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ORIGINAL RESEARCH

Monitoring of Perioperative Microcirculation Dysfunction by Near-Infrared Spectroscopy for Neurological Deterioration and Prognosis of Aneurysmal Subarachnoid Hemorrhage: An Observational, Longitudinal Cohort Study

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ABSTRACT

Introduction: No evidence has established a direct causal relationship between early microcirculation disturbance after aneurysmal subarachnoid hemorrhage (aSAH) and neurological function prognosis, which is the key pathophysiological mechanism of early brain injury (EBI) in patients with aSAH.

Methods: A total of 252 patients with aSAH were enrolled in the Neurosurgical Intensive Care Unit of Southwest Hospital between January 2020 and December 2022 and divided into the no neurological deterioration, early neurological deterioration, and delayed neurological deterioration groups. Indicators of microcirculation disorders in EBI included regional cerebral oxygen saturation (rSO_2) measured by near-infrared spectroscopy (NIRS), brain oxygen monitoring, and other clinical parameters for

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evaluating neurological function and determining the prognosis of patients with aSAH.
Results: Our data suggest that the rSO_2 is generally lower in patients who develop neurological deterioration than in those who do not and that there is at least one time point in the population of patients who develop neurological deterioration where left and right cerebral hemisphere differences can be significantly monitored by NIRS. An unordered multiple-classification logistic regression model was constructed, and the results revealed that multiple factors were effective predictors of early neurological deterioration: reoperation, history of brain surgery, World Federation of Neurosurgical Societies (WFNS) grade 4–5, Fisher grade 3–4, SAFIRE grade 3–5, abnormal serum sodium and potassium levels, and reduced rSO_2 during the perioperative period. However, for delayed neurological deterioration in patients with aSAH, only a history of brain surgery and perioperative RBC count were predictive indicators.
Conclusions: The rSO_2 concentration in patients with neurological deterioration is generally lower than that in patients without neurological deterioration, and at least one time point in the population with neurological deterioration can be significantly monitored via NIRS. However, further studies are needed to determine the role of microcirculation and other predictive factors in the neurocritical management of EBI after aSAH, as these factors can reduce the incidence of adverse outcomes and mortality during hospitalization.

Keywords: Subarachnoid hemorrhage; Microcirculation; Early brain injury; Regional cerebral oxygen saturation; Near-infrared spectroscopy

Key Summary Points

Why carry out this study?

No evidence has established a direct causal relationship between early microcirculation disturbance after aneurysmal subarachnoid hemorrhage and neurological function prognosis.

We sought to evaluate the relationship between regional cerebral oxygen saturation measured by near-infrared spectroscopy and other indicators in the early phase after subarachnoid hemorrhage (SAH) and neurological changes during hospitalization.

What was learned from the study?

Our data suggest that regional cerebral oxygen saturation (rSO_2) levels are generally lower in patients with neurological deterioration than in those without neurological deterioration and that near-infrared spectroscopy can be used to monitor at least one time point in the population with neurological deterioration.

However, further studies are needed to determine the role of microcirculation and other predictive factors in the neurocritical management of early brain injury (EBI) after aneurysmal subarachnoid hemorrhage, as these factors can reduce the incidence of adverse outcomes and mortality during hospitalization.

INTRODUCTION

Subarachnoid hemorrhage (SAH) is one of the most common and severe injuries in the central nervous system and is mostly caused by ruptured intracranial aneurysms. In recent years, with the extensive application of surgical techniques and intensive neurological care, most ruptured aneurysms can be effectively treated by craniotomy clipping or endovascular embolization. However, according to a new survey in the USA, the in-hospital mortality rate of patients with SAH in the last 15 years has remained at approximately 13–14% [1], while the rate of in-hospital death/unordered discharge is as high as 20.6% [2]. Delayed cerebral ischemia (DCI) caused by intracranial artery spasm after SAH has long been considered a key pathophysiological mechanism leading to poor

patient prognosis [3]. With the landmark clinical trials CONSCIOUS-2 (registration number NCT00558311) and CONSCIOUS-3 (registration number NCT00940095), we gradually realized the importance of early brain injury (EBI) after SAH, but there is still a lack of in-depth understanding of the pathophysiological changes in EBI and effective clinical monitoring and intervention [3–5].

Since the EBI concept of SAH was proposed, there have been many studies on its pathophysiological mechanism. Among these abnormalities, sudden aneurysm rupture leads to blood entering the subarachnoid space, induces autonomic cerebral blood flow regulation disorders and intracranial microcirculation disorders, and causes brain tissue ischemia and hypoxia, which are the most important pathophysiological changes in the early stage of SAH [6]. The vast majority of patients with SAH lack brain tissue ischemic focus on imaging; even among patients with high-grade SAH, secondary cerebral infarction accounts for only 21% of the brain tissue [7]. However, cerebrospinal fluid (CSF) metabolomics analysis suggests that, with or without intracranial vasospasm, the tissue hypoxia marker 2-hydroxyglutarate is significantly associated with long-term neurological function prognosis in patients with SAH [8]. Helbok et al. adopted brain tissue microdialysis and other methods and reported that more than 60% of patients with SAH had brain tissue hypoxia within 24 h after the onset of the disease ($PbtO_2 < 20$ mmHg) [9]. In 2003, Uhl et al. observed segmental and bead-like intracranial microvascular spasm for the first time during the process of craniotomy clipping of ruptured aneurysms, causing 75% cortical microcirculation dysfunction [10]. Our previous studies also confirmed in a mouse model that oxygenated hemoglobin can induce the contraction of pericapillary cells and can cause beaded microvascular spasm and microcirculation disturbance, similar to what occurs in the human body [11, 12]. It has been preliminarily confirmed that intracranial microcirculation disturbance in the very early and subsequent periods after SAH is the direct cause of delayed ischemia and poor prognosis of neurological function [13], and the results of the CONSCIOUS-2 clinical trial have been further interpreted, suggesting that intracranial microvascular spasm is at least partially independent of endothelin receptors. The mechanism of delayed ischemia is different from that of symptomatic intracranial great vascular spasm [14]. However, rather than merely considering the predictive correlation mentioned in previous studies, no evidence has established a direct causal relationship between early microcirculation disturbance after SAH and neurological function prognosis, which has become the key pathophysiological mechanism of EBI in patients with SAH.

In the present study, we sought to (1) evaluate the relationship between regional cerebral oxygen saturation (rSO_2) and other indicators in the early phase after SAH and neurological changes during hospitalization and (2) identify the early predictors associated with neurological deterioration during the hospitalization period in patients with SAH. The results will help medical care personnel better understand this critical period, improve their ability to perceive EBI indicators, identify those patients at risk early, and provide more positive strategies.

METHODS

Study Design

We retrospectively enrolled aneurysmal patients with SAH admitted to the Neurosurgical Intensive Care Unit of Southwest Hospital between January 2020 and December 2022. All patient data were extracted from medical records, and all patients had angiographically documented aneurysms with SAH, confirmed by either computed tomography (CT) or lumbar puncture. The study protocol was reviewed and approved by the Ethics Committee of Southwest Hospital of Army Medical University (No. (B) KY2023040). Written informed consent to participate was waived by the ethical committee because of the observational nature of the study. This study was conducted in accordance with the ethical guidelines of the Helsinki Declaration and reported in accordance with the Strengthening the Reporting of

Observational Studies in Epidemiology (STROBE) checklist.

The inclusion criteria for patients were as follows: (1) aged between 18 and 80 years, (2) less than 72 h from the time of rupture to admission for treatment, (3) had ruptured bleeding from a single aneurysm, and (4) underwent either surgical clipping (SC) or endovascular coiling (EC) surgery. The exclusion criteria were as follows: (1) a previous history of ruptured aneurysm or SAH; (2) severe cardiac, brain, or lung decompensation; (3) nonaneurysmal SAH; (4) discharge against medical advice; (5) long-term use of antiplatelet drugs; (6) rebleeding; and (7) missing medical, radiological, or laboratory information.

A total of 252 consecutive patients with SAH were eventually enrolled (Fig. 1) and then divided into three groups based on the National Institute of Health Stroke Scale (NIHSS) score. Neurosurgical nurses who had been systematically trained used the NIHSS scale to independently assess daily changes in nervous system function during patient hospitalization. Neurological function deterioration was defined as an NIHSS score ≥ 4 according to previous studies [15, 16]. The enrolled patients were divided into the no neurological deterioration (NND) group (NIHSS score < 4 points during hospitalization; $n = 158$). For the early neurological deterioration group (END), the NIHSS score change within 72 h after surgery was ≥ 4 points ($n = 70$); for delayed neurological deterioration (DND), the NIHSS score change after 72 h of surgery was ≥ 4 points ($n = 24$). The flow diagram of the enrolled cohort is illustrated in Fig. 1.

