

In-Hospital Risk Factors and Short-Term Outcomes for Subarachnoid Hemorrhage

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Objective: To explore the relevant factors affecting the prognosis of subarachnoid hemorrhage.

Methods: 284 patients with subarachnoid hemorrhage who were hospitalized in our hospital from January 1, 2022 to June 30, 2024 were selected and divided into a good prognosis group and a poor prognosis group according to the modified Rankin Scale (mRS) score. The general clinical data of the patients were also collected, and the independent risk factors affecting the poor prognosis of the patients were screened by univariate logistic regression analysis.

Results: Patients with a favorable prognosis had a lower incidence rate of rebleeding (4.72% vs 17.65%; $P=0.001$), electrolyte disturbances (21.46% vs 41.18%; $P<0.001$), lower respiratory tract infection (5.58% vs 35.29%; $P<0.001$), urinary tract infection (1.72% vs 15.69%; $P<0.001$) and gastrointestinal infection (2.15% vs 11.76%; $P<0.001$) than patients with an unfavorable prognosis. Therefore, coinfection is an independent risk factor for prognosis. After adjusting for covariates, logistic regression analysis identified the prognosis of subarachnoid hemorrhage was related to coinfections (adjusted odds ratio =2.057; 95% CI: 1.516~2.791; $P<0.001$).

Conclusion: Coinfection is a very important independent risk factor affecting prognosis, and clinical care should focus on how to reduce coinfection during hospitalization in patients with subarachnoid hemorrhage and treat it aggressively to reduce mortality and disability and improve patient prognosis.

Keywords: subarachnoid hemorrhage, prognosis, infections, risk factors, treatment

Introduction

Subarachnoid hemorrhage (SAH) is a clinical syndrome caused by the rupture of a diseased vessel on the surface or base of the brain and the direct entry of blood into the subarachnoid space; it is a devastating neurological disease with high disability and mortality rates and a poor overall prognosis.¹⁻³ Therefore, it is necessary to study the treatment and prognosis of SAH. According to the literature, prognosis is influenced by a number of factors, and available studies suggest that infection may be an important factor affecting prognosis.^{4,5} It has also been shown that age, underlying disease, Hunt-Hess classification, World Federation of Neurological Societies (WFNS) classification, and Fisher classification are independent risk factors affecting the prognosis of subarachnoid hemorrhage.⁶⁻¹¹ There are different views and controversies about the factors affecting the prognosis of subarachnoid hemorrhage. In this study, we retrospectively analyzed the relevant factors affecting the prognosis of subarachnoid hemorrhage, aiming to screen out the independent risk factors affecting the prognosis of patients, intervene early on the risk factors affecting the prognosis of patients, and clarify the key directions of clinical prevention and treatment to provide a theoretical basis for the treatment of SAH. In short, this study aims to explore how to intervene in SAH before patients get worse: such an early warning algorithm could be better explored. The following is reported.

Methods

Data Source

Patients were screened at the Affiliated Jiangning Hospital with Nanjing Medical University. The hospital ethics committee approved the study (approved number, 2021-03-033-K01, May 11(th), 2021). Hospitalized patients aged 18

years or older with a diagnosis of acute SAH were consecutively enrolled from January 1, 2022 to June 30, 2024. Data on patient demographics, clinical and imaging characteristics, and treatment details were collected from the inpatient medical record system. Data were collected on demographics, medical history, clinical presentation, laboratory findings, management and outcomes.

Study Design and Population

This observational, prospective and single-center study was conducted in adults with acute SAH. Participants were included if they met all of the following criteria: 1) age 18 years or older at baseline; 2) a clear history of head injury prior to the onset of symptoms 3) cranial CT was performed within 12 hours of admission and DWI sequence review of cranial MRI was performed before discharge; 4) two experienced neuroradiologists diagnosed SAH by CT scan; and 5) higher image quality was available for subsequent neuroimaging evaluation. Patients with acute intracranial hemorrhage, acute cardiovascular disease, severe cardiopulmonary insufficiency, severe hepatic insufficiency, severe renal insufficiency, a clear history of previous brain injury, and intracranial tumors were excluded. A total of 361 patients aged 18 years or older with SAH were enrolled. All patients provided informed consent and were enrolled if they met all inclusion criteria. At the end of the study, only 284 eligible patients were analyzed, and a detailed study flowchart is shown in Figure 1.

