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ORIGINAL ARTICLE

Correlation between CVS and SII in Aneurysmal Subarachnoid Hemorrhage and Construction of Risk Assessment System

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SUMMARY

Background: **This study aimed to investigate the correlation between cerebral vasospasm (CVS) and systemic immune-inflammation index (SII) in aneurysmal subarachnoid hemorrhage (aSAH) patients and to construct a risk assessment system based on SII.**

Methods: **This study included 230 eligible patients with aSAH from June 1, 2021, through December 30, 2024. By retrospective analysis method, clinical information and laboratory data of the patients were collected. Patients were divided into two groups: those with CVS (CVS^+) and those without CVS (CVS^-). The clinical characteristics of patients were compared, and the correlation between SII index and CVS was analyzed. The risk assessment system was constructed using a Cox regression model, which analyzed independent variables with significant differences.**

Results: **Age of CVS^+ patients was significantly higher than that of CVS^- patients. The CVS^+ group exhibited higher proportions of patients with medium-sized aneurysms, more severe CT imaging features of hemorrhage, increased electrolyte disturbances, and elevated immune system markers compared to the CVS^- group. The median time for CVS onset was 7.5 days when SII was at least 1.58, considerably shorter than the 16 days for SII less than 0.64 and 15 days for SII between 0.64 and 0.93 ($p < 0.0001$). When the SII index was elevated, the risk of CVS increased. The SII-based risk assessment system reduced the significance of age and modified Fisher grade in endpoint event prediction, while increasing the overall predictive value of the model.**

Conclusions: **This study revealed a significant correlation between CVS and SII index in aSAH patients and successfully constructed a risk assessment system based on SII. This system can more accurately predict the risk of CVS in aSAH patients and provides an important reference for clinical decision-making.**

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INTRODUCTION

Subarachnoid hemorrhage (SAH) is a prevalent and severe type of hemorrhagic cerebrovascular condition in neurosurgery [1]. It refers to a common clinical syndrome caused by a lesion at the base or surface of the brain that ruptures a blood vessel and directs blood into the subarachnoid space. Ruptured aneurysms account for a significantly larger share of SAH cases compared to other causes [2]. Common major complications of

aneurysmal SAH (aSAH) include cerebral vasospasm (CVS), hydrocephalus, rebleeding, and in a small percentage of patients, epilepsy, stress-related upper-gastrointestinal bleeding, and pulmonary edema [3]. CVS is a common and serious complication, with an incidence rate of 30% to 70% (4). CVS is a persistent condition where cerebral arterioles constrict due to impaired contractile and dilatory functions of intracranial arteries, following blood entering the subarachnoid space after aSAH. It indirectly causes delayed cerebral ischemia, neurological deficits, and poor clinical outcomes by increasing intracranial pressure, thereby prolonging hospitalization and increasing the healthcare burden for patients [5]. In recent years, CVS resulting from aSAH has emerged as a significant topic of study in brain surgery.

The classification of CVS usually involves two forms, based on the timing of its onset [6]. Mechanical stimulation-induced CVS is the results of blood entering the cerebrospinal fluid post-SAH, frequently referred to as transient, premature, or acute CVS. Generally, the acute/ultra-early cerebral vasospasm arises within the first 24 - 48 hours after SAH. Unlike the delayed vasospasm, this early form is often transient and may resolve within hours.

The second type is the sustained CVS with an undetermined mechanism, identified as persistent or delayed CVS (DCV). Typical DCV usually occurs 3 days after the onset of the disease and peaks at 7 - 8 days, with a duration of approximately 7 - 21 days. The exact mechanism of CVS has not been fully elucidated despite decades of extensive research [7]. In the past few years, improvements in neuroimaging have made it easier to detect vasospasm, but treatment protocols still vary greatly among neurosurgical facilities. For patients suffering from SAH, CVS can cause irreversible ischemic injury [8], with its onset being related to various elements, including blood decomposition products and inflammation [9].

Early systemic inflammatory response after SAH is associated with delayed cerebral ischemia and poor functional outcome [10]. The systemic immune inflammation index (SII), a cutting-edge inflammatory index, has been frequently used to assess the prognosis of individuals with acute ischemic stroke [11]. Also, SII could be used to predict the occurrence of DCV after aSAH [12]. In summary, there is a significant correlation between SII index and CVS occurring after SAH. Monitoring SII and additional inflammatory markers can be useful in anticipating and managing the prognosis of patients with aSAH, helping to lessen the incidence of secondary brain injury. Most studies investigating aSAH-induced CVS have focused on risk factors, with limited attention given to the timing of onset as a significant variable.

In view of this, the aim of this study was to deeply explore the correlation between CVS and SII in aSAH patients and to construct a scientific and effective risk assessment system based on this correlation.