Parameter Retraction

All patient data were collected from patient medical records. The selection of indicators associated with the prognosis of EBI in patients with aSAH was guided by the underlying concept and pathophysiological mechanism [17]. Several of these indicators have been previously reported to be correlated with EBI prognosis. We collected demographic information, medical history, history of brain surgery, size and location of the aneurysm, in-hospital complications, and indicators theoretically correlated with EBI. The indicators of microcirculation disorder in EBI included regional cerebral oxygen saturation (rSO_2) measured by near-infrared spectroscopy (NIRS), brain oxygen monitoring [17, 18], laboratory examination, clinical signs and symptoms; the consciousness scores included loss of consciousness and postictus at admission; and the World Federation of Neurosurgical Societies (WFNS) grade. The imaging characteristics and scores included acute hydrocephalus, the Barrow Neurological Institute (BNI) grading scale before surgical treatment [19], after neurological recovery World Federation of Neurosurgical Societies (rWFNS) grade [20], and the SAFIRE grade [21], which was previously reported to be associated with the prognosis of SAH.

Laboratory examinations included routine blood examination (white blood cell count, red blood cell count, hemoglobin, neutrophil count, lymphocyte count, platelet count, monocyte count, and neutrophil-to-lymphocyte ratio (NLR) [22]); blood biochemical examination (albumin, potassium ion, sodium ion, glucose, total cholesterol, triglyceride, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and anion gap); partial clotting indices (fibrinogen mean, D-dimer, FDP); and procalcitonin. In addition, the operation time, operation modality, and dynamic NIHSS score during hospitalization were also collected.

Statistical Analysis

Prior to conducting the data analyses, all the variables were thoroughly examined for missing values. Among the predictors, the percentage of missing data varied from 0 to 23%. To incorporate these data into the analysis, we employed multiple imputations using mean imputations to address the missing values. Any variables with a missing data rate exceeding 50% were removed from the analysis.

The sum test was used to compare the quantitative variables. We compared differences in demographic information, clinical

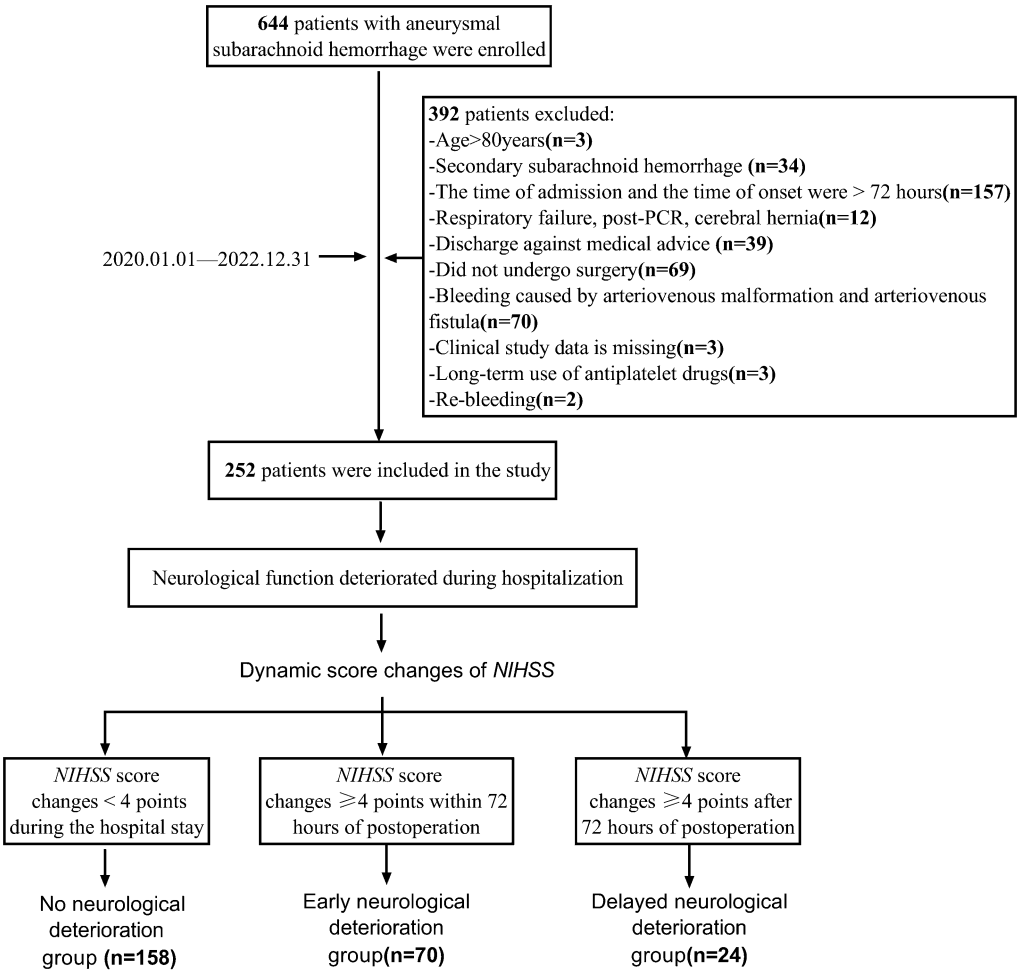

Fig. 1 Flow diagram of patient inclusion. *NIHSS* National Institute of Health Stroke Scale, *PCR* polymerase chain reaction

symptoms, grading of scales, laboratory findings, and treatments between patients in the three groups. The descriptive variables are presented as the means (standard deviations) or medians with interquartile ranges (IQRs) for continuous variables and as frequencies (percentages) for categorical variables. Chi-squared tests or Fisher's exact tests were used to compare categorical variables, one-way analysis of variance (ANOVA) or the Kruskal–Wallis rank test with $p < 0.05$ in the univariate analysis were used for univariate logistic regression, and only variables with $p < 0.05$ in the univariate logistic regression were included in the multivariate unordered multiple classification logistic regression analysis to identify the independent EBI risk factors associated with early and delayed neurological deterioration during the perioperative period. Associations are expressed as odds ratios (ORs) and 95% confidence intervals (CIs). To further investigate the changes in regional cerebral oxygen saturation with the location and duration of major diffuse intracranial hemorrhage, we used repeated measures ANOVA to determine the differences and trends. Moreover, a receiver operating characteristic (ROC) curve was generated to determine the role of potential predictors of neurological deterioration in patients with aSAH, and $p < 0.05$ (two-tailed) was considered to indicate statistical significance. All the statistical analyses were performed using SPSS Statistics 25.0 (IBM, Armonk, New York, USA), and the ROC curve and line chart of the changes in regional cerebral oxygen concentrations were drawn with GraphPad Prism 8.0.2.

RESULTS

Patient Characteristics

Of all 252 patients included in the study, 158 (62.7%) patients were included in the no neurological deterioration group, 70 (27.8%) patients were included in the early neurological deterioration (END) group, and 24 (9.5%) patients were included in the delayed neurological deterioration (DND) group (Fig. 1). The demographic and clinical characteristics are shown in Table 1. The mean age was 56 years (SD 10.91), and 38.5% of the patients were male. There were 119 (47.2%) patients with preoperative hypertension, 18 (7.1%) with diabetes mellitus, 6 (2.4%) with coronary heart disease, 58 (23.0%) with a smoking history, 60 (23.8%) with a drinking history, and 12 (4.8%) with a history of brain surgery. In this study, 19 (7.5%) patients had acute hydrocephalus at admission, 197 (78.17%) patients had WFNS grades of 4–5, 131 (51.98%) had Fisher grade of 3–4, and 129 (51.20%) had BNI score of 4–5. In addition, 128 (50.8%) patients had SAFIRE grades 3–5 within 24 h after surgery. Aneurysms were more commonly found in the anterior circulation in 235 (93.3%) patients in the present study. Among all the patients, 184 (73.02%) underwent interventional radiological procedures, whereas 68 (26.98%) underwent surgical clipping. Twenty-two (8.7%) patients underwent a second surgery within a short period, 5 (22.73%) of whom underwent decompressive craniectomy (DC) via implantation of an intracranial pressure probe for cerebral edema and 17 (77.27%) of whom underwent extraventricular drainage for acute hydrocephalus. The remaining related variables were collected, and the characteristics of the three groups are also summarized in Supplementary Table 1.

Compared with those in the non deterioration group, the median age was greater in the END and DND groups (58 versus 54 years, 59 versus 54 years, $p = 0.029$). All three groups were predominantly female; however, the sex difference was not significant. The END and DND groups had a greater proportion of patients with a history of hypertension, brain surgery, acute hydrocephalus, reoperation, surgical clipping, BNI score 4–5, Fisher grade 3–4, or SAFIRE grade 3–5. On the other hand, these groups exhibited a lower proportion of patients with coronary heart disease, a history of smoking and drinking, those who received endovascular coiling, and those with BNI scores 1–3, Fisher grade 1–2, or SAFIRE grade 1–2. Additionally, a greater proportion of patients in the early deterioration group had diabetes mellitus and a WFNS grade of 1–3 than did those in the no deterioration group, whereas a lower proportion of patients in the delayed deterioration group had these characteristics than did those in the no deterioration group. However, there was no significant difference in the location of the responsible aneurysm among the three groups. No COVID-19 cases were observed in our study cohort, despite the ongoing COVID-19 pandemic.