Prognostic Assessment

The mRS score was used to evaluate all patients who met the enrollment criteria at 3 months. The primary outcome was the distribution of mRS scores at 3 months after SAH. An mRS score < 3 indicated a favorable prognosis, while an mRS score > 2 indicated an unfavorable prognosis.¹² Patients were then classified as having a favorable prognosis (mRS score

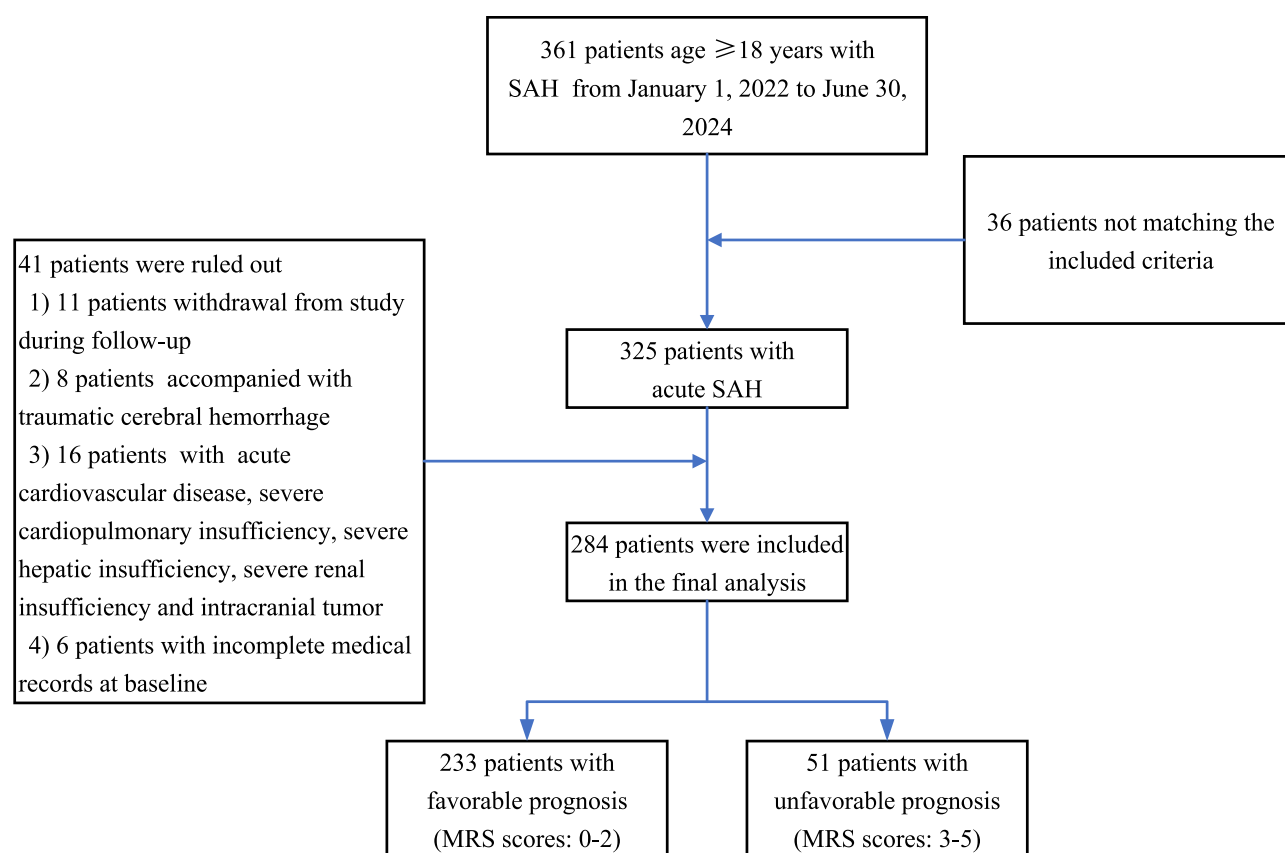


Figure 1 Flow diagram of patient selection.

of 0–2) or an unfavorable prognosis (mRS score of 3–6). Patients who died during follow-up were eligible for inclusion and were classified as having an unfavorable prognosis.