MATERIALS AND METHODS

Study population

From June 1, 2021, through December 30, 2024, 213 patients admitted to the Department of Neurosurgery at The Third People's Hospital of Hubei Province who were eligible for aSAH were included. Inclusion criteria: 1) spontaneous aSAH due to ruptured intracranial aneurysm, in which the diagnosis of intracranial aneurysm was confirmed by computed tomography (CT), magnetic resonance imaging, or lumbar puncture. The diagnosis of aSAH was followed by digital subtraction angiography (DSA) to confirm the intracranial aneurysm; 2) The duration of the disease was within 48 hours (time from disease onset to the first medical contact), and the length of hospitalization was greater than 7 days; and 3) information on the admission routine blood tests was complete. Any of the following were excluded: 1) hemorrhage due to rupture of craniocerebral tumor or craniocerebral metastasis; 2) history of previous craniocerebral trauma; 3) severe endocrine, hematologic, and hepatic/renal diseases; 4) long-term regular or recent history of antiplatelet/anticoagulant medication; 5) refusal of surgical treatment; and 6) death within 14 days of admission to the hospital.

In this retrospective study, informed consent was obtained from patients or their guardians. The study was approved by the Third People's Hospital of Hubei Province Ethics Committee.

Data collection

Subjective indicators were validated by at least two experienced clinicians or technologists, especially in cases of disagreement, whereas objective indicators were directly obtained; 1) demographic characteristics: gender, age, smoking, and comorbidities; 2) basic disease profile: aneurysm size (if there are multiple aneurysms, the one causing the hemorrhage is used as the reference), number, location, secondary rupture, and modified Fisher grade and Hunt-Hess classification; 3) surgical and perioperative information: treatment modality, time of intervention, perioperative period with or without lumbar drainage, and electrolyte disorders (normal range of serum potassium: 3.5 to 5.5 mmol/L, sodium: 135 to 145 mmol/L, and chloride: 96 to 106 mmol/L); 4) laboratory tests: blood calcium, red blood cell (RBC) count, hematocrit (HCT), hemoglobin (Hb), platelet count (PLT), lymphocyte count (LYM), and neutrophil count (NE). The SII index was calculated as (PLT × NE/LYM)/1,000. Case information was retrieved through the hospital electronic case and hospital information system platform.

Hunt-Hess classification and Fisher grade

The Hunt-Hess scale is globally utilized to assess the severity of aneurysm bleeding, decide on the timing for imaging and surgery, and assess treatment efficacy [13]: Grade I: asymptomatic, or with mild headache and cervical stiffness.

Grade II: severe headache, neck stiffness, no neurologic conditions except for brain nerves such as the oculomotor nerve.
Grade III: mild consciousness disorder, agitation, and mild cerebral symptoms.
Grade IV: semi-coma, hemiparesis, early decerebrate rigidity, and autonomic deficits.
Grade V: deep coma, decerebrate rigidity, and endangered state.
Fisher grade [14] allows for the categorization of early onset aSAH patients by the first CT evidence of hemorrhage:
Grade I: small, diffuse hemorrhage with no clot formation and no CT evidence.
Grade II: thin blood clots or 1 clot > 2 mm in thickness.
Grade III: 2 or more blood clots greater than 2 mm in thickness.
Grade IV: intracerebral or intraventricular hematoma with or without clot formation in the subarachnoid space.

Patient management

All patients received routine SAH treatment in the emergency room, which involved checking vital signs, lying down, inhaling oxygen, and fluid administration. The procedure followed the applicable standards and did not include any clinical trials of medications or therapies. In the absence of angiographic data [CT angiography (CTA), CTA/magnetic resonance angiography (MRA), MRA/DSA], the examination was organized according to the patient's condition, with CTA usually performed first. In the absence of contraindications, the perioperative standard involved intravenous use of 20% mannitol for cranial pressure reduction and 0.02% nimodipine (60 mg every 4 hours) for CVS prevention and control. The decision on the surgical approach took into account the patient's age, clinical condition, aneurysm characteristics, and the preferences of the patient or their family. Discharge from the hospital was granted only after patients' postoperative conditions were stable and complications were basically controlled.

CVS diagnosis and outcome

The time between the initial hemorrhage and the first CVS was recorded. There is currently an absence of clear and standardized criteria for defining CVS. Therefore, by using prior literature and clinical experience, the diagnostic criteria were established as follows:
1) aSAH symptoms improved or stabilized by treatment, and then deteriorated or progressively aggravated, with fever, high blood level, and no signs of infection;
2) there was a decline in consciousness from wakefulness to drowsiness or coma, or a coma resurfaced after initially changing to wakefulness;
3) depending on the site of CVS, focal signs such as aphasia, dysarthria, hemiparesis, and agnosia were observed. Symptoms of localized neurological damage may appear gradually over several days or may peak several minutes to 1 hour after a sudden onset;
4) symptoms of increased intracranial pressure, such as headache, vomiting, and optic papilla edema were detected;
5) CVS was detected on DSA or MRA, CTA;
6) transcranial Doppler revealed an increase in blood flow velocity with an abnormal spectrum and turbulence.
The diagnosis of CVS was made if both of the following conditions were met: a) the presence of one or more new clinical symptoms or signs (criteria 1 - 4), and b) the confirmation of vasospasm by either vascular imaging (criterion 5) or transcranial Doppler (criterion 6), after the exclusion of other causes such as hydrocephalus, rebleeding, intracranial hematoma, and electrolyte disturbances. Disagreements were resolved by consensus. Upon confirmation, patients received endovascular treatment, including intra-arterial injection of nimodipine into the ipsilateral internal carotid or vertebral artery in the affected area, particularly in cases of associated posterior circulation vasospasm or percutaneous endoluminal angioplasty via ballooning of the affected vascular segments or temporary stenting.