Laboratory Findings in Patients with aSAH in the EBI Period

The laboratory data collected during the perioperative period are summarized in Table 1. Routine blood examinations, biochemical blood examinations, and blood clotting index examinations were conducted at four time points (i.e., at admission, within 24 h of surgery, within 24–48 h of surgery, and within 48–72 h of surgery). The results showed that the mean white blood cell (WBC) counts were 12.62 (SD 4.32), 25.44 (SD 3.42), 10.98 (SD 3.57), and 9.75 (SD 3.59), respectively, with only the WBC count at admission being significantly different ($p = 0.008$) between the three groups. The average red blood cell (RBC) counts were 4.32 (SD 0.56), 5.58 (SD 0.56), 3.80 (SD 0.57), and 3.80 (SD 0.69), respectively, with only the RBC count within 24 h of surgery being significantly different ($p = 0.001$) among the three groups. The median neutrophil counts were 10.04 (IQR 7.69–13.06), 8.27 (IQR 6.52–10.32), 9.15 (IQR 7.31–11.67), and 8.05 (IQR 6.06–10.15), respectively, with the neutrophil count at admission ($p = 0.007$), within 24–48 h ($p = 0.031$), and within 48–72 h of surgery

Table 1 Demographic, baseline characteristics and laboratory findings of patients with aneurysmal subarachnoid hemorrhage

Variable	Neurological deterioration				*P*
	Early deterioration (*n* = 70)	No deterioration (*n* = 158)	Delayed deterioration (*n* = 24)	Total (*n* = 252)	
Demographic					
Age, years, mean (SD)	57.94 (10.93)	54.46 (10.82)	58.93 (10.23)	55.86 (10.91)	0.029
With history of brain surgery, *n* (%)	5 (7.10)	3 (1.90)	4 (16.70)	12 (4.8)	0.040
Reoperation, *n* (%)	16 (22.9)	3 (1.9)	3 (12.5)	22 (8.7)	< 0.001
Treatment modality					
Surgical clipping, *n* (%)	21 (30)	39 (24.68)	8 (33.33)	68 (26.98)	0.046
Endovascular coiling, *n* (%)	49 (70)	119 (75.32)	16 (66.67)	184 (73.02)	
At admission					
WFNS grade 1–3, *n* (%)	12 (17.14)	30 (18.99)	13 (54.17)	55 (21.83)	< 0.001
WFNS grade 4–5, *n* (%)	58 (82.86)	128 (81.01)	11 (45.83)	197 (78.17)	
Fisher grade 1–2, *n* (%)	29 (41.4)	85 (53.8)	7 (29.2)	121 (48.02)	0.034
Fisher grade 3–4, *n* (%)	41 (58.6)	73 (46.2)	17 (70.8)	131 (51.98)	
BNI 1–3 score, *n* (%)	32 (45.70)	85 (53.80)	6 (25.00)	123 (48.80)	0.026
BNI 4–5 score, *n* (%)	38 (54.30)	73 (46.20)	18 (75.00)	129 (51.20)	
WBC count[a], mean (SD)	12.00 (4.32)	13.48 (4.82)	14.28 (5.01)	12.62 (4.32)	0.008
Neutrophil count[a], median (IQR)	10.59 (7.96–14.91)	9.38 (7.2–12.66)	11.67 (9.62–14.82)	10.04 (7.69–13.06)	0.007
Serum sodium ion[d], mean (SD)	139.51 (3.43)	138.85 (3.25)	137.45 (3.30)	138.90 (3.34)	0.031
Within 24 h of surgery					
SAFIRE grade 1–2, *n* (%)	6 (8.60)	110 (69.60)	8 (33.30)	124 (49.2)	< 0.001
SAFIRE grade 3–5, *n* (%)	64 (91.40)	48 (30.40)	16 (66.70)	128 (50.8)	
RBC count[b], mean (SD)	3.86 (0.55)	3.95 (0.53)	3.51 (0.64)	5.58 (0.56)	0.001
Albumin[c], mean (SD)	33.37 (5.42)	35.30 (4.91)	33.41 (6.81)	46.50 (5.32)	0.021
Procalcitonin[e], median (IQR)	0.09 (0.05–0.23)	0.08 (0.04–0.23)	0.16 (0.07–0.57)	0.09 (0.04–0.23)	0.022

Table 1 continued

Variable	Neurological deterioration				*P*
	Early deterioration (*n* = 70)	No deterioration (*n* = 158)	Delayed deterioration (*n* = 24)	Total (*n* = 252)	
rSO_2 left (%), mean (SD)	67.01 (8.21)	69.37 (4.80)	69.75 (4.51)	68.75 (5.60)	0.016
Within 24–48 h of surgery					
Neutrophil count[a], median (IQR)	9.79 (7.63–11.50)	8.82 (7.00–11.52)	10.6 (8.33–12.61)	9.15 (7.31–11.67)	0.031
NIR, median (IQR)	16.62 (11.80–26.48)	14.50 (9.23–21.15)	21.00 (10.91–43.61)	15.71 (9.92–22.85)	0.018
Albumin[c], mean (SD)	34.59 (3.56)	36.05 (3.42)	35.76 (3.55)	35.62 (3.52)	0.014
Serum potassium ion[d], mean (SD)	3.72 (0.36)	3.85 (0.38)	3.69 (0.48)	3.80 (0.39)	0.021
Anion gap[d], mean (SD)	12.31 (2.81)	11.81 (2.24)	13.21 (2.32)	12.08 (2.45)	0.021
rSO_2 left (%), mean (SD)	68.59 (4.98)	69.68 (5.19)	67.00 (3.49)	69.12 (5.05)	0.030
Within 48–72 h of surgery					
Neutrophil count[a], median (IQR)	8.74 (6.94–11.09)	7.57 (5.69–9.30)	9.37 (6.93–10.89)	8.05 (6.06–10.15)	0.014
Lymphocyte count[a], median (IQR)	0.56 (0.38–0.81)	0.73 (0.46–1.06)	0.53 (0.37–0.79)	0.65 (0.43–0.94)	0.002
NLR, median (IQR)	15.77 (9.42–24.27)	10.86 (5.95–17.23)	17.01 (9.81–24.69)	12.42 (7.82–19.72)	0.001
Serum sodium ion[d], mean (SD)	142.68 (4.58)	140.79 (3.88)	143.50 (5.49)	141.57 (4.36)	0.003
Anion gap[d], mean (SD)	11.83 (2.10)	11.63 (2.35)	12.96 (3.00)	11.81 (2.37)	0.037
rSO_2 left (%), mean (SD)	68.34 (5.04)	69.61 (5.09)	66.46 (2.41)	68.96 (4.97)	0.007

Table 1 continued

Variable	Neurological deterioration				*P*
	Early deterioration (*n* = 70)	No deterioration (*n* = 158)	Delayed deterioration (*n* = 24)	Total (*n* = 252)	
rSO_2 right (%), mean (SD)	70.39 (4.09)	71.90 (4.75)	70.05 (3.17)	71.31 (4.50)	0.023

IQR interquartile range, *n* numbers, *SD* standard deviation, *WFNS* World Federation of Neurological Societies, *BNI* Barrow Neurological Institute Grading Scale, *WBC* white blood cell count, *RBC* red blood cell, *NLR* neutrophil-to-lymphocyte ratio, *FDP* fibrinogen degradation product, rSO_2 oxygen saturation of cerebral arterial blood

[a]Unit of measurement: 10^9/L

[b]Unit of measurement: 10^{12}/L

[c]Unit of measurement: g/L

[d]Unit of measurement: mmol/L

[e]Unit of measurement: ng/ml

($p = 0.014$) being significantly different between the three groups. The median lymphocyte counts were 1.06 (IQR 0.75–1.48), 1.09 (IQR 0.72–1.66), 0.60 (IQR 0.42–0.86), and 0.65 (IQR 0.43–0.94), respectively, with only the lymphocyte count within 48–72 h of surgery being significantly different ($p = 0.002$) between the three groups.