Scale Evaluation

The modified Fisher Scale is useful in predicting the risk of complications and outcomes after SAH, such as the development of cerebral vasospasm, which can cause stroke-like symptoms.¹³ The severity of SAH was assessed at baseline using the modified Fisher scale according to the results of the CT scan at the time of admission. Clinical severity of SAH was measured on hospital admission using the Hunt and Hess Scale, which is a graded scale used to predict the rate of mortality based solely on clinical features in a patient presenting with aneurysmal SAH.¹⁴

Complications

There are four major complications of SAH. These complications are vasospasm (leading to delayed cerebral infarction), hydrocephalus, seizure, and rebleeding. According to the previous literature, we have collected the complications of rebleeding, delayed cerebral infarction, hydrocephalus, seizure, electrolyte disturbances and co-infections.^{15,16} The definition of complications was as previously reported in the literature.^{17,18} Concomitant infection is our focus, so we record whether patients have the following infections, including upper respiratory tract infection, lower respiratory tract infection, gastrointestinal tract infection, and urinary tract infection. Upper respiratory tract infection was defined as an acute infection involving the upper respiratory tract, including the nose, sinuses, pharynx, or larynx.¹⁹ A lower respiratory tract infection was defined as either pneumonia, difficulty breathing, or respiratory problems.²⁰ Gastrointestinal infection was defined as having either diarrhea, nausea, cramps, loss of appetite, and fever.²¹ Urinary tract infection was defined as clinical symptoms and positive urine culture.²²

Statistical Methods

Continuous data are summarized as means with SDs for data with a normal distribution or as medians with interquartile ranges for data with a skewed distribution. Categorical data are presented as frequencies with proportions. A two-sample *t*-test was used to compare continuous data. Categorical data were analyzed using the chi-squared test. Logistic multivariate analyses were performed to identify risk factors for SAH prognosis. All statistical analyses were performed with SPSS 25.0 software (SPSS, Chicago, IL). Differences were considered statistically significant at $P < 0.05$.

Results

Baseline Characteristics of the Subjects

Of the 284 enrolled patients, 233 (82.04%) were identified as with, and 51 (17.96%) as without favorable prognosis. Patients with a favorable prognosis had a lower ratio of current smoker (14.16% vs 29.41%; $P < 0.01$) than those without. Patients with a favorable prognosis had a lower Serum uric acid level (259.11 ± 107.95 vs 315.28 ± 125.42 $\mu\text{mol/L}$; $P < 0.01$) than those without. For scale scores at admission, patients with a favorable prognosis had lower scores on both the modified Fisher scale (Grade 1, 28.76% vs 7.84%; Grade 2, 40.77% vs 25.49%; Grade 3, 16.31% vs 25.49%; Grade 4, 14.16% vs 41.76%; $P < 0.001$) and the Hunt and Hess scale (Grade 1, 18.03% vs 9.80%; Grade 2, 69.10% vs 41.18%; Grade 3, 11.16% vs 25.49%; Grade 4, 1.72% vs 15.69%; Grade 5, 0.00% vs 7.84%; $P < 0.001$). For complications, patients with a favorable prognosis had a lower incidence rate of rebleeding (4.72% vs 17.65%; $P = 0.001$), electrolyte disturbances (21.46% vs 41.18%; $P < 0.001$), lower respiratory tract infection (5.58% vs 35.29%; $P < 0.001$), urinary tract infection (1.72% vs 15.69%; $P < 0.001$) and gastrointestinal infection (2.15% vs 11.76%; $P < 0.001$) than patients with an unfavorable prognosis. The details are shown in Table 1.