Statistical analysis

The sample size of the study was estimated using G*Power software version 3.1.9.2 with a significance level of $\alpha = 0.05$, power of $1-\beta = 0.8$, effect size of $d = 0.5$, and two-sided tests. Statistical analyses were performed using SPSS 22.0 software. Normality of the data was determined using the Shapiro-Wilk test. When data followed a normal distribution, they were represented as mean ± standard deviation and analyzed comparatively using Student's *t*-test. For distributions that were skewed, continuous variable data were presented as median (interquartile range, IQR), and the Mann-Whitney U test was employed for comparisons. Count data were expressed as frequencies (n) and ratios (%) and tested by chi-squared test or Fisher's exact test. Kaplan-Meier curves for the occurrence of CVS in groups with different levels of SII were plotted using the occurrence of CVS as the endpoint event and the time of the event as the time variable. Variables with significant differences in the univariate analyses were included in Cox risk regression analyses and risk assessment models were constructed with or without SII to predict the occurrence of CVS in aSAH. The predictive value of the models was evaluated in terms of ROC and area under the curve (AUC). Data were plotted using an online platform https://hiplot.cn. $p < 0.05$ was considered statistically significant.

Table 1. Demographic and clinical parameters of patients with subarachnoid hemorrhage.

Independent variable	CVS^- (n = 132)	CVS^+ (n = 98)	p-value
General characteristics			
Age, years	56.6 ± 12.3	61.3 ± 10.8	< 0.001
Male	52 (39.39%)	40 (40.82%)	0.828
Smoking	12 (9.09%)	10 (10.20%)	0.777
Comorbidities			
Hypertension	59 (44.70%)	49 (50.00%)	0.426
Diabetes	10 (7.58%)	15 (15.31%)	0.063
Dyslipidemia	5 (3.79%)	5 (5.10%)	0.747
Aneurysm size			
≤ 0.5 cm	93 (70.45%)	52 (53.06%)	0.036
0.6 - 1.5 cm	36 (27.27%)	44 (44.90%)	
1.6 - 2.5 cm	2 (1.52%)	2 (2.04%)	
> 2.5 cm	1 (0.76%)	0 (0.00%)	
Multiple aneurysms	26 (19.70%)	13 (13.27%)	0.199
Aneurysm location			
AcoA	53 (40.15%)	37 (37.76%)	0.257
MCA	27 (20.45%)	20 (20.41%)	
ICA	25 (18.94%)	21 (21.43%)	
ACA	4 (3.03%)	3 (3.06%)	
PCA	23 (17.42%)	17 (17.35%)	
Secondary rupture of aneurysm	1 (0.76%)	4 (4.08%)	0.166
Modified Fisher grade			
1	92 (69.70%)	34 (34.69%)	< 0.001
2	4 (3.03%)	6 (6.12%)	
3	30 (22.73%)	43 (43.88%)	
4	6 (4.55%)	15 (15.31%)	
Hunt-Hess classification			
I	89 (67.42%)	33 (33.67%)	< 0.001
II	20 (15.15%)	6 (6.12%)	
III	18 (13.64%)	43 (43.88%)	
IV	4 (3.03%)	15 (15.31%)	
V	1 (0.76%)	1 (1.02%)	
Surgical approach			
Surgical clipping	31 (23.48%)	30 (30.61%)	0.226
Intervention therapy	101 (76.52%)	68 (69.39%)	
Time from onset to surgery			
≤ 24 hours	20 (15.15%)	26 (26.53%)	0.1
24 - 48 hours	33 (25.00%)	20 (20.41%)	
> 48 hours	79 (59.85%)	52 (53.06%)	
Lumbar drainage	7 (5.30%)	10 (10.20%)	0.16
Electrolyte disturbance	52 (39.39%)	66 (67.35%)	< 0.001

Table 1. Demographic and clinical parameters of patients with subarachnoid hemorrhage (continued).

Independent variable	CVS^- (n = 132)	CVS^+ (n = 98)	p-value
Laboratory tests			
Ca^{2+} (mmol/L)	2.23 (2.16, 2.33)	2.26 (2.14, 2.35)	0.572
RBC ($\times 10^{12}$/L)	4.56 ± 0.49	4.61 ± 0.48	0.325
HCT (%)	41.21 ± 4.36	41.32 ± 4.03	0.394
Hb (g/L)	138.65 ± 15.69	141.66 ± 14.37	0.241
PLT ($\times 10^9$/L)	210.01 ± 37.45	223.83 ± 42.18	0.01
NE ($\times 10^9$/L)	9.0 (6.2, 11.1)	10.6 (7.7, 13.5)	< 0.001
LYM ($\times 10^9$/L)	0.85 (0.62, 1.66)	1.02 (0.69, 1.55)	0.706
SII	1.70 (0.98, 2.52)	2.37 (1.79, 3.02)	< 0.001

AcoA anterior communicating artery, MCA middle cerebral artery, ICA internal carotid artery, ACA anterior cerebral artery, PCA posterior cerebral artery. Electrolyte disturbance was defined when any of serum potassium, sodium, or chloride exceeded the normal range. RBC red blood cell count, HCT hematocrit, Hb hemoglobin, PLT platelet count, LYM lymphocyte count, NE neutrophil count, SII systemic immunoinflammatory index. Values were expressed as X ± S or median (IQR). $p < 0.05$ was statistically significant.

Table 2. Demographic and clinical parameters of patients with vasospasm at different time periods.

	CVS^+ < 8 days (n = 49)	$CVS^+ \geq 8$ days (n = 49)	p-value
General characteristics			
Age, years	59.8 ± 10.2	64.0 ± 10.5	0.046
Male	22 (44.90%)	18 (36.73%)	0.411
Smoking	5 (10.20%)	5 (10.20%)	1
Comorbidities			
Hypertension	20 (40.82%)	29 (59.18%)	0.069
Diabetes	6 (12.24%)	9 (18.37%)	0.4
Dyslipidemia	3 (6.12%)	2 (4.08%)	1
Aneurysm size			
≤ 0.5 cm	32 (65.31%)	20 (40.82%)	0.049
0.6 - 1.5 cm	16 (32.65%)	28 (57.14%)	
1.6 - 2.5 cm	1 (2.04%)	1 (2.04%)	
Multiple aneurysms	5 (10.20%)	8 (16.33%)	0.372
Aneurysm location			
AcoA	18 (36.73%)	19 (38.78%)	0.875
MCA	9 (18.37%)	12 (24.49%)	
ICA	12 (24.49%)	9 (18.37%)	
ACA	2 (4.08%)	1 (2.04%)	
PCA	8 (16.33%)	8 (16.33%)	
Secondary rupture of aneurysm	2 (4.08%)	2 (4.08%)	1
Modified Fisher grade			
1	22 (44.90%)	12 (24.49%)	0.093
2	4 (8.16%)	2 (4.08%)	
3	18 (36.73%)	25 (51.02%)	
4	5 (10.20%)	10 (20.41%)	

Table 2. Demographic and clinical parameters of patients with vasospasm at different time periods (continued).

	CVS^+ < 8 days (n = 49)	CVS^+ ≥ 8 days (n = 49)	p-value
Hunt-Hess classification			
I	21 (42.86%)	12 (24.49%)	0.063
II	5 (10.20%)	1 (2.04%)	
III	18 (36.73%)	25 (51.02%)	
IV	5 (10.20%)	10 (20.41%)	
V	0 (0.00%)	1 (2.04%)	
Surgical approach			
Surgical clipping	13 (26.53%)	17 (34.69%)	0.381
Intervention therapy	36 (73.47%)	32 (65.31%)	
Time from onset to surgery			
≤ 24 hours	16 (32.65%)	10 (20.41%)	0.388
24 - 48 hours	9 (18.37%)	11 (22.45%)	
> 48 hours	24 (48.98%)	28 (57.14%)	
Lumbar drainage	5	5	1
Electrolyte disturbance	30 (61.22%)	36 (73.47%)	0.196
Laboratory tests			
Ca^{2+} (mmol/L)	2.24 (2.12, 2.40)	2.28 (2.19, 2.30)	0.589
RBC ($\times 10^{12}$/L)	4.49 ± 0.42	4.67 ± 0.62	0.125
HCT (%)	41.01 ± 3.59	41.92 ± 4.33	0.829
Hb (g/L)	145.3 ± 13.25	138.46 ± 17.27	0.394
PLT ($\times 10^9$/L)	188.22 ± 26.46	217.46 (185.8, 262.16)	< 0.001
NE ($\times 10^9$/L)	8.45 ± 2.57	10.24 (7.42, 13.08)	0.006
LYM ($\times 10^9$/L)	1.39 (0.74, 2.02)	0.81 (0.63, 1.34)	0.013
SII	1.91 (1.58, 2.38)	3.19 (2.83, 3.51)	< 0.001

AcoA anterior communicating artery, MCA middle cerebral artery, ICA internal carotid artery, ACA anterior cerebral artery, PCA posterior cerebral artery. Electrolyte disturbance was defined when any of serum potassium, sodium, or chloride exceeded the normal range. RBC red blood cell count, HCT hematocrit, Hb hemoglobin, PLT platelet count, LYM lymphocyte count, NE neutrophil count, SII systemic immunoinflammatory index. Values were expressed as X ± S or median (IQR). $p < 0.05$ was statistically significant.

Table 3. Multifactorial Cox proportional risk analysis for the risk assessment system of developing CVS after aneurysmal subarachnoid hemorrhage.

	Variables	β	S.E	Z	p	HR (95% CI)
Model 1	Age	0.03	0.01	2.37	0.018	1.03 (1.01 - 1.06)
	Fisher grade	0.7	0.3	2.33	0.02	2.01 (1.12 - 3.63)
	Electrolytes	0.93	0.32	2.93	0.003	2.55 (1.36 - 4.75)
Model 2	Age	0.02	0.01	1.86	0.063	1.02 (1.00 - 1.05)
	Fisher grade	0.5	0.31	1.62	0.105	1.66 (0.90 - 3.05)
	Electrolytes	0.98	0.32	3.07	0.002	2.67 (1.42 - 4.99)
	SII	0.46	0.2	2.29	0.022	1.59 (1.07 - 2.36)

HR hazards ratio, CI confidence interval. Independent variables included in model 1: age (continuous values), aneurysm size (small vs. medium and above), modified Fisher grade (1/2 vs. 3/4), Hunt-Hess classification (I/II/III vs. IV/V), and electrolyte disturbance (no vs. yes). The independent variable incorporated in model 2 adds SII (continuous values) to model 1.

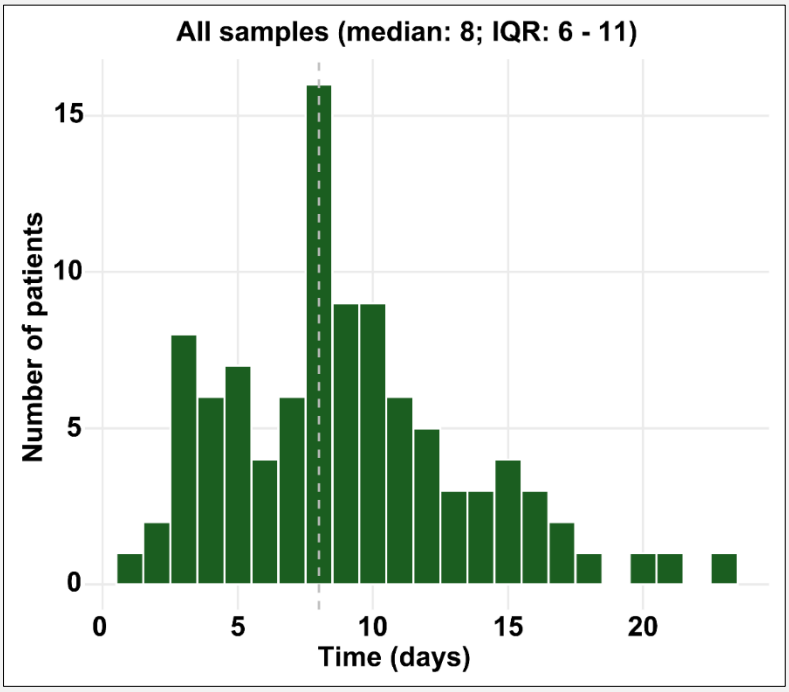

Figure 1. Distribution of CVS over time.

RESULTS

Clinical parameters of patients

A total of 230 patients with aSAH were studied, all of whom received appropriate treatment within a set time. Out of the total, 92 (40.00%) were males and 138 (60.00%) were females, with a mean age of 58.6 years ± 11.5 years. CVS occurred in 98 (42.61%) patients during their stay in the hospital. Patients' clinical data are summarized in Table 1. The age of the patients with CVS was significantly higher than that of the patients without CVS ($p < 0.001$). In the CVS group, the proportion of patients with medium-sized aneurysms (0.6 - 1.5 cm) was higher than that of the patients in the group without CVS. Consistent with expectations, patients in the CVS group had more severe hemorrhagic CT imaging features, as evidenced by a higher proportion of patients with Fisher grades 3 and 4 and Hunt-Hess grades III and IV, than those in the group without CVS. In addition, we observed a significantly higher proportion of electrolyte disturbances in the CVS group than in the group without CVS ($p < 0.001$). On the immune system, patients with CVS had increased PLT, NE, and SII. The two groups did not show statistically significant differences in gender, comorbidities, aneurysm location, surgical technique, procedure length, and lumbar drainage performance (all $p > 0.05$).

Distribution of CVS occurrence and risk modeling

The median duration of CVS detected in this study was 8 days (IQR 6 - 11 days), as shown in Figure 1. The mean duration of CVS was 2 days (IQR 1 - 5 days). The $CVS^+ < 8$ days group and the $CVS^+ \geq 8$ days group were set according to the median duration of CVS occurrence, with a median threshold of 8 days. Table 2 compares the clinical characteristics of the two groups of patients. Patients in the $CVS^+ < 8$ days group had a higher age ($p = 0.046$) and a higher proportion of medium-sized aneurysms ($p < 0.05$) compared with the $CVS^+ \geq 8$ days group. In addition, PLT, NE, LYM, and SII also had higher levels in the $CVS^+ < 8$ days group (all $p < 0.05$). The $CVS^+ < 8$ days group had a higher percentage of patients with Fisher grades 3 and 4 and Hunt-Hess grades III and IV, even though no difference was seen in the modified Fisher grade and Hunt-Hess classification between the groups.

By using Kaplan-Meier curves, the first occurrence of CVS after admission was the focal event, and events not observed before discharge were censored or truncated. Grouping was performed according to SII index, SII < 0.64, SII = 0.64 - 0.93, and SII ≥ 1.58. As shown in Figure 2, the number of CVS that occurred in the three groups was 11, 49, and 38, respectively. When SII ≥ 1.58, the median time until occurrence of CVS was 7.5 days, which was significantly shorter than that of the

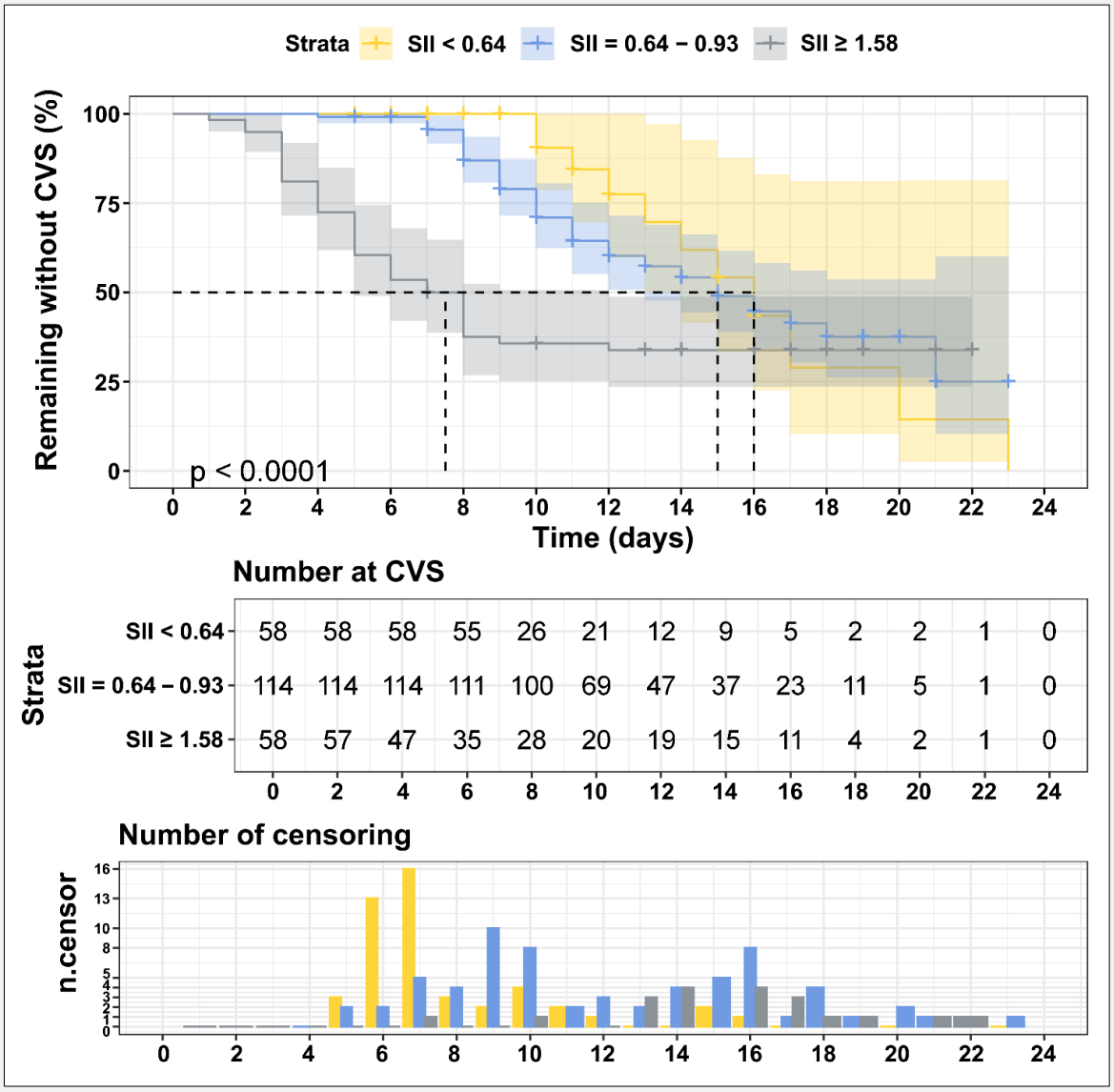

Figure 2. Kaplan-Meier curves.

p-values were calculated by log-rank test.

other two groups (16 days for SII < 0.64, and 15 days for SII = 0.64 - 0.93, p < 0.0001). From this basis, a risk assessment system for CVS was constructed using a Cox regression model, which included independent variables with significant differences in the univariate analysis, including age, aneurysm size, modified Fisher grade (grade 1/2 vs. grade 3/4), Hunt-Hess classification (I/II/III vs. IV/V), electrolyte disturbances (no vs. yes), and SII (continuous values). As shown in Table 3, in model 1 (without the inclusion of SII), increasing age, higher modified Fisher grade, and electrolyte disturbances were independent risk factors influencing the development of CVS in patients with aSAH. While incorporating SII into model lessened the influence of age and modified Fisher grade on predicting endpoint events, it enhanced the model's overall risk assessment predictive value, as shown in Figure 3A and B (Molde 1 vs. Moled 2, AUC = 0.67 vs. AUC = 0.73).

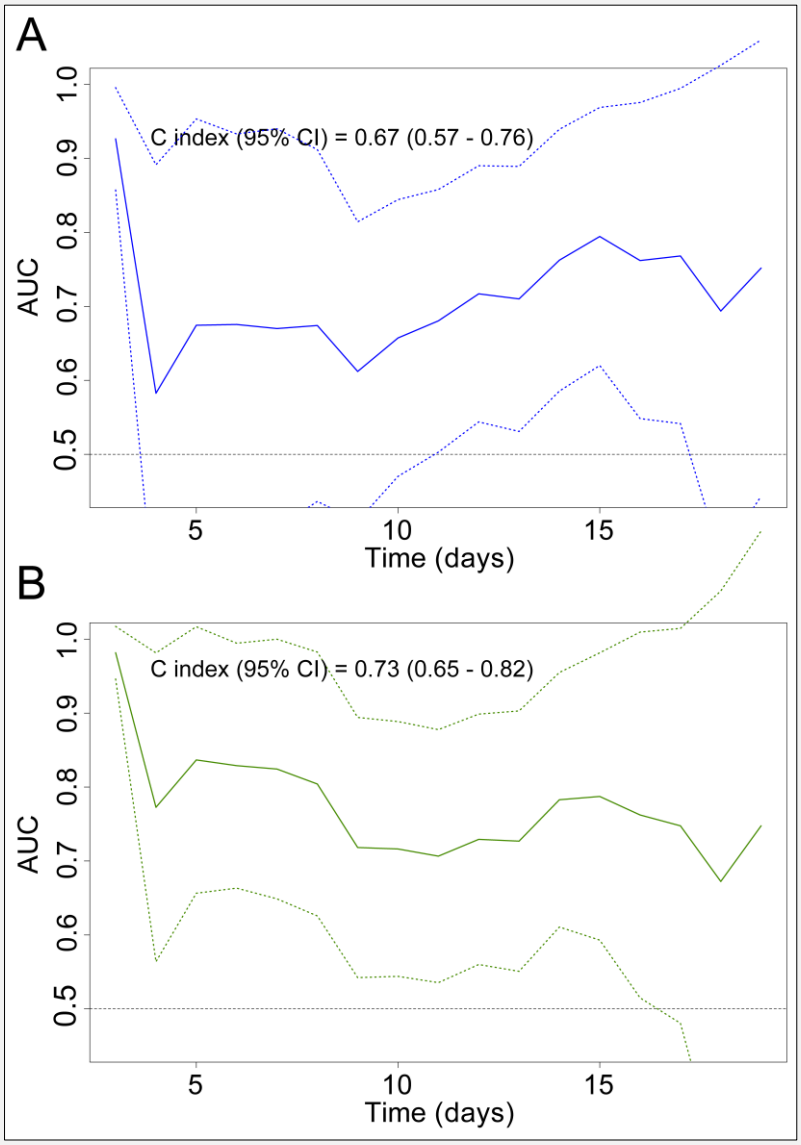

Figure 3. ROC curves based on Cox' proportional risk model.

A Model 1 and B Model 2.

DISCUSSION

aSAH is a serious cerebrovascular disease often accompanied by CVS, and this may occur both preoperatively and postoperatively. This study demonstrated for the first time that SII was associated with time to CVS in aSAH, with a median time to CVS of 7.5 days when SII was ≥ 1.58, which was significantly shorter than that in the other two groups (16 days for SII < 0.64 and 15 days for SII = 0.64-0.93, $p < 0.0001$). The inclusion of SII in the model reduced the predictive value of age and modified Fisher grade on endpoint events but improved the predictive value of the overall risk assessment model. It is also of interest that electrolyte disturbances were an independent risk factor influencing the occurrence of CVS in patients with aSAH in this study, which seems to be less frequently found in other studies. Although techniques such as transcranial Doppler ultrasound and DSA have been used to diagnose patients who are experiencing CVS [15], there is a lack of an accurate and objective predictive tool that can effectively assess the development of symptoms before they appear. The

Fisher grade [16] and Hunt-Hess classification [13], in their modified versions, serve as imaging assessment methods to determine CVS risk according to the admission CT scan. Although the scale demonstrates high sensitivity, its specificity and inter-assessor agreement need to be improved. The newly proposed SII index [17], which combines changes in peripheral blood NE, LYM, and PLT counts, provides an additional specificity advantage as a novel, easily accessible, and noninvasive biomarker. This index can help to precisely identify a group of patients at high risk for CVS and provide a strong rationale for early intervention in treatment.

The present study observed a significant difference in SII index between aSAH patients with or without CVS, a finding that suggests that the early inflammatory response may play a key role in the development of delayed neurological dysfunction after aSAH.

The relationship between systemic inflammatory response syndrome and the prognosis of aSAH is a complex and multifaceted topic. In a retrospective study, SII and SIRI levels on the third postoperative day independently predict poor prognosis in aSAH [18]. Although CVS also occurs in patients with preoperative aSAH, there may be some minor vascular changes or underlying spasmodic tendencies prior to bleeding that are usually not easily detected and quantified. Postoperative CVS, on the other hand, is influenced by a number of factors and has a high incidence. Therefore, in order to minimize the occurrence of postoperative CVS, both clinicians and patients need to pay close attention to the postoperative situation. In aSAH, elevated NLR is closely associated with poor clinical outcomes and not only predicts clinical outcomes in patients with aSAH but also correlates with the risk of complications such as delayed cerebral ischemia or rebleeding [19]. There is also evidence that PLT activation plays a non-negligible role in aSAH adverse outcomes. It has been shown that PLR, a new marker of atherosclerotic inflammation, is recognized as a predictor in cardiovascular disease, and elevated PLR is associated with adverse outcomes and mortality [20]. A major highlight of this study is that by integrating NE changes and LYM and PLT counts to form the SII index, it was found to perform better in predicting CVS than its components alone. This finding provides new perspectives and tools for risk assessment and prognostic prediction in patients with aSAH.

The median time to CVS in this study aSAH was 8 days. However, in the cohort with SII $\geq$ 1.58, the median time to develop CVS was shortened to 7.5 days, whereas the median time to develop CVS was more than 14 days in both the SII < 0.64 and SII = 0.64 - 0.93 cohorts. This suggests that there is a correlation between increased SII and earlier CVS events in patients with aSAH.

In multivariate analysis, advanced age and higher Fisher grade remained independent risk factors for CVS events in aSAH patients. Age has been found to be negatively associated with the risk of CVS [21]. Data on aneurysm location and incidence of vasospasm are less clear, although some studies have shown an increased incidence of anterior circulation aneurysms. This study observed a significant difference in electrolyte disturbances between the CVS^- and CVS^+ groups. A previous study has developed a column-line graph model for predicting the risk of postoperative CVS in patients with aSAH and revealed that electrolyte disturbance is one of the independent risk factors for CVS [22]. In this investigation, the occurrence time of CVS was employed as a time variable to build a risk assessment model for CVS in aSAH, a method seemingly not used in earlier studies. Multifactorial Cox regression analysis showed that the predictive value of the overall risk assessment model was improved (AUC from 0.67 to 0.73) after SII was included as a continuous-valued independent variable in the base model (model 1).

Some limitations are present in this study. It used a retrospective study design, which can analyze existing medical record data but may be limited by the completeness, accuracy, and consistency of the data. Retrospective studies might not completely account for all possible confounding factors, potentially impacting the accuracy and reliability of the results. Although most CVS occur postoperatively, there may be significant differences in pathogenesis, clinical manifestations, and treatment strategies between preoperative and postoperative CVS. Therefore, failure to compare the two separately may confound the findings and make the understanding of the relationship between SII and CVS less thorough and accurate. On the therapeutic side, the management of postoperative CVS remains a challenge. Interventional endovascular therapy is a standard treatment for CVS, but it does not substantially reduce delayed ischemia incidence and may result in poorer clinical outcomes [23]. Therefore, the management of postoperative cerebral vasospasm requires a combination of factors, including individual patient differences and preoperative and postoperative hemodynamic changes. In summary, patients with aSAH are at risk for CVS both preoperatively and postoperatively. Future studies need to further explore effective preventive and therapeutic strategies to improve the clinical outcomes of patients.

CONCLUSION

This study revealed the clinical characteristics, distribution pattern, and risk assessment model of CVS in patients with aSAH. SII predicts the occurrence of CVS with its elevated level. This research not only enhances the comprehension of the pathophysiological processes of aSAH and its complications but is also anticipated to offer new and more accurate biological markers for clinical treatment and prognosis evaluation. Meanwhile, by constructing a risk assessment system, it is expected to provide strong support for the early intervention and precise treatment of aSAH patients, thus further improving the therapeutic effects and quality of life of patients.

Data Availability Statement:
Data is available from the corresponding author on request.

Consent to Participate:
Written informed consent was obtained from each subject.

Consent to Publish:
Written informed consent for publication was obtained from all participants.

Ethical Approval Statement:
All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. All subjects were approved by the Third People's Hospital of Hubei Province (No. 202012WH-21).

Declaration of Interest:
The authors have no conflicts of interest to declare.

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