The median neutrophil-to-lymphocyte ratio (NLR) values were 10.42 (IQR 5.77–14.55), 7.20 (IQR 4.60–13.14), 15.71 (IQR 9.92–22.85), and 12.42 (IQR 7.82–19.72), respectively, there were significant difference in NLR between 24–48 h and 48–72 h ($p = 0.018$, $p = 0.001$, respectively). The mean albumin levels were 43.04 (SD 3.77), 46.50 (SD 5.32), 35.62 (SD 3.52), and 35.39 (SD 3.91), respectively, with albumin levels within 24 h ($p = 0.021$) and 24–48 h of surgery ($p = 0.014$) being significantly different. The mean serum potassium ion levels were 3.74 (SD 0.40), 5.94 (SD 0.51), 3.80 (SD 0.39), and 3.79 (SD 0.38), respectively, with only the serum potassium ion level within 24–48 h of surgery ($p = 0.021$) being significantly different among the three groups. The mean anion gap were 12.04 (SD 3.73), 10.53 (SD 3.42), 12.08 (SD 2.45), and 11.81 (SD 2.37), respectively, with the anion gap occurring within 24–48 h of surgery ($p = 0.021$) and within 48–72 h of surgery ($p = 0.037$) being significantly different. The median procalcitonin (PCT) levels were 0.05 (IQR 0.04–0.11), 0.09 (IQR 0.04–0.23), 0.13 (IQR 0.05–0.32), and 0.21 (IQR 0.06–0.80), respectively, with only the PCT within 24 h of surgery being significantly different ($p = 0.022$) among the three groups. Regarding cerebral oxygen saturation (rSO_2), within 24 h ($p = 0.016$), 24–48 h ($p = 0.030$), and 48–72 h of surgery ($p = 0.007$) of surgery, the left brain rSO_2 concentration significantly differed among the three groups. However, there were no significant differences in the remaining variables.

Compared with those in the no neurological deterioration group, patients in the early deterioration group had higher neutrophil counts; serum sodium ion levels at admission; procalcitonin levels within 24 h of surgery; neutrophil count; NIR and anion gap within 24–48 and 48–72 h of surgery; and serum sodium ion within 48–72 h of surgery. Additionally, these patients had lower WBC counts; RBC counts; albumin levels; serum potassium ion counts; and lymphocyte counts. The delayed neurological deterioration group also had the same result, excluding the WBC count at admission and the left rSO_2 within 24 h of surgery.

Table 2 Predictors of neurological deterioration in patients

	Early deterioration				Delayed deterioration			
	B	***P***	**OR**	**95% CI**	**B**	***P***	**OR**	**95% CI**
Univariate analysis								
Demographic								
Age > 55	0.89	0.003	2.45	1.37–4.38	0.31	0.485	1.36	0.58–3.21
Reoperation	2.73	< 0.001	15.31	4.29–54.59	2.00	0.019	7.38	1.40–38.97
Endovascular coiling	− 0.27	0.401	0.77	0.41–1.43	− 0.42	0.369	0.66	0.26–1.65
With history surgery of brain	1.38	0.064	3.97	0.92–17.12	2.34	0.004	10.33	2.16–49.56
At admission								
WFNS grade 4–5	− 0.13	0.740	0.88	0.42–1.85	1.62	< 0.001	5.04	2.06–12.35
Fisher grade 3–4	0.50	0.086	1.65	0.93–2.91	1.04	0.003	4.78	1.70–13.43
BNI grade 4–5	0.32	0.261	1.38	0.79–2.43	1.25	0.012	3.49	1.32–9.27
WBC count[a]	0.08	0.016	1.09	1.02–1.16	0.12	0.014	1.12	1.02–1.23
Neutrophil count[a]	0.09	0.009	1.10	1.02–1.17	0.13	0.009	1.14	1.03–1.25
Serum sodium ion[d]	0.06	0.163	1.07	0.98–1.16	− 0.12	0.048	0.89	0.79–1.00
Within 24 h of surgery								
SAFIRE grade 3–5	3.20	< 0.001	24.44	9.91–60.30	1.52	0.001	4.58	1.84–11.43
RBC count[b]	− 0.29	0.283	0.75	0.44–1.27	− 1.49	0.001	0.23	0.10–0.52
Albumin[c]	− 0.07	0.012	0.93	0.88–0.99	− 0.07	0.100	0.93	0.86–1.01
Procalcitonin[c]	0.18	0.652	1.20	0.55–2.64	0.93	0.019	2.54	1.16–5.53
rSO_2 left (%)	− 0.08	0.018	0.92	0.86–0.99	0.02	0.716	1.02	0.93–1.11
Within 24–48 h of surgery								
Neutrophil count[a]	0.07	0.094	1.08	0.99–1.17	0.14	0.029	1.15	1.01–1.30
NIR	0.00	0.668	10.00	0.99–1.02	0.02	0.022	1.02	1.00–1.04
Albumin[c]	− 0.12	0.004	0.89	0.81–0.96	− 0.03	0.701	0.98	0.86–1.11
Serum potassium ion[d]	− 0.92	0.020	0.40	0.18–0.87	− 1.15	0.061	0.32	0.10–1.05
Anion gap[d]	0.09	0.144	1.09	0.97–1.23	0.23	0.010	1.25	1.06–1.49
rSO_2 left (%)	− 0.05	0.139	0.96	0.90–1.02	− 0.14	0.018	0.87	0.78–0.98
Within 48–72 h of surgery								
Neutrophil count[a]	0.08	0.058	1.08	1.00–1.176	0.09	0.149	1.09	0.97–1.23
Lymphocyte count[a]	− 1.16	0.003	0.31	0.15–0.68	− 1.14	0.062	0.32	0.10–1.06
NLR	0.03	0.026	1.03	1.00–1.05	0.04	0.005	1.04	1.01–1.07
Serum sodium ion[d]	0.11	0.003	1.11	1.04–1.19	0.15	0.004	1.16	1.05–1.28
Anion gap[d]	0.04	0.540	1.04	0.92–1.17	0.23	0.012	1.26	1.05–1.50

Table 2 continued

	Early deterioration				Delayed deterioration			
	B	*P*	OR	95% CI	B	*P*	OR	95% CI
rSO_2 left (%)	− 0.06	0.084	0.95	0.89–1.01	− 0.21	0.004	0.81	0.70–0.93
rSO_2 right (%)	− 0.08	0.022	0.92	0.86–0.99	− 0.11	0.064	0.90	0.80–1.01
Multivariate analysis								
Reoperation	2.94	0.002	18.864	2.91–122.49				
With history surgery of brain	3.34	0.013	28.231	1.20–398.68	2.64	0.038	14.052	1.16–170.50
At admission								
WFNS grade 4–5	− 5.13	< 0.001	0.006	0.00–0.06				
Fisher grade 3–4	1.73	0.01	5.617	1.52–20.77				
Serum sodium ion[d]	0.24	0.016	1.266	1.05–1.53				
Within 24 h of surgery								
SAFIRE grade 3–5	5.52	< 0.001	153.46	30.53–771.40				
RBC count[b]					− 2.809	0.002	0.06	0.01–0.36
rSO_2 left (%)	− 0.17	0.007	0.841	0.74–0.95				
Within 24–48 h of surgery								
Serum potassium ion[d]	− 1.51	0.049	0.22	0.05–0.99				
Within 48–72 h of surgery								
rSO_2 left (%)	0.15	0.024	1.166	1.02–1.31				
rSO_2 right (%)	− 0.28	0.001	0.756	0.89–0.92				

Used the logistic regression analysis

CI confidence interquartile, *OR* odds ratio, *WFNS* World Federation of Neurological Societies, *BNI* Barrow Neurological Institute Grading Scale, *WBC* white blood cell count. *RBC* red blood cell, rSO_2 oxygen saturation of cerebral arterial blood, *NLR* neutrophil-to-lymphocyte ratio

[a]Unit of measurement: 10^9/L

[b]Unit of measurement: 10^{12}/L

[c]Unit of measurement: g/L

[d]Unit of measurement: mmol/L

[e]Unit of measurement: ng/ml

Factors Predictive of Neurological Deterioration

The univariate and multivariate analyses for predictive indicators of neurological deterioration among patients with aSAH are summarized in Table 2. A logistic regression model was constructed to reveal the potential indicators for END and DND in patients with aSAH. According to the univariate analysis, the following risk factors were associated with END: age > 55 years, reoperation, SAFIRE grade 3–5, reduced WBC count and increased neutrophil count at admission, NIR, and serum sodium ion

Table 3 Cerebral oxygen saturation characteristics of the subjects

	Bleeding from ruptured aneurysms is mainly diffuse in the cerebral hemisphere		
	Left hemisphere (n = 38), mean (SD)	**Right hemisphere (n = 38), mean (SD)**	**Bilateral hemisphere (n = 18), mean (SD)**
Left frontal part of brain rSO_2 (%)			
Δ At admission	69.29 (5.38)	69.26 (5.16)a	70.28 (7.14)
Δ Within 24 h of surgery	67.73 (4.17)a	68.26 (3.53)	66.50 (15.54)
Δ Within 24–48 h of surgery	68.50 (5.12)a	68.89 (4.63)	67.28 (3.89)
Δ Within 48–72 h of surgery	67.66 (5.86)a	67.55 (2.98)	68.94 (4.39)a
Right frontal part of brain rSO_2 (%)			
Δ At admission	71.53 (5.36)	72.42 (5.59)*b	73.06 (6.15)
Δ Within 24 h of surgery	69.92 (2.38)b	69.87 (3.77)	72.33 (3.91)
Δ Within 24–48 h of surgery	71.13 (3.79)b	69.58 (3.12)	69.44 (4.41)
Δ Within 48–72 h of surgery	70.56 (2.95)b	68.94 (3.52)*	72.67 (5.03)b
Integral inspection			
Inter-group (F, P)	14.374, < 0.001	12.205, 0.001	6.841, 0.013
Time (F, P)	2.536, 0.063	4.032, 0.010	2.451, 0.081
Interaction (F, P)	0.156, 0.926	0.566, 0.639	0.375, 0.772

Used the repeated measures analysis of variance (ANOVA); Since the spherical hypothesis was not satisfied, multivariate tests were used for repeated measures ANOVA

SD standard deviation

*Indicated within ipsilateral differences at the $P < 0.05$

a, b indicates that there is a significant difference ($P < 0.05$) in the change of left and right scores at a fixed time point. All P values reflect the Bonferroni correction

within 48–72 h of surgery; decreased albumin and rSO_2 within 24 h of surgery; decreased albumin and serum potassium ion within 24–48 h of surgery; and decreased lymphocyte count and rSO_2 within 48–72 h of surgery.

In the DND group, the following risk factors were identified: reoperation, with history of brain surgery, WFNS grade 4–5, Fisher grade 3–4, BNI score 4–5, SAFIRE grade 3–5, increased WBC and neutrophil count at admission; procalcitonin within 24 h of surgery; neutrophil count; NIR and anion gap within 24–48 h of surgery; NIR, serum sodium ion, and anion gap within 48–72 h of surgery; and decreased RBC count within 24 h of surgery and rSO_2 in the left frontal area within 24–48 h.

Multivariate logistic regression revealed early predictors of END in patients with aSAH. The results showed that reoperation, with history surgery of brain, WFNS grade 4–5, Fisher grade 3–4, serum sodium ion concentration at admission, SAFIRE grade 3–5, rSO_2 (left frontal

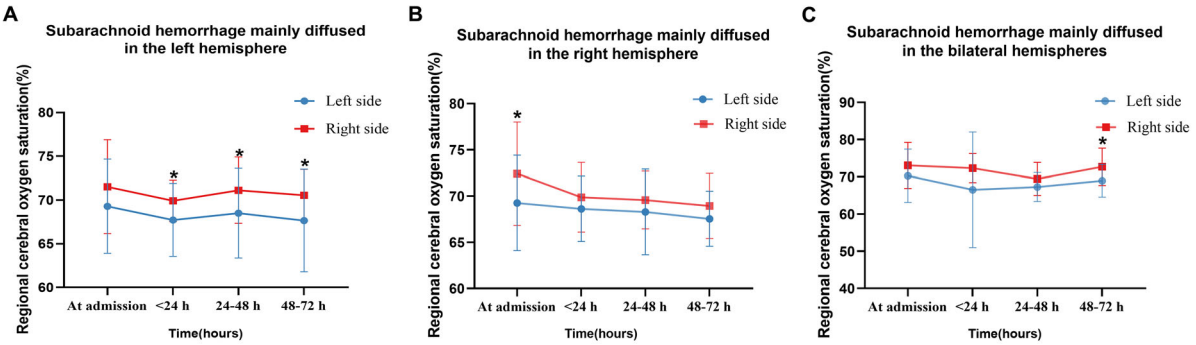

Fig. 2 **a–c** Changes in regional oxygen saturation on the left and right sides of the brain, respectively. *Significant difference ($P < 0.05$) in the change in the left and right scores at a fixed time point

area) within 24 h of surgery, serum potassium ion concentration within 24–48 h of surgery, and rSO_2 (left and right frontal areas) within 48–72 h of surgery were independent predictive indicators of early neurological deterioration. However, only with history of surgery in the brain and a decreased of RBC count within 24 h of surgery were potential independent predictive indicators for DND.

By CT scanning, we found that according to the degree of primary and secondary intracranial distribution of ruptured aneurysm hemorrhage can be divided into the cerebral hemispheres located on the left side, the right hemisphere, and bilateral cerebral hemispheres of the left and right sides of the brain equally. To further determine the changes and relationship between the primary diffuse cerebral hemisphere and regional cerebral oxygen saturation (rSO_2) of aneurysmal hemorrhage in patients with neurological deterioration, repeated ANOVA was conducted (Table 3, Fig. 2). The changes in rSO_2 in the left and right frontal areas of the brain of patients with aSAH with neurological deterioration during the perioperative period (i.e., at admission, within 24 h of surgery, within 24–48 h of surgery, and within 48–72 h of surgery) are shown in Table 3. The results showed that the oxygen saturation in the left and right frontal areas of the brain of the three groups of patients exhibited significant differences ($p < 0.001$, $p = 0.001$, and $p = 0.013$, respectively) during the perioperative period, and changes in the rSO_2 values of the three groups of patients over time are graphically presented in Fig. 2.

To further confirm the role of the aforementioned (in Table 2) covariates collectively for the prediction of aSAH among patients with neurological deterioration, a ROC curve analysis was conducted (Table 4, Fig. 3). The area under the curve (AUC) for early neurological deterioration was 0.928 (95% CI 0.896–0.920, $p < 0.001$), which provided a sensitivity and specificity of 88.57% and 84.18%, respectively. The AUC of delayed neurological deterioration was 0.652 (95% CI 0.537–0.772, $p = 0.008$), which provided a sensitivity and specificity of 60% and 72.78%, respectively.

DISCUSSION

In this study, the rSO_2 was typically lower in patients who experienced neurological deterioration than in those who did not and at least one point in time, and near-infrared spectroscopy could be used to significantly monitor cerebral oxygen differences between the left and right cerebral hemispheres in patients with neurological deterioration. An unordered multiple-classification logistic regression model was constructed, and the results revealed that multiple factors were effective predictors of early neurological deterioration: reoperation, history of brain surgery, WFNS grade 4–5, Fisher grade 3–4, SAFIRE grade 3–5, abnormal serum sodium and potassium levels, and reduced regional cerebral oxygen saturation during the

Table 4 Receiver operating characteristic (ROC) curve data

Factors	AUC	95% CI	*P*	Cutoff	Sensitivity, %	Specificity, %
Early neurological deterioration						
Reoperation	0.605	0.520–0.689	0.012	–	22.86	98.10
With history of brain surgery	0.526	0.443–0.609	0.528	–	7.14	98.10
Admission						
WFNS grade 4–5	0.509	0.428–0.590	0.824	–	82.86	18.99
Fisher grade 3–4	0.562	0.481–0.642	0.137	–	58.57	53.80
Serum sodium ion[a]	0.553	0.469–0.637	0.201	140.20	40.43	70.87
Within 24 h of surgery						
SAFIRE grade 3–5	0.805	0.746–0.864	< 0.001	–	91.43	69.62
rSO_2 left (%)	0.597	0.520–0.673	0.020	69.50	75.71	45.57
Within 24–48 h of surgery						
Serum potassium ion[a]	0.604	0.523–0.682	0.012	3.91	80.00	41.77
Within 48–72 h of surgery						
rSO_2 left (%)	0.586	0.508–0.664	0.039	68.50	60.00	55.70
rSO_2 right (%)	0.591	0.509–0.672	0.029	69.50	41.43	74.05
Combination	0.928	0.896–0.920	< 0.001	–	88.57	84.18
Delayed neurological deterioration						
With history of brain surgery	0.574	0.440–0.707	0.244	–	16.67	98.10
Within 24 h of surgery						
RBC count[b]	0.699	0.585–0.813	0.002	3.73	66.67	69.92
Combination	0.652	0.537–0.772	0.008	–	60.00	72.78

AUC area under the curve, *CI* confidence interval, *WFNS* World Federation of Neurological Societies, *RBC* red blood cell, *rSO_2* regional cerebral oxygen saturation
[a]Unit of measurement: mmol/L
[b]Unit of measurement: 10^{12}/L

perioperative period. However, for delayed neurological deterioration in patients with aSAH, only a history of brain surgery and perioperative decreased RBC count were predictive indicators. Nevertheless, in the preceding step of the statistical analysis, local cerebral oxygen saturation and biochemical markers were shown to be associated with early and delayed neurological deterioration in patients with EBI, revealing an important role and potential clinical significance of microcirculatory function in neurological deterioration.

In our previous review, we proposed that post-SAH microcirculation disorders can be divided into three stages: compensatory, decompensated, and irreversible [17]. The compensation period for microcirculation disorders mainly depends on the autonomic regulation of cerebral vessels, the effective perfusion of brain tissue that has decreased perfusion, the beginning of the accumulation of harmful

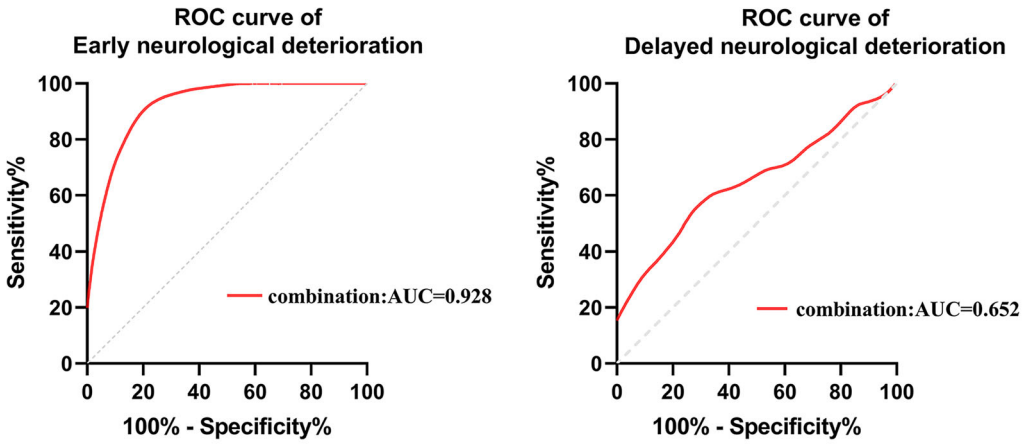

Fig. 3 Receiver operating characteristic (ROC) curve. *AUC* area under the curve

substances other than blood disintegration products, and the beginning of brain tissue ischemia and hypoxia. During the decompensation period, as a result of intracranial inflammatory reactions, the blood–brain barrier is damaged, vasogenic edema and other pathophysiological changes occur, and microcirculation blood stasis and effective perfusion are further reduced, resulting in more severe cerebral ischemia and hypoxia. In the irreversible stage, as a result of the extensive formation of microthrombi, a neutrophil trapping network, neuroinflammation, and other factors [23], regardless of systemic circulation and intracranial perfusion pressure, the intracranial microcirculation completely fails, and the blood flow is in a state of "no entry and no exit", presenting a classic "no-reflow" phenomenon [24]. Therefore, identifying the early microcirculation status of patients with SAH to facilitate timely intervention and treatment in the compensatory and decompensated stages of microcirculation disorders is urgently needed for disease monitoring in the diagnosis and treatment of patients with SAH and EBI.

The changes in rSO_2 during the perioperative period also differed between patients with aSAH with neurological deterioration (END and DND) and patients without neurological deterioration. However, the rSO_2, an independent predictor of the DND model, was removed from the multivariate logistic regression analysis. The rSO_2 measured by NIRS appears to be a reliable marker of regional cerebral tissue oxygenation, indirectly reflecting cerebral perfusion [25]. A review analysis concluded that higher rSO_2 monitored during cardiopulmonary resuscitation (CPR) was consistently associated with an increase in the return of spontaneous circulation (ROSC) rate. However, the differential ability of the rSO_2 to predict neurological outcomes is unclear [26]. One study involving 163 patients with aSAH showed that the rSO_2 was related to DCI and poor 3-month functional outcomes [27]. In contrast, we collected data on rSO_2 during the perioperative period in patients with aSAH, which can also be understood as the EBI period (i.e., 1–3 or 4 days after bleeding); this study collected data 5–10 days after bleeding. This difference could help us explain why the rSO_2 was not significant in the independent predictive DND model but was an independent predictor of the END model. Notably, we discovered that not all rSO_2 values, both bilaterally and at all stages, had a significant impact. When the hemorrhage mainly spread in both hemispheres, there was a significant difference between the left and right rSO_2, and the difference was also found on the fourth day after hemorrhage. This pathological change during hypoperfusion showed a similar process in the mouse model; that is, the phenomenon of red cell block or red cell-free capillaries occurred on the fourth day after bleeding [28], which may help explain why at least one time point can be significantly monitored. Regarding the

significant differences in bilateral rSO_2, in our cohort, the degree of diffusion of ruptured aneurysm hemorrhage in the right and left cerebral hemispheres was characterized by a primary–secondary distribution difference. The combination of a hemorrhage-induced neuroinflammatory response, neuronal cell death, and microvascular spasm due to microcirculatory ischemia results in tissue damage and altered local cerebral oxygenation. Hemodynamic differences before and after rupture of cerebral aneurysms, assessed by quantitative methods, have been explored and found [29]. We cannot deny that penetrating factors such as scalp hair and light scattering affect the infrared light emitted by NIRS during monitoring, but despite these potential confounders, NIRS is still a reliable technique for measuring temporal changes in brain oxygenation over time [30]. Differences in outcomes due to potential influencing factors and the retrospective nature of the study need to be further explored in larger prospective studies.

In the present study, the demographic and clinical manifestations were similar to those in previous studies [31]. Age was significantly associated with neurological deterioration among patients with aSAH. The older the patient is, the worse the basic condition is. In elderly patients, cerebral parenchyma atrophy is common, and the subarachnoid space is enlarged to contain additional blood from ruptured aneurysms [32]. The degree of meningeal fibrosis increases with age, which further leads to impaired CSF circulation on the basis of hemorrhage and reduced CSF absorption [33]; these patients are more prone to hydrocephalus and even neuron damage. In one study involving elderly patients ($\geq$ 60 years) with poor-grade aSAH (WFNS IV and V), survival analysis revealed that increasing age was associated with an increased risk of death after aSAH [34]. Notably, patient chronological age and lower functional status were both independent predictors of worsening clinical and radiological status at admission, as defined by a WFNS grade 4–5 and Fisher grade 3–4, respectively [35]. In the present study, patients who experienced neurological deterioration (END and DND) were not only older but also had a significantly greater proportion of worsening clinical and radiological states than patients without neurological deterioration. Similarly, the higher the Hunt–Hess grade, WFNS grade, and Fisher grade were in patients with aSAH, the greater the risk of poor prognosis was [36–38]. The BNI, which predicts symptomatic vasospasm based on the maximum clot thickness of any pool or fissure, was significantly superior to the Fisher grade in predicting the occurrence of DCI according to multicenter external validation analyses [19]. Both showed similar predictive efficacy in our cohort, but only the Fisher grade was included in the final model of END. Heterogeneity in the selection and definition of various primary endpoints (including symptomatic vasospasm, neurodegeneration, DCI) may contribute to the observed disparity. In addition, the selection bias inherent in retrospective studies contributes to the uneven distribution of sample size characteristics to some extent.

Furthermore, we noted that undergoing a second surgery within a short period is a significant contributing factor to neurological complications. We analyzed the reasons for reoperation in our dataset and found that 77.27% of the patients had acute hydrocephalus. This could lead to poor neurological outcomes and severe cognitive deficits [39–42]. However, complete statistics on the occurrence of hydrocephalus after surgery were not available in our study. The reasons for this were as follows: acute hydrocephalus requires intraventricular drainage (EVD) to reduce harmful secondary reactions and CSF flow obstruction after bleeding [36]. However, the prolonged use of an EVD may complicate the treatment of aSAH and increase the risk of meningitis and/or ventriculitis triggering neurological deterioration. To date, two-sided characterizations of the effectiveness of DC in reducing mortality and the development of neurological deficits due to the loss of brain protection from DC cranial defects and interference with CSF dynamics [37, 38, 43, 44] have been performed.

A large-scale study revealed that patients with responsible aneurysms (< 5 mm in diameter) located in the anterior communicating region had a lower incidence of focal neurological deficits during hospitalization than did

those with nonanterior communicating aneurysms. Additionally, aneurysms within the diameter range of 5–25 mm were identified as independent risk factors for new focal neurological deficits and poor mRS scores during hospitalization [45]. However, our statistical analysis demonstrated no significant association between location or size and neurological deterioration. In this study, among patients who did not experience neurological deterioration, the responsible aneurysm was found to have a smaller diameter than was found in the other two groups of patients with neurological deterioration, and a greater proportion of these aneurysms were located in the anterior circulation. Although these differences did not reach statistical significance, they prompted us to consider certain details, including (1) variations in sample size included in the study, hierarchical classification of aneurysm location and size, and definition and measurement of the study endpoint and (2) inherent selection bias that cannot be completely avoided in retrospective real-world studies.