Logistic Regression Analysis Affecting the Prognosis of Subarachnoid Hemorrhage

After adjusting for covariates, logistic regression analysis identified the prognosis of SAH was related to coinfections (adjusted odds ratio = 2.057; 95% CI: 1.516–2.791; $P < 0.001$). Moreover, current smoker (adjusted odds ratio = 0.340; 95% CI: 0.142–0.814; $P < 0.05$), modified Fisher scale (adjusted odds ratio = 1.617; 95% CI: 1.067–2.451; $P < 0.05$), Hunt

Table I Clinical Characteristics of Patients with and without a Favorable Prognosis at Baseline (n = 284)

Variables	Patients with Favorable Prognosis (n = 233)	Patients with Unfavorable prognosis (n = 51)	P value
Demographic characteristics			
Age, y, mean ± SD	59.75 ± 11.39	60.20 ± 13.49	0.805
Male, n (%)	93 (39.91)	27 (52.94)	0.088
Medical history, n (%)			
Hypertension	107 (45.92)	29 (56.86)	0.157
Diabetes	44 (18.88)	8 (15.69)	0.593
Coronary artery disease	20 (8.58)	3 (5.88)	0.522
Previous ischemic stroke	37 (15.88)	7 (13.73)	0.700
Hyperlipidemia	42 (18.03)	15 (29.41)	0.066
Current smoker	33 (14.16)	15 (29.41)	0.008
Current alcohol user	35 (15.02)	9 (17.65)	0.639
Score on admission, n (%)			
Modified Fisher scale			0.000
Grade 0	–	–	
Grade 1	67 (28.76)	4 (7.84)	
Grade 2	95 (40.77)	13 (25.49)	
Grade 3	38 (16.31)	13 (25.49)	
Grade 4	33 (14.16)	21 (41.76)	0.000
Hunt and Hess scale			
Grade 1	42 (18.03)	5 (9.80)	
Grade 2	161 (69.10)	21 (41.18)	
Grade 3	26 (11.16)	13 (25.49)	
Grade 4	4 (1.72)	8 (15.69)	0.000
Grade 5	0 (0.00)	4 (7.84)	
Laboratory findings, mean ± SD			
Homocysteine, μmol/L	12.92 ± 5.64	14.91 ± 8.85	0.122
D-dimer, mg/L	1.06 ± 1.29	1.14 ± 1.07	0.757
Uric acid, μmol/L	259.11 ± 107.95	315.28 ± 125.42	0.002
Creatinine, μmol/L	69.13 ± 69.14	63.31 ± 21.72	0.569
Complications, n (%)			
Rebleeding	11 (4.72)	9 (17.65)	0.001
Delayed cerebral infarction	50 (21.46)	13 (25.49)	0.530
Hydrocephalus	68 (29.18)	68 (43.14)	0.052
Seizure	14 (6.01)	6 (11.76)	0.146
Electrolyte disturbances	50 (21.46)	21 (41.18)	0.003
Coinfections			0.000
Upper respiratory tract infection	11 (4.72)	1 (1.96)	
Lower respiratory tract infection	13 (5.58)	18 (35.29)	
Urinary tract infection	4 (1.72)	8 (15.69)	
Gastrointestinal infection	5 (2.15)	6 (11.76)	
Therapy, n (%)			
Medication	108 (46.35)	24 (47.06)	0.927
Medication and coil embolization	125 (53.65)	27 (52.94)	

Notes: Continuous variables are shown as the mean $\pm$ standard deviation (SD), categorical variables are shown as numbers combined with percentage (%).

