



Predictors of Outcome in Aneurysmal Subarachnoid Hemorrhage: A Tertiary Center Experience

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ABSTRACT

AIM: To determine the risk factors affecting the mortality rate and outcomes of patients with subarachnoid hemorrhage (SAH).

MATERIAL and METHODS: The records of patients who underwent aneurysm treatment and intensive care unit (ICU) follow-up in our hospital between 2013-2021 were reviewed retrospectively. Demographics of the patients, aneurysm characteristics, complications in the ICU, the Hunt Hess score, Glasgow Coma Scale (GCS), Acute Physiologic Assessment and Chronic Health Evaluation II score (APACHE II), sepsis status, and mechanical ventilation (MV) needed during ICU admission were collected. The generalized linear mixed modeling method was used to determine independent risk factors affecting mortality.

RESULTS: The records of 91 patients who met the inclusion criteria were analyzed. The age of the patients ranged from 21 to 86 years, and the female-to-male ratio was 6 / 7, with a mean age of 49.9 ± 13.06 years. The aneurysm treatment modality was surgical in 79 patients (86.8%) and endovascular in 12 patients (13.2%). The length of the ICU stay was mean 10.96 ± 13.66 days. While 64.8% (n=59) of the patients were discharged, 7.7% (n=7) were referred to palliative care units, and 25% (n=25) died. A one-unit increase in the APACHE II score was determined to increase the risk of vasospasm 1.154 times (p<0.001). Analysis showed that a one-day increase in the MV day increased the mortality risk 1.838 times (p<0.001), and vasospasm increased the mortality risk 32.151 times (p=0.004)

CONCLUSION: The length of hospital stay, the day of MV, and the presence of vasospasm were determined as independent risk factors affecting mortality. Early diagnosis and rapid treatment of vasospasm, which increases mortality during ICU follow-up, positively impact patient outcomes.

KEYWORDS: Intracranial aneurysm, Subarachnoid hemorrhage, Intracranial vasospasm, Mortality, APACHE, Intensive care

ABBREVIATIONS: SAH: Subarachnoid hemorrhage, ICU: Intensive care unit, CT: Computed tomography, ICP: Intracranial pressure, MV: Mechanical ventilation, GCS: Glasgow coma scale, APACHE: Acute physiologic assessment and chronic health evaluation, DCI: Delayed cerebral ischemia

■ INTRODUCTION

Aneurysmal subarachnoid hemorrhage (aSAH) is a serious disease that occurs at a rate of 9:100,000 population worldwide and causes 30% of the patients to die. Only 30% of survivors continue their lives independently after discharge (4). Acute, severe headache, typically the worst headache the patient has ever experienced, is typical in anamnesis (39). The gold standard for diagnostic evaluation of SAH is non-contrast head computed tomography (CT), followed by lumbar puncture if the CT does not show any bleeding (1).

Considering many factors such as the patient's age, general medical condition, location of the aneurysm, and the size of the bleeding, the most appropriate option either endovascular coiling or neurosurgical clipping is determined, and the risk of bleeding is controlled. The first step of treatment is to stop the bleeding (25). All patients should be followed closely in the intensive care unit (ICU) to detect complications early and prevent new bleeding. It is crucial to avoid vasospasm and hydrocephalus and avoid rebleeding and cerebral ischemia with optimal hemodynamic monitoring during follow-up (28).

Guidelines are published regularly on the issues to be considered in the ICU follow-up of patients (3,4,33,39). In this way, patients can be followed more carefully regarding complications that may arise, and treatment is faster and more effective. Although mortality and morbidity have decreased over the years as surgical and ICU treatments have been updated through research, they are still high. Many studies are conducted to predict and reduce mortality rates (17,18,20,31,36,37,40,45,46,49).

In this study, we aimed to evaluate the risk factors affecting the mortality rate and outcomes of patients with SAH.

■ MATERIAL and METHODS

This study was designed retrospectively and was carried out at Marmara University Pendik Training and Research Hospital.

This study was performed in compliance with the Helsinki Declaration and approved by the Marmara University Faculty of Medicine Clinical Research Ethics Committee (Number: 09.2020.1152).

All patients diagnosed with aneurysmal SAH who underwent an occlusive operation in our hospital and were followed up in the ICU between 2013 and 2021 were evaluated. Each patient's follow-up period was defined as the time between admission to the hospital and discharge.

Patients who underwent the occlusive procedure or ICU follow-up in an external center were excluded from the study.

Patients who met the inclusion criteria were analyzed. In addition to the patient's demographic information, the Hunt-Hess score, Glasgow coma scale (GCS), Acute Physiologic Assessment and Chronic Health Evaluation II (APACHE II) score, sepsis status, and mechanical ventilation (MV) requirements during ICU admission were collected.