According to the laboratory findings, previous research has shown that inflammatory/immunologic reactions markedly influence outcomes and predict the clinical course of stroke [46, 47]; in particular, the neutrophil-to-lymphocyte ratio [NIR] has received increased amounts of attention [22, 48, 49]. This study was similar to multiple other studies and showed that NIR radiation is significantly associated with adverse functional outcomes in patients with aSAH, but this association was no longer significant after stepwise regression analysis [31, 50]. As the most common type of leukocyte, neutrophils play a major role in inflammation. Elevated neutrophil counts have been associated with poor outcomes [51]. In this study, higher neutrophil counts were significantly associated with neurological deterioration and were an independent predictor of neurological deterioration. A recent multicenter observational study of 6041 patients with aSAH in China revealed that, compared to lower neutrophil counts, higher neutrophil counts were associated with an increased risk of in-hospital mortality, hospital-acquired infections, and delayed nerve ischemia defects [52]. Interestingly, the NIR was also reported to be an independent predictor of poor neurological outcomes. Possible explanations include the following: (1) Neutrophil counts representing acquired infections shortly before or after the aSAH ictus. (2) Neutrophil-derived free oxygen radicals, proteolytic enzymes, and other products are widely considered involved in the pathogenesis of brain–blood barrier dysfunction [53, 54]. For example, our previous study indicated that neutrophil-derived neutrophil extracellular traps lead to microthrombosis and microcirculation dysfunction [55]. Therefore, aSAH severity and mortality could be tightly associated with neutrophil counts [52], and neurological physicians should pay more attention to patients with aSAH and higher neutrophil counts during the perioperative period.

As previously discussed, we propose that clinical medical care personnel should prioritize the EBI clinical stage (high stage of microcirculation disorders) and pay closer attention to biological indicators; additionally, correcting electrolyte imbalances and improving systemic circulation are crucial for optimizing cerebral perfusion and oxygenation. It has been reported that there is a positive correlation between rSO_2 and cardiac output [56], independent of the mean arterial blood pressure (MAP). However, it is worth noting that rSO_2 may improve as a result of adequate blood flow perfusion and normal blood pressure levels. Furthermore, rSO_2 also relies on a sufficient oxygen supply, with the concentration of hemoglobin in the blood potentially contributing to increased rSO_2. The integration of neurointensive care techniques can enable monitoring of cerebral blood flow and electroencephalography (EEG) signals. The latter is extremely sensitive to ischemia and hypoxia, can reflect rSO_2 to a certain extent by recording changes in brain electrical activity, and can be used to evaluate the metabolic state of brain tissue oxygen demand and oxygen consumption; moreover, the latter has been proven to have excellent ability to predict ischemia in the ICU environment [57]. Sedative drugs are often used to maintain sedation during neurological intensive care. It may affect cerebral blood flow and oxygenation, and

professional scientific evaluation methods can help surgeons avoid confusion in clinical judgment.

Limitations

Several limitations of the current study cannot be ignored. First, as a result of its retrospective nature, the bias introduced by the nature of the study type cannot be completely avoided. Second, the sample sizes of patients with early neurological deterioration and delayed neurological deterioration were relatively small; thus, the validity of the predictors derived from our cohort requires further verification in a future study with a larger sample size. Third, as the data were collected from electronic medical records, several severity score data, such as the SAPS, SOFA, Graeb, and SEBES scores, were not analyzed or collected to better supplement and support the conclusions. In addition, subsequent multicenter prospective clinical trials are needed to further verify the effects of these risk factors, and subsequent basic experiments are needed to explore their pathophysiological mechanism and understand their role in disease progression to guide clinicians in the treatment and judgment of disease.

CONCLUSION

We retrospectively and dynamically collected clinical information on EBI after aSAH. After reoperation, a history of brain surgery, WFNS grades 4–5, Fisher grades 3–4, SAFIRE grades 3–5, abnormal serum sodium and potassium levels, and reduced rSO_2 during the perioperative period were predictive indicators of early neurological deterioration, whereas a history of brain surgery and a decreased perioperative RBC count were predictive indicators of delayed neurological deterioration. However, further studies are needed to determine the role of microcirculation and other predictive factors in the neurocritical management of EBI after SAH, as these factors can reduce the incidence of adverse outcomes and mortality during hospitalization.

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Data Availability. The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Conflict of Interest. Shunyan Yang, Binbin Tan, Jie Lin, Xia Wang, Congying Fu, Kaishan Wang, Jinyu Qian, Jin Liu, Jishu Xian, Liang Tan, Hua Feng, Yujie Chen and Lihua Wang declare that they have no competing interests.

Ethical Approval. The study protocol was reviewed and approved by the Ethics Committee of Southwest Hospital of Army Medical University (No. (B) KY2023040). Written informed consent to participate was waived by the ethical committee as a result of the observational nature of the study. This study was

conducted in accordance with the ethical guidelines of the Helsinki Declaration and reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist.

REFERENCES

1. Wahood W, Rizvi AA, Alexander AY, et al. Trends in admissions and outcomes for treatment of aneurysmal subarachnoid hemorrhage in the United States. Neurocrit Care. 2022;37(1):209–18.

2. Wang YJ, Li ZX, Gu HQ, et al. China Stroke Statistics 2019: A Report From the National Center for Healthcare Quality Management in Neurological Diseases, China National Clinical Research Center for Neurological Diseases, the Chinese Stroke Association, National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention and Institute for Global Neuroscience and Stroke Collaborations. Stroke Vasc Neurol. 2020;5(3):211–39.

3. Neifert SN, Chapman EK, Martini ML, et al. Aneurysmal subarachnoid hemorrhage: the last decade. Transl Stroke Res. 2021;12(3):428–46.

4. Andersen CR, Presseau J, Saigle V, et al. Core outcomes for subarachnoid haemorrhage. Lancet Neurol. 2019;18(12):1075–6.

5. Claassen J, Park S. Spontaneous subarachnoid haemorrhage. Lancet. 2022;400(10355):846–62.

6. Chen Y, Galea I, Macdonald RL, Wong GKC, Zhang JH. Rethinking the original changes in subarachnoid haemorrhage: focusing on real-time metabolism during early brain injury. EBioMedicine. 2022;83: 104223.

7. Taran S, Trivedi V, Singh JM, English SW, McCredie VA. The use of standardized management protocols for critically ill patients with non-traumatic subarachnoid hemorrhage: a systematic review. Neurocrit Care. 2020;32(3):858–74.

8. Lu AY, Damisah EC, Winkler EA, Grant RA, Eid T, Bulsara KR. Cerebrospinal fluid untargeted metabolomic profiling of aneurysmal subarachnoid hemorrhage: an exploratory study. Br J Neurosurg. 2018;32(6):637–41.

9. Helbok R, Schiefecker AJ, Beer R, et al. Early brain injury after aneurysmal subarachnoid hemorrhage: a multimodal neuromonitoring study. Crit Care. 2015;19:75.

10. Uhl E, Lehmberg J, Steiger HJ, Messmer K. Intraoperative detection of early microvasospasm in patients with subarachnoid hemorrhage by using orthogonal polarization spectral imaging. Neurosurgery. 2003;52(6):1307–15 (discussion 15-7).

11. Li Q, Chen Y, Li B, et al. Hemoglobin induced NO/cGMP suppression deteriorate microcirculation via pericyte phenotype transformation after subarachnoid hemorrhage in rats. Sci Rep. 2016;6:22070.

12. Chen Y, Li Q, Tang J, Feng H, Zhang JH. The evolving roles of pericyte in early brain injury after subarachnoid hemorrhage. Brain Res. 2015;1623:110–22.

13. Naraoka M, Matsuda N, Shimamura N, Ohkuma H. Role of microcirculatory impairment in delayed cerebral ischemia and outcome after aneurysmal subarachnoid hemorrhage. J Cereb Blood Flow Metab. 2022;42(1):186–96.

14. Liu H, Dienel A, Scholler K, et al. Microvasospasms after experimental subarachnoid hemorrhage do not depend on endothelin A receptors. Stroke. 2018;49(3):693–9.

15. Seners P, Baron JC. Revisiting "progressive stroke": incidence, predictors, pathophysiology, and management of unexplained early neurological deterioration following acute ischemic stroke. J Neurol. 2018;265(1):216–25.

16. Seners P, Turc G, Oppenheim C, Baron JC. Incidence, causes and predictors of neurological deterioration occurring within 24 h following acute

ischaemic stroke: a systematic review with pathophysiological implications. J Neurol Neurosurg Psychiatry. 2015;86(1):87–94.

17. Zhou J, Guo P, Guo Z, Sun X, Chen Y, Feng H. Fluid metabolic pathways after subarachnoid hemorrhage. J Neurochem. 2022;160(1):13–33.

18. Kistka H, Dewan MC, Mocco J. Evidence-based cerebral vasospasm surveillance. Neurol Res Int. 2013;2013:256713.

19. Neidert MC, Maldaner N, Stienen MN, et al. The Barrow Neurological Institute grading scale as a predictor for delayed cerebral ischemia and outcome after aneurysmal subarachnoid hemorrhage: data from a nationwide patient registry (Swiss SOS). Neurosurgery. 2018;83(6):1286–93.

20. Giraldo EA, Mandrekar JN, Rubin MN, et al. Timing of clinical grade assessment and poor outcome in patients with aneurysmal subarachnoid hemorrhage. J Neurosurg. 2012;117(1):15–9.

21. van Donkelaar CE, Bakker NA, Birks J, et al. Prediction of outcome after aneurysmal subarachnoid hemorrhage. Stroke. 2019;50(4):837–44.

22. Giede-Jeppe A, Reichl J, Sprügel MI, et al. Neutrophil-to-lymphocyte ratio as an independent predictor for unfavorable functional outcome in aneurysmal subarachnoid hemorrhage. J Neurosurg. 2019;132(2):400–7.

23. Hao X, Zeng Z, Liang L, et al. The role of neutrophil extracellular traps in early microthrombosis and brain injury after subarachnoid hemorrhage in mice. Transl Stroke Res. 2023;14(5):752–65.

24. Asano T, Sano K. Pathogenetic role of no-reflow phenomenon in experimental subarachnoid hemorrhage in dogs. J Neurosurg. 1977;46(4):454–66.

25. Mutoh T, Kobayashi S, Tamakawa N, Ishikawa T. Multichannel near-infrared spectroscopy as a tool for assisting intra-arterial fasudil therapy for diffuse vasospasm after subarachnoid hemorrhage. Surg Neurol Int. 2011;2:68.

26. Schnaubelt S, Sulzgruber P, Menger J, Skhirtladze-Dworschak K, Sterz F, Dworschak M. Regional cerebral oxygen saturation during cardiopulmonary resuscitation as a predictor of return of spontaneous circulation and favourable neurological outcome–a review of the current literature. Resuscitation. 2018;125:39–47.

27. Yousef KM, Balzer JR, Crago EA, Poloyac SM, Sherwood PR. Transcranial regional cerebral oxygen desaturation predicts delayed cerebral ischaemia and poor outcomes after subarachnoid haemorrhage: a correlational study. Intensive Crit Care Nurs. 2014;30(6):346–52.

28. Anzabi M, Angleys H, Aamand R, et al. Capillary flow disturbances after experimental subarachnoid hemorrhage: a contributor to delayed cerebral ischemia? Microcirculation. 2019;26(3):e12516.

29. Fujimura S, Yamanaka Y, Takao H, et al. Hemodynamic and morphological differences in cerebral aneurysms between before and after rupture. J Neurosurg. 2023. https://doi.org/10.3171/2023.6.JNS23289.

30. Kampf S, Schramm P, Klein KU. Transcranial Doppler and near infrared spectroscopy in the perioperative period. Curr Opin Anaesthesiol. 2013;26(5):543–8.

31. Wang L, Zhang Q, Zhang G, et al. Risk factors and predictive models of poor prognosis and delayed cerebral ischemia in aneurysmal subarachnoid hemorrhage complicated with hydrocephalus. Front Neurol. 2022;13:1014501.

32. Jeong TS, Yoo CJ, Kim WK, Yee GT, Kim EY, Kim MJ. Factors related to the development of shunt-dependent hydrocephalus following subarachnoid hemorrhage in the elderly. Turk Neurosurg. 2018;28(2):226–33.

33. Dorai Z, Hynan LS, Kopitnik TA, Samson D. Factors related to hydrocephalus after aneurysmal subarachnoid hemorrhage. Neurosurgery. 2003;52(4):763–9 (**discussion 9-71**).

34. Goldberg J, Schoeni D, Mordasini P, et al. Survival and outcome after poor-grade aneurysmal subarachnoid hemorrhage in elderly patients. Stroke. 2018;49(12):2883–9.

35. Zumofen DW, Roethlisberger M, Achermann R, et al. Factors associated with clinical and radiological status on admission in patients with aneurysmal subarachnoid hemorrhage. Neurosurg Rev. 2018;41(4):1059–69.

36. Qian C, Yu X, Chen J, et al. Effect of the drainage of cerebrospinal fluid in patients with aneurismal subarachnoid hemorrhage: a meta-analysis. Medicine (Baltimore). 2016;95(41):e5140.

37. Smith M, Servadei F, Hutchinson PJ. What is new in decompressive craniectomy in neurological emergencies: the good, the bad and the ugly. Intensive Care Med. 2020;46(5):1023–6.

38. Lu C, Feng Y, Li H, et al. Microsurgical treatment of 86 anterior choroidal artery aneurysms: analysis of factors influencing the prognosis. J Neurol Surg A Cent Eur Neurosurg. 2020;81(6):501–7.

39. Paisan GM, Ding D, Starke RM, Crowley RW, Liu KC. Shunt-dependent hydrocephalus after aneurysmal subarachnoid hemorrhage: predictors and long-term functional outcomes. Neurosurgery. 2018;83(3):393–402.

40. Haug Nordenmark T, Karic T, Sorteberg W, Sorteberg A. Predictors of cognitive function in the acute phase after aneurysmal subarachnoid hemorrhage. Acta Neurochir (Wien). 2019;161(1):177–84.

41. Di Russo P, Di Carlo DT, Lutenberg A, Morganti R, Evins AI, Perrini P. Shunt-dependent hydrocephalus after aneurysmal subarachnoid hemorrhage. J Neurosurg Sci. 2020;64(2):181–9.

42. Zaidi HA, Montoure A, Elhadi A, et al. Long-term functional outcomes and predictors of shunt-dependent hydrocephalus after treatment of ruptured intracranial aneurysms in the BRAT trial: revisiting the clip vs coil debate. Neurosurgery. 2015;76(5):608–13 (discussion 13-4; quiz 14).

43. Rosengart AJ, Schultheiss KE, Tolentino J, Macdonald RL. Prognostic factors for outcome in patients with aneurysmal subarachnoid hemorrhage. Stroke. 2007;38(8):2315–21.

44. van Lieshout JH, Mijderwijk HJ, Nieboer D, et al. Development and internal validation of the ARISE prediction models for rebleeding after aneurysmal subarachnoid hemorrhage. Neurosurgery. 2022;91(3):450–8.

45. Roethlisberger M, Aghlmandi S, Rychen J, et al. Impact of very small aneurysm size and anterior communicating segment location on outcome after aneurysmal subarachnoid hemorrhage. Neurosurgery. 2023;92(2):370–81.

46. Boisseau W, Desilles JP, Fahed R, et al. Neutrophil count predicts poor outcome despite recanalization after endovascular therapy. Neurology. 2019;93(5):e467–75.

47. Zhu B, Liu H, Pan Y, et al. Elevated neutrophil and presence of intracranial artery stenosis increase the risk of recurrent stroke. Stroke. 2018;49(10):2294–300.

48. Al-Mufti F, Amuluru K, Damodara N, et al. Admission neutrophil-lymphocyte ratio predicts delayed cerebral ischemia following aneurysmal subarachnoid hemorrhage. J Neurointerv Surg. 2019;11(11):1135–40.

49. Guo Y, Liu J, Zeng H, et al. Neutrophil to lymphocyte ratio predicting poor outcome after aneurysmal subarachnoid hemorrhage: a retrospective study and updated meta-analysis. Front Immunol. 2022;13:962760.

50. Li R, Lin F, Chen Y, et al. A 90-day prognostic model based on the early brain injury indicators after aneurysmal subarachnoid hemorrhage: the TAPS score. Transl Stroke Res. 2023;14(2):200–10.

51. Maestrini I, Strbian D, Gautier S, et al. Higher neutrophil counts before thrombolysis for cerebral ischemia predict worse outcomes. Neurology. 2015;85(16):1408–16.

52. Zhang Y, Li L, Jia L, et al. Neutrophil counts as promising marker for predicting in-hospital mortality in aneurysmal subarachnoid hemorrhage. Stroke. 2021;52(10):3266–75.

53. Manda-Handzlik A, Demkow U. The brain entangled: the contribution of neutrophil extracellular traps to the diseases of the central nervous system. Cells. 2019;8(12):1477.

54. Chou ML, Babamale AO, Walker TL, Cognasse F, Blum D, Burnouf T. Blood-brain crosstalk: the roles of neutrophils, platelets, and neutrophil extracellular traps in neuropathologies. Trends Neurosci. 2023;46(9):764–79.

55. Hao X, Zeng Z, Liang L, et al. The role of neutrophil extracellular traps in early microthrombosis and brain injury after subarachnoid hemorrhage in mice. Transl Stroke Res. 2023;14(5):752–65.

56. Schramm P, Tzanova I, Hagen F, et al. Cerebral oxygen saturation and cardiac output during anaesthesia in sitting position for neurosurgical procedures: a prospective observational study. Br J Anaesth. 2016;117(4):482–8.

57. Hoedemaekers C, Hofmeijer J, Horn J. Value of EEG in outcome prediction of hypoxic-ischemic brain injury in the ICU: a narrative review. Resuscitation. 2023;189:109900.