Table 2 The Multivariate Logistic Regression Analysis of Patients with and without a Favorable Prognosis

Variables	β	Wals	OR (95% CI)	P value
Current smoker	-1.079	5.864	0.340 (0.142~0.814)	0.015
Modified Fisher scale	0.481	5.139	1.617 (1.067~2.451)	0.023
Hunt and Hess scale	0.632	4.413	1.882 (1.043~3.394)	0.036
Rebleeding	0.857	1.446	2.357 (0.583~9.530)	0.229
Electrolyte disturbances	0.905	4.388	2.471 (1.060~5.761)	0.036
Uric acid	0.003	3.139	1.003 (1.000~1.006)	0.076
Coinfections	0.721	21.428	2.057 (1.516~2.791)	0.000

Notes: Logistic regression analysis adjusted for Current smoker, Modified Fisher scale, Hunt and Hess scale, Electrolyte disturbances and Uric acid at baseline.

Abbreviations: OR, odds ratio; CI, confidence interval.

and Hess scale (adjusted odds ratio =1.882; 95% CI: 1.043~3.394; $P<0.05$) and electrolyte disturbances (adjusted odds ratio =2.471; 95% CI: 1.060~5.761; $P<0.001$) were also associated with the prognosis of SAH (Table 2).

Comparison of Coinfections

In the favorable prognosis group, 2 patients were complicated with lower respiratory tract infection and urinary tract infection, and 1 patient was complicated with upper respiratory tract infection and gastrointestinal tract infection. In the poor prognosis group, 5 patients were complicated with lower respiratory tract infection and urinary tract infection, and 2 patients were complicated with lower respiratory tract infection, urinary tract infection, and gastrointestinal infection. A total of 30 (12.88%) patients with good prognosis were infected, while 24 (47.06%) patients with poor prognosis were infected. There were significant differences in the proportion of lower respiratory tract infection, urinary tract infection, and digestive tract infection between the two groups (all $P<0.01$), suggesting that bacterial infection during hospitalization may be an important risk factor for poor prognosis in patients with subarachnoid hemorrhage. The specific infection situation of the two groups of patients is shown in Figure 2.

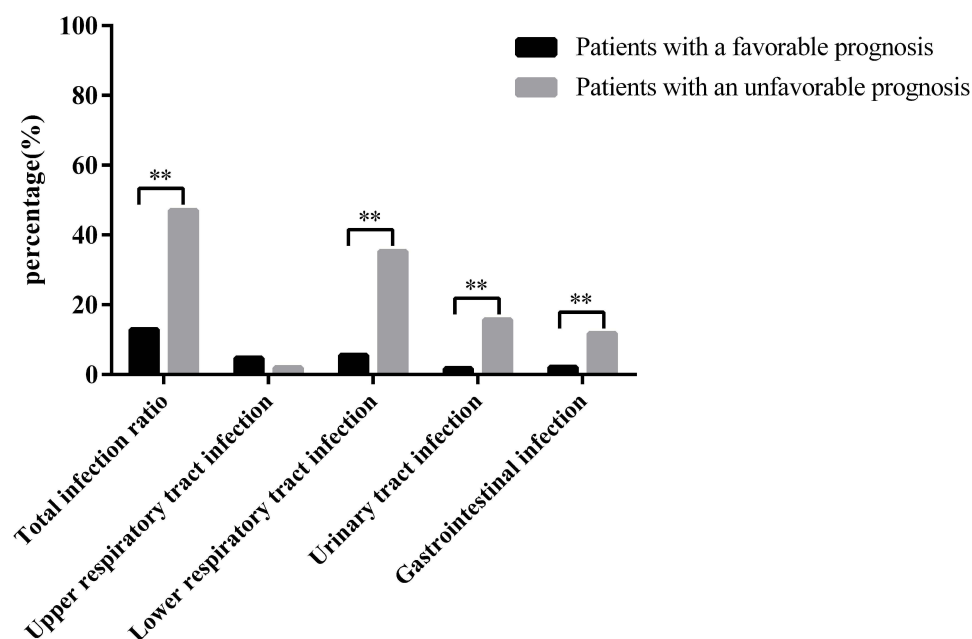


Figure 2 Comparison of coinfections in patients with favorable and unfavorable prognosis. ** $P<0.01$.