Sepsis and septic shock were defined according to Sepsis-3 criteria. (38). The diagnosis of acute kidney injury was made according to the Kidney Disease Improving Global Outcomes (KDIGO) criteria (7). The type of electrolyte imbalance that developed during ICU hospitalization was examined. Intracranial pressure (ICP) was measured directly in some patients via external ventricular drain (EVD) and lumbar drainage; in other patients, it was measured indirectly by measuring the optic nerve diameter with ultrasonography (USG). The upper limit is 22 cm H₂O for direct measurements and 6 mm for USG measurements (9). The diagnosis of vasospasm was made via transcranial Doppler (TCD) examinations based on clinical suspicion. Patients with a middle cerebral artery (MCA) mean flow velocity >120 cm/s were considered positive (35). Each patient's ICU length of stay and discharge type were recorded.

■ RESULTS

The medical records of patients who developed SAH due to intracranial aneurysm rupture and who were admitted to our center between April 2013 and September 2021 were evaluated retrospectively. A total of 183 patients enrolled in the study in neurosurgery and interventional radiology clinics. Eighteen patients transferred to the external ICU after the procedures; 63 patients who were followed up in the postoperative service and 11 patients whose files could not be reached were excluded from the study. A total of 91 patients from two clinics were included in the study (Figure 1).

The age of the patients ranged from 21 to 86 years, and the female-to-male ratio was 42:49, with a mean age of 49.9 ± 13.06 years. The mean Hunt-Hess scores, GCS, and APACHE II scores at the initial presentation were 2.35 ± 1.12 , 11.05 ± 4.61 , and 17.42 ± 7.66 , respectively. The mean length of stay in the ICU was 11 days. The aneurysm treatment modality was surgical in 79 patients (86.8%) and endovascular in 12 patients (13.2%). Whereas 64.8% (n=59) of the patients were discharged, 7.7% (n=7) were referred to palliative care units, and 27.5% (n=25) died. Detailed information about the need for MV, infection status, aneurysm type and distribution, and complications is given in Table I.

When the clinical features of the patients were compared in terms of mortality, Hunt-Hess scores ($p < 0.001$), APACHE II scores ($p < 0.001$), the number of MV days ($p < 0.001$), and the lengths of ICU stay ($p = 0.045$) were higher in the patients who were non-survivors. The mortality percentage was higher in cases with sepsis ($p = 0.002$), septic shock ($p = 0.047$), MV ($p < 0.001$), acute kidney injury ($p < 0.001$), vasospasm ($p < 0.001$), and ICP requiring intervention ($p < 0.001$) (Table II).

The generalized linear mixed modeling method was used to determine the factors affecting mortality. Whereas mortality was included in the model as a dependent variable, variables found to be associated with mortality in univariate analyzes were included as independent variables. In this context, the independent variables were the Hunt-Hess score, ICU admission GCS score, APACHE II score, number of MV days, length of ICU stay, length of hospital stay, sepsis, septic shock, MV requirement, acute kidney injury, vasospasm, and

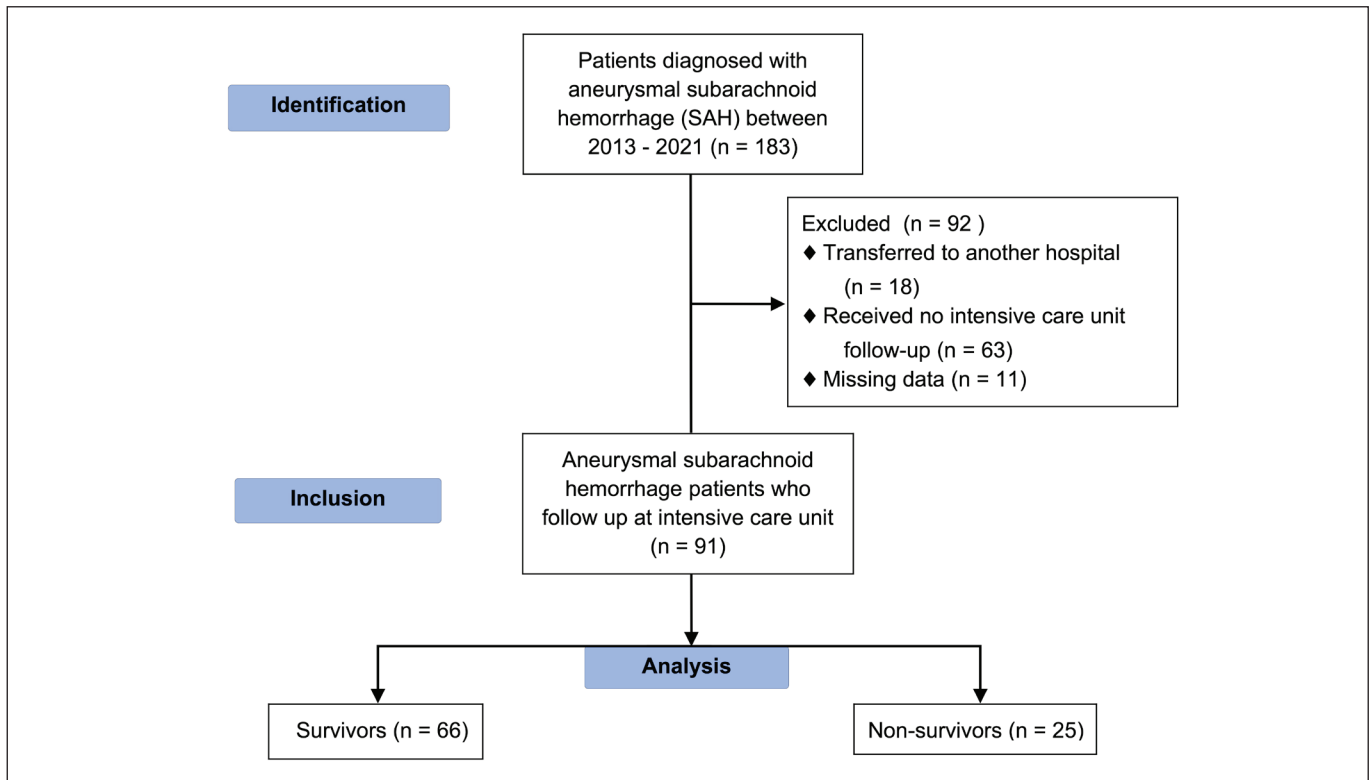


Figure 1: Flowchart of patient selection.

Table I: Demographic and Clinical Characteristics

| Parameters | Min-Max | Mean ± SD |
|--------------------------------------|----------|---------------|
| Age (years) | 21-86 | 49.9 ± 13.06 |
| Hunt Hess score | 1-5 | 2.35 ± 1.12 |
| Initial GCS at ICU | 3-15 | 11.05 ± 4.61 |
| GCS at discharge from ICU | 7-15 | 14.36 ± 1.92 |
| APACHE II score | 3-35 | 17.42 ± 7.66 |
| Mechanical ventilation (days) | 0-72 | 7.24 ± 14.38 |
| Diagnosis-intervention period (days) | 0-18 | 1.18 ± 2.38 |
| Length of ICU stay (days) | 2-76 | 10.96 ± 13.66 |
| Length of hospital stay (days) | 2-110 | 17.35 ± 18.43 |
| | n | % |
| Sex | | |
| Female | 42 | 46.2 |
| Male | 49 | 53.8 |
| Sepsis | 26 | 28.6 |
| Septic shock | 23 | 25.3 |
| Need for mechanical ventilation | 43 | 47.3 |
| Acute kidney injury | 15 | 16.5 |

Table I: Cont.

| Parameters | Number of patient | Percentage |
|--|-------------------|------------|
| Vasospasm | 38 | 41.8 |
| Increased intracranial pressure (ICP) requiring intervention | 28 | 30.8 |
| Location of Aneurysm | | |
| ACOM | 32 | 35.2 |
| MCA | 30 | 33.0 |
| PCOM | 11 | 12.1 |
| Others | 22 | 24.2 |
| Aneurysm Treatment | | |
| Clip occlusion | 79 | 86.8 |
| Coil embolization | 12 | 13.2 |
| Rebleeding of aneurysm | 9 | 10.0 |
| Diabetes insipidus | 9 | 9.9 |
| Syndrome of inappropriate antidiuretic hormone secretion (SIADH) | 9 | 9.9 |
| Cerebral salt wasting (CSW) | 16 | 17.6 |
| Discharge type from ICU | | |
| Hospital ward | 59 | 64.8 |
| Palliative care | 7 | 7.7 |
| Exitus | 25 | 27.5 |

APACHE II: Acute physiology and chronic health evaluation II score, **GCS:** Glasgow Coma Scale, **ICU:** Intensive care unit, **ACOM:** anterior communicating artery, **MCA:** middle cerebral artery; **PCOM:** posterior communicating artery.

Table II: Comparison of Variables According to Mortality

| Parameters | Mortality | | Test value (z) | p-value |
|------------------------------------|---------------------|-------------------------|-------------------------|----------------------|
| | Survivors (n=66) | Non-survivors (n=25) | | |
| | Median (Q1, Q3) | Median (Q1, Q3) | | |
| Age (years) | 50.5 (43, 57) | 50 (40, 59) | -0.076 | ^a 0.940 |
| Hunt Hess score | 2 (1, 3) | 3 (2, 4) | -3.888 | ^a <0.001* |
| Initial GCS at ICU | 15 (10, 15) | 7 (3, 13) | -4.029 | ^a <0.001* |
| APACHE II score | 13.5 (10, 18) | 25 (21, 26) | -4.182 | ^a <0.001* |
| Mechanical ventilation (days) | 0 (0, 1) | 8 (4, 12) | -5.545 | ^a <0.001* |
| Diagnosis-intervention time (days) | 1 (0, 2) | 0 (0, 1) | -1.233 | ^a 0.218 |
| Length of ICU stay (days) | 6 (3, 10) | 10 (6, 12) | -2.009 | ^a 0.045* |
| Length of hospital stay (days) | 12 (9, 19) | 10 (6, 12) | -2.651 | ^a 0.008* |
| | n (%) | n (%) | Test value (χ^2) | p-value |
| Sex | | | 1.345 | ^b 0.246 |
| Female | 28 (66.7) | 14 (33.3) | | |
| Male | 38 (77.6) | 11 (22.4) | | |
| Sepsis | | | 9.271 | ^b 0.002* |
| Absent | 53 (81.5) | 12 (18.5) | | |
| Present | 13 (50) | 13 (50) | | |

Table II: Cont.

| | n (%) | n (%) | Test value (χ^2) | p-value |
|--|-----------|-----------|-------------------------|-------------------------------|
| Septic shock | | | 3.957 | ^b0.047* |
| Absent | 53 (77.9) | 15 (22.1) | | |
| Present | 13 (56.5) | 10 (43.5) | | |
| Need for mechanical ventilation | | | 38.478 | ^b<0.001* |
| Absent | 48 (100) | 0 (0) | | |
| Present | 18 (41.9) | 25 (58.1) | | |
| Acute kidney injury | | | - | ^c <0.001* |
| Absent | 62 (81.6) | 14 (18.4) | | |
| Present | 4 (26.7) | 11 (73.3) | | |
| Vasospasm | | | - | ^c <0.001* |
| Absent | 50 (94.3) | 3 (5.7) | | |
| Present | 16 (42.1) | 22 (57.9) | | |
| Increased intracranial pressure (ICP) requiring intervention | | | 22.430 | ^b<0.001* |
| Absent | 55 (87.3) | 8 (12.7) | | |
| Present | 11 (39.3) | 17 (60.7) | | |
| ACOM aneurysms | | | 1.885 | ^b 0.170 |
| Absent | 40 (67.8) | 19 (32.2) | | |
| Present | 26 (81.3) | 6 (18.8) | | |
| MCA aneurysm | | | 3.525 | ^b 0.060 |
| Absent | 48 (78.7) | 13 (21.3) | | |
| Present | 18 (60) | 12 (40) | | |
| PCOM aneurysm | | | - | ^c 0.721 |
| Absent | 57 (71.3) | 23 (28.8) | | |
| Present | 9 (81.8) | 2 (18.2) | | |
| Other aneurysms | | | - | ^c 0.981 |
| Absent | 50 (72.5) | 19 (27.5) | | |
| Present | 16 (72.7) | 6 (27.3) | | |
| Aneurysm Treatment | | | - | ^c 0.999 |
| Clip occlusion | 57 (72.2) | 22 (27.8) | | |
| Coil embolization | 9 (75) | 3 (25) | | |
| Rebleeding of aneurysm | | | - | ^c 0.257 |
| Absent | 61 (74.1) | 21 (25.9) | | |
| Present | 5 (55.6) | 4 (44.4) | | |
| Diabetes insipidus | | | - | ^c 0.252 |
| Absent | 61 (74.4) | 21 (25.6) | | |
| Present | 5 (55.6) | 4 (44.4) | | |
| Syndrome of inappropriate antidiuretic hormone secretion (SIADH) | | | - | ^c 0.999 |
| Absent | 59 (72) | 23 (28) | | |
| Present | 7 (77.8) | 2 (22.2) | | |
| Cerebral salt wasting (CSW) | | | - | ^c 0.542 |
| Absent | 53 (70.7) | 22 (29.3) | | |
| Present | 13 (81.3) | 3 (18.8) | | |

Q1: First quartile, **Q3:** Third quartile, ^aMann-Whitney U test, ^bPearson chi-square test ^cFisher's exact test * $p < 0.05$, **APACHE II:** Acute physiology and chronic health evaluation II score, **ACOM:** Anterior communicating artery, **MCA:** Middle cerebral artery, **PCOM:** Posterior communicating artery.

ICP requiring intervention. In the first stage, all independent variables were included in the analysis, the variable with the lowest level of significance (the highest p-value) in the obtained model was removed from the model, and the analysis was repeated. This process was repeated until only variables with a statistically significant effect remained in the model. Information about the obtained model is presented in Table III.

In the model obtained at the last stage, it was determined that the length of hospital stay, the days of MV, and the presence of vasospasm were significantly included. A one-day increase in the length of hospital stay increased the risk of mortality 0.503 times ($p<0.001$). Analysis showed that a one-day increase in the MV days increased the mortality risk by 1.838 times ($p<0.001$), and vasospasm increased the mortality risk by 32.151 times ($p=0.004$) (Table III).

The clinical characteristics of the patients were compared in terms of vasospasm, the Hunt-Hess scores ($p=0.001$), APACHE II scores ($p<0.001$), the numbers of MV days ($p<0.001$), and lengths of stay in the ICU ($p<0.001$) were found to be higher in patients with vasospasm, and lower ICU initial GCS score ($p<0.001$). The percentage of vasospasm was higher in patients with sepsis ($p<0.001$), septic shock ($p<0.001$), MV requirement ($p<0.001$), acute kidney injury ($p<0.001$), and ICP requiring intervention ($p=0.004$) (Table IV).

The generalized linear mixed modeling method was used to determine the factors affecting vasospasm. Whereas vasospasm was included in the model as a dependent variable, variables found to be associated with vasospasm in univariate analyzes were included as independent variables. In this context, the independent variables were the Hunt-

Table III: Factors Affecting Mortality

| | OR | 95% CI | t | p-value |
|--------------------------------|--------|---------------|--------|-------------------|
| Reference | 5.517 | 0.644-47.291 | 1.594 | 0.117 |
| Length of hospital stay (days) | 0.503 | 0.353-0.718 | -3.869 | <0.001* |
| Mechanical ventilation (days) | 1.838 | 1.329-2.540 | 3.768 | <0.001* |
| Vasospasm | 32.151 | 3.243-318.750 | 3.033 | 0.004* |

* $p<0.05$, **OR:** Odds ratio, **CI:** Confidence interval.

Table IV: Comparison of Variables According to Vasospasm

| Parameters | Vasospasm | | Test value (z) | p-value |
|------------------------------------|-----------------|-----------------|-------------------------|--------------------------------|
| | Absent (n=53) | Present (n=38) | | |
| | Median (Q1, Q3) | Median (Q1, Q3) | | |
| Age (years) | 50 (42, 56) | 52.5 (41, 59) | -0.862 | ^a 0.389 |
| Hunt Hess score | 2 (1, 2) | 3 (2, 4) | -3.335 | ^a 0.001* |
| Initial GCS at ICU | 15 (12, 15) | 7.5 (3, 15) | -3.793 | ^a <0.001* |
| APACHE II score | 13 (10, 17) | 24 (14, 26) | -4.289 | ^a <0.001* |
| Mechanical ventilation (days) | 0 (0, 0) | 8 (3, 19) | -6.474 | ^a <0.001* |
| Diagnosis-intervention time (days) | 1 (0, 2) | 0 (0, 1) | -1.277 | ^a 0.202 |
| Length of ICU stay (days) | 5 (3, 8) | 10 (6, 22) | -4.025 | ^a <0.001* |
| Length of hospital stay (days) | 11 (9, 13) | 14 (9, 33) | -1.677 | ^a 0.093 |
| | n (%) | n (%) | Test value (χ^2) | p |
| Sex | | | 0.039 | ^b 0.844 |
| Female | 24 (57.1) | 18 (42.9) | | |
| Male | 29 (59.2) | 20 (40.8) | | |
| Sepsis | | | 932.645 | ^b <0.001* |
| Absent | 50 (76.9) | 15 (23.1) | | |
| Present | 3 (11.5) | 23 (88.5) | | |
| Septic shock | | | 25.854 | ^b <0.001* |
| Absent | 50 (73.5) | 18 (26.5) | | |
| Present | 3 (13) | 20 (87) | | |

Table IV: Cont.

| | n (%) | n (%) | Test value (χ^2) | p |
|--|-----------|-----------|-------------------------|----------------------|
| Need for mechanical ventilation | | | 41.028 | ^b <0.001* |
| Absent | 43 (89.6) | 5 (10.4) | | |
| Present | 10 (23.3) | 33 (76.7) | | |
| Acute kidney injury | | | 19.644 | ^b <0.001* |
| Absent | 52 (68.4) | 24 (31.6) | | |
| Present | 1 (6.7) | 14 (93.3) | | |
| Increased intracranial pressure (ICP) requiring intervention | | | 8.439 | ^b 0.004* |
| Absent | 43 (68.3) | 20 (31.7) | | |
| Present | 10 (35.7) | 18 (64.3) | | |
| ACOM aneurysms | | | 0.368 | ^b 0.544 |
| Absent | 33 (55.9) | 26 (44.1) | | |
| Present | 20 (62.5) | 12 (37.5) | | |
| MCA aneurysm | | | 2.465 | ^b 0.116 |
| Absent | 39 (63.9) | 22 (36.1) | | |
| Present | 14 (46.7) | 16 (53.3) | | |
| PCOM aneurysm | | | - | ^c 0.757 |
| Absent | 46 (57.5) | 34 (42.5) | | |
| Present | 7 (63.6) | 4 (36.4) | | |
| Other aneurysms | | | 0.009 | ^b 0.926 |
| Absent | 40 (58) | 29 (42) | | |
| Present | 13 (59.1) | 9 (40.9) | | |
| Aneurysm Treatment | | | 1.596 | ^b 0.206 |
| Clip occlusion | 44 (55.7) | 35 (44.3) | | |
| Coil embolization | 9 (75) | 3 (25) | | |
| Rebleeding of aneurysm | | | - | ^c 0.160 |
| Absent | 50 (60.5) | 32 (39.5) | | |
| Present | 3 (33.3) | 6 (66.7) | | |
| Diabetes insipidus | | | - | ^c 0.157 |
| Absent | 50 (61) | 32 (39) | | |
| Present | 3 (33.3) | 6 (66.7) | | |
| Syndrome of inappropriate antidiuretic hormone secretion (SIADH) | | | - | ^c 0.999 |
| Absent | 48 (58.5) | 34 (41.5) | | |
| Present | 5 (55.6) | 4 (44.4) | | |
| Cerebral salt wasting (CSW) | | | 0.542 | ^b 0.462 |
| Absent | 45 (60) | 30 (40) | | |
| Present | 8 (50) | 8 (50) | | |

Q1: First quartile, **Q3:** Third quartile, ^aMann-Whitney U test, ^bPearson chi-square test ^cFisher's exact test * $p < 0.05$, **APACHE II:** Acute physiology and chronic health evaluation II score, **ACOM:** Anterior communicating artery, **MCA:** Middle cerebral artery, **PCOM:** Posterior communicating artery.

Table V: Factors Affecting Vasospasm

| | OR | 95% CI | t | p-value |
|-----------------|-------|-------------|--------|---------|
| Reference | 0.056 | 0.022-0.145 | -6.236 | <0.001* |
| APACHE II score | 1.154 | 1.098-1.212 | 5.969 | <0.001* |

APACHE II: Acute physiology and chronic health evaluation II score, **OR:** Odds ratio, **CI:** Confidence interval.

Hess score, GCS score at time of ICU admission, APACHE II score, number of MV days, and length of ICU stay. In the first stage, all independent variables were included in the analysis, the variable with the lowest level of significance (the highest p-value) in the obtained model was removed from the model, and the analysis was repeated. This process was repeated until only variables with a statistically significant effect remained in the model, and the results are given in Table V.

It was determined that only the APACHE II score was statistically significant in the model obtained in the last stage. One-unit increase in the APACHE II score was determined to increase the risk of vasospasm by 1.154 times ($p < 0.001$) (Table V).

DISCUSSION

We performed a retrospective study on aneurysmal SAH patients who were followed up in the ICU of our hospital. We showed that SAH was associated with 27% mortality. Previous studies indicated that bleeding in the acute stage and late complications in ICU follow-up are important causes of mortality. We identified the length of hospital stay, the days of MV, and the presence of vasospasm as independent risk factors affecting mortality.

In our study, mortality was 27% ($n=25$) in 91 patients with aneurysmal SAH who were followed up and treated in the ICU. Mortality rates between 20% and 44% are reported in patients with aneurysmal SAH, and our mortality rate is consistent with the literature (4,28,30,32,34,39,41,44). In a study by Mourelo-Farina et al., 536 patients followed in the ICU due to SAH were examined, and it was reported that patients who were non-survivors had higher APACHE II and Hunt-Hess scores (HH) at the time of admission and lower GCS scores, in line with our results (27). In addition, recent studies have shown HH5 grade at 48 hours to be an independent risk factor for mortality and a better tool than the initial HH grade (23).

In the International Subarachnoid Aneurysm Trial (ISAT) study, it was reported that if there is a possibility of both surgical and radiological intervention to the aneurysm, the method of choice should be neuroradiological coiling, and mortality and morbidity are significantly reduced in these patients. In patients with a ruptured intracranial aneurysm, for which endovascular coiling and neurosurgical clipping are therapeutic options, the outcome in terms of survival free of disability at one year is significantly better with endovascular coiling (24,25). In our study, we did not observe any difference in mortality between surgical clipping and neuroradiological coiling, which is used as an aneurysm intervention method, but this result may be

due to the low number of patients who underwent coiling.

In our study, the median number of days spent on MV during the ICU stay was eight in the group of patients who were non-survivors and zero in the patients who survived. MV duration was identified as an independent risk factor that increased mortality by 1.8 times. Udy et al. stated that 63% of aneurysmal SAH patients need MV, and the presence of MV is an independent risk factor that increases mortality by 1.69 times (42). The study by Bouvet et al. showed that the overall one-year mortality is high, and the functional status is poor, in critical stroke patients who need MV (2).

Although the development of sepsis and septic shock prolonged ICU and hospital stays in our study, they were not identified as independent risk factors for mortality. A recent study demonstrated that sepsis was one of the main systemic complications during the hospital stay in patients with aneurysmal SAH, and sepsis was a modifiable factor associated with poor functional outcomes at long-term follow-up (11).

Complications frequently encountered in patients with aneurysmal SAH include increased ICP, rebleeding, and disturbances in serum sodium values. In our study, increased ICP requiring intervention was higher in non-survivors. van Donkelaar et al. reported a higher rate of ICP requiring intervention in non-survivors (43). In our study, rebleeding rates were similar in both groups. Due to the small number of patients with rebleeding, no significant difference could be found in mortality. In many studies, rebleeding has been found to be an independent risk factor for mortality (16,19).

Vasospasm developed during ICU hospitalization, prolonged ventilation, and prolonged hospitalization were identified as independent risk factors for mortality. The most influential risk factor for mortality was vasospasm, with a 32-fold increased risk. The incidence of vasospasm in patients was 41%, and mortality was 58% in patients who developed vasospasm. Many studies have shown that vasospasm directly affects the survival of patients (15). Depending on the criteria used, the incidence of vasospasm after SAH reaches up to 70 percent (9,14). In a review by Neifert et al., 43% of patients had angiographic vasospasm, and 33% had delayed cerebral ischemia (DCI). It has been shown that the development of DCI in patients increases mortality by 3.7 times (28).

Many studies have also searched for methods to reduce vasospasm risk, the most important risk factor for mortality in our study. Foudhaili et al. showed that early out-of-bed mobilization after subarachnoid hemorrhage is associated with better functional outcomes and lower rates of vasospasm

(10).

APACHE II and Hunt-Hess scores were significantly higher in our vasospasm patients group. A review showed the presence of signs of SAH severity on CT as a risk factor for the development of cerebral vasospasm (12). Various scoring systems have been proposed to predict vasospasm and DCI (8,22,33). However, there is not yet a widely used scoring system. Therefore, in our study, the Hunt-Hess score was used for SAH staging, and the APACHE II score was used to determine the severity of the patient's condition during hospitalization in the ICU.

In our study, initial GCS score at time of ICU admission was lower in the vasospasm group. The World Federation of Neurological Surgeons (WFNS) scoring system used for SAH severity staging includes the patient's GCS and clinical evaluation. The score increases with a decrease in GCS and clinical worsening. Although the WFNS scoring system is used in SAH staging, various studies have proven that it can predict vasospasm and is a risk factor for vasospasm (22).

Forty-seven percent of our patients required MV during their stay in the ICU, 86% of the patients who developed vasospasm needed MV, and the median number of MV days was eight days. In a study evaluating the risk factors for cerebral vasospasm in patients with SAH, 51.5% of patients with vasospasm needed MV (29). In addition to the more prolonged need for MV in patients with vasospasm, these patients also require longer ICU stays. Sepsis and septic shock are more common in the vasospasm group.

In our study, vasospasm was observed in 65% of patients with elevated ICP requiring intervention. Studies showed the development of acute hydrocephalus as an independent risk factor for vasospasm (21,26). In our study, the presence of hypertension was similar in both groups. However, there are studies in the literature in which hypertension is an independent risk factor for the development of vasospasm (9,13). In our study, aneurysm treatment procedures and localization did not affect vasospasm. Many studies have not shown a relationship between vasospasm and aneurysm localization (5,6,13,26,47,48).

Our study's limitations include its retrospective and single-center nature and its small patient population. We do not know the status of the patients who were referred to an external center after aneurysm treatment, and the number of patients who underwent endovascular coiling is small.

CONCLUSION

In our study to determine the risk factors affecting mortality and patient outcomes in patients with SAH, we determined the mortality rate to be 28%. The length of hospital stay, the days of MV, and the presence of vasospasm were identified as independent risk factors affecting mortality. Although the severity of the patient's disease at the time of admission is a crucial factor affecting mortality, it is a risk factor that cannot be mitigated. Early diagnosis and rapid treatment of vasospasm, which increases mortality during ICU follow-up, has a positive effect on patient outcomes. These identified

risk factors should be carefully considered during follow-up of SAH patients in the ICU.

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AUTHORSHIP CONTRIBUTION

Study conception and design: ME, AS, YB, IC, BB

Data collection: ME, AS, YB, IC, BB

Analysis and interpretation of results: ME, AS, YB, IC, BB

Draft manuscript preparation: ME, AS, YB, IC, BB

Critical revision of the article: ME, AS, YB, IC, BB

Other (study supervision, fundings, materials, etc...): ME, AS, YB, IC, BB

All authors (ME, AS, YB, IC, BB) reviewed the results and approved the final version of the manuscript.

REFERENCES

1. Abraham MK, Chang WW: Subarachnoid hemorrhage. *Emerg Med Clin North Am* 34:901-916, 2016. <https://doi.org/10.1016/j.emc.2016.06.011>
2. Bouvet P, Murgier M, Pons B, Darmon M: Long-term outcomes of critically ill patients with stroke requiring mechanical ventilation. *Am J Crit Care* 28:477-480, 2019. <https://doi.org/10.4037/ajcc2019310>
3. Committee for Guidelines for Management of Aneurysmal Subarachnoid Hemorrhage, Japanese Society on Surgery for Cerebral Stroke: Evidence-based guidelines for the management of aneurysmal subarachnoid hemorrhage. English Edition. *Neurol Med Chir* 52:355-429, 2012. <https://doi.org/10.2176/nmc.52.355>
4. Connolly ES, Jr., Rabinstein AA, Carhuapoma JR, Derdeyn CP, Dion J, Higashida RT, Hoh BL, Kirkness CJ, Naidech AM, Ogilvy CS, Patel AB, Thompson BG, Vespa P, American Heart Association Stroke C, Council on Cardiovascular R, Intervention, Council on Cardiovascular N, Council on Cardiovascular S, Anesthesia, Council on Clinical C: Guidelines for the management of aneurysmal subarachnoid hemorrhage: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 43:1711-1737, 2012. <https://doi.org/10.1161/STR.0b013e3182587839>
5. Crobeddu E, Mittal MK, Dupont S, Wijdicks EF, Lanzino G, Rabinstein AA: Predicting the lack of development of delayed cerebral ischemia after aneurysmal subarachnoid hemorrhage. *Stroke* 43:697-701, 2012. <https://doi.org/10.1161/STROKEAHA.111.638403>

6. Dupont SA, Wijdicks EF, Manno EM, Lanzino G, Rabinstein AA: Prediction of angiographic vasospasm after aneurysmal subarachnoid hemorrhage: Value of the Hijdra sum scoring system. *Neurocritical Care* 11:172-176, 2009. <https://doi.org/10.1007/s12028-009-9247-3>
7. Eagles ME, Powell MF, Ayling OGS, Tso MK, Macdonald RL: Acute kidney injury after aneurysmal subarachnoid hemorrhage and its effect on patient outcome: An exploratory analysis. *J Neurosurg* 12:1-8, 2019
8. Fang YJ, Mei SH, Lu JN, Chen YK, Chai ZH, Dong X, Araujo C, Reis C, Zhang JM, Chen S: New risk score of the early period after spontaneous subarachnoid hemorrhage: For the prediction of delayed cerebral ischemia. *CNS Neurosci Ther* 25:1173-1181, 2019. <https://doi.org/10.1111/cns.13202>
9. Findlay JM, Nisar J, Darsaut T: Cerebral vasospasm: A review. *Can J Neurol Sci* 43:15-32, 2016. <https://doi.org/10.1017/cjn.2015.288>
10. Foudhaili A, Barthélémy R, Collet M, de Roquetaillade C, Kerever S, Vitiello D, Mebazaa A, Chousterman BG: Impact of early out-of-bed mobilization on functional outcome in patients with aneurysmal subarachnoid hemorrhage: A retrospective cohort study. *World Neurosurg* 175:e278-e287, 2023. <https://doi.org/10.1016/j.wneu.2023.03.073>
11. Gonçalves B, Rynkowski C, Turon R, Charris N, Miranda F, de Caro V, Prazeres M, Santos T, Greer DM, Sharshar T, Guillaume T, Bozza FA, Righy C, Kurtz P: Clinical characteristics and outcomes of patients with aneurysmal subarachnoid hemorrhage: A prospective multicenter study in a middle-income country. *Neurocrit Care* 38:378-387, 2022. <https://doi.org/10.1007/s12028-022-01629-6>
12. Inagawa T: Risk factors for cerebral vasospasm following aneurysmal subarachnoid hemorrhage: A review of the literature. *World Neurosurg* 85:56-76, 2016. <https://doi.org/10.1016/j.wneu.2015.08.052>
13. Inagawa T, Yahara K, Ohbayashi N: Risk factors associated with cerebral vasospasm following aneurysmal subarachnoid hemorrhage. *Neurol Med Chir* 54:465-473, 2014. <https://doi.org/10.2176/nmc.oa.2013-0169>
14. Janjua N, Mayer SA: Cerebral vasospasm after subarachnoid hemorrhage. *Curr Opin Crit Care* 9:113-119, 2003. <https://doi.org/10.1097/00075198-200304000-00006>
15. Kistka H, Dewan MC, Mocco J: Evidence-based cerebral vasospasm surveillance. *Neurol Res Int* 2013:256713, 2013. <https://doi.org/10.1155/2013/256713>
16. Lantigua H, Ortega-Gutierrez S, Schmidt JM, Lee K, Badjatia N, Agarwal S, Claassen J, Connolly ES, Mayer SA: Subarachnoid hemorrhage: Who dies, and why? *Crit Care* 19:309, 2015. <https://doi.org/10.1186/s13054-015-1036-0>
17. Li Y, Yang S, Zhou X, Lai R: Poor expression of miR-195-5p can assist the diagnosis of cerebral vasospasm after subarachnoid hemