in NLR between 24 and 72 hours postoperatively (rather than absolute values at individual time points) may possess additional predictive value, providing a basis for its application as a dynamic monitoring parameter; third, developing a prognostic model incorporating

dynamic NLR parameters and anatomical indicators (tumor neck), which was internally validated via Bootstrap 1000 simulations, with calibration curves demonstrating good model fit. These findings suggest that dynamic monitoring of NLR changes holds greater clinical significance than single measurements.

It facilitates the early identification of high-risk patients postoperatively and enables stratified management.

4.4 Research Limitations and Conclusions

This study has the following limitations: First, it employed a single-center, retrospective observational design with a limited sample size (248 cases, only 55 with poor prognosis), which may introduce selection bias and overfitting risks; further validation through multicenter, large-scale studies is warranted. Second, NLR measurement is susceptible to influences such as infection status and glucocorticoid use; although confirmed infections were excluded, not all confounding factors were fully controlled. Third, other inflammatory markers such as IL-6 and TNF-α were not measured, preventing direct comparison of NLR's predictive efficacy with those biomarkers. Fourth, only internal Bootstrap validation was conducted, lacking an external validation cohort, thus the model's generalizability remains unverified. Fifth, the interaction between NLR and aneurysm treatment modality (embolization versus clipping) was not analyzed, and measurements of aneurysm neck width may exhibit observer variability.

Conclusion: A significant elevation in NLR at 72 hours postoperatively is an independent risk factor for poor prognosis in patients with aSAH at discharge, when evaluated combined with other factors.

The predictive model constructed using Hunt-Hess grading and tumor neck width demonstrated excellent discrimination capability. Dynamic monitoring of early postoperative NLR variation trajectories aids in identifying high-risk patients and provides a reference for clinical decision-making.

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