Discussion

This study demonstrated that hospital-acquired coinfection was an independent risk factor for poor prognosis of SAH after adjustment for multiple confounders. It is imperative that physicians rapidly screen and aggressively treat patients at high risk for coinfection because of the poor outcomes of these patients. Thus, the data of this study are reliable, and the results of this study further provide a theoretical basis for the clinical control of arachnoid infections.

This study also demonstrated that the difference in the modified Fisher scale and Hunt-Hess scale scores comparison between the two groups was statistically significant. This is consistent with the established findings that modified Fisher scale and Hunt-Hess grading is used to assess the severity of the patient's condition and can better predict clinical prognosis,²³ with higher grading associated with worse prognosis. In addition, current smoker and electrolyte disturbances were also related to poor prognosis. These results suggest that in the diagnosis and treatment of SAH patients, we should strengthen the prevention and treatment of complications to improve the prognosis of patients.

Regarding the relationship between infection and the prognosis of SAH, we speculate that this may be caused by the following reasons. Some studies have reported subarachnoid hemorrhage hospital infection as a high incidence disease,^{24,25} probably due to the need for absolute bed rest in patients with subarachnoid hemorrhage, which increases the chance of pulmonary infection. Additionally, the release of inflammatory factors is promoted after subarachnoid hemorrhage, invading the affected tissues and releasing cytokines, leading to inflammation.²⁶ Previous studies have also supported the conclusion of this study that hospital-acquired infections, as a complication of SAH, are directly associated with poor prognosis and that the frequency of hospital-acquired infections is significantly associated with disability in patients with SAH.^{27,28} The possible reason is that pulmonary infection not only decreases the immunity of the patient, delays the recovery process, and prolongs the course of the disease but also directly leads to the deterioration of the patient's condition in severe cases, which leads to a poor prognosis and increased mortality. Therefore, the active prevention and treatment of hospital-acquired infections is a major and meaningful task.

To the best of our knowledge, this is the first hospitalized study demonstrating that the presence of coinfection was associated with an increased risk of poor outcomes in patients with SAH. All data were subjected to rigorous quality controls, and rigorous statistical analyses were performed. This finding will prompt scholars to pay more attention to the prognostic value of coinfection in patients with SAH. However, there are some limitations in the current study, which are listed as follows. First and most importantly, this is an observational study, we followed the prognosis of the patients only 3 months after the onset of the disease, without further follow-up and dynamic observation of the progress of SAH. Second, this was a retrospective single center study, and further validation with large samples and multicenter data is needed. Although most patients underwent CTA or DSA of the cerebral artery to determine the presence of intracranial aneurysms, we did not further analyze the size, location, and shape of the aneurysms. We only quantitatively evaluated the bleeding and the severity of the patients' symptoms using the modified Fisher scale and Hunt-Hess scale. In addition, we did not further analyze the severity of infection, which may affect disease prognosis. Moreover, there is still a lack of comprehensive discussion and analysis of potential factors that may affect infection or prognosis of patients during hospitalisation, such as length of hospital stay and different treatment regimens for patients. At the same time, we did not analyse the treatment of patients with infection. However, the information in this study is authentic and reliable, and the findings may provide a basis for conducting a multicenter, large-scale clinical prospective study.

Taken together, our findings suggest that coinfection is a very important independent risk factor affecting prognosis. Therefore, clinicians should focus on how to reduce coinfection during hospitalization in patients with subarachnoid hemorrhage and treat it aggressively to reduce mortality and disability and improve the prognosis of patients.

Abbreviations

mRS, modified Rankin Scale; SAH, subarachnoid hemorrhage; WFNS, World Federation of Neurological Societies.

Data Sharing Statement

Study data are available from the corresponding author upon request.

Ethics Approval and Consent to Participate

We obtained ethical approval for this study from the ethics committee of the Affiliated Jiangning Hospital of Nanjing Medical University and performed in accordance with the Declaration of Helsinki (reference number, 2021-03-033-K01). Written informed consent was obtained from all study participants.

Consent for Publication

All patients gave informed consent for publication.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no competing financial interests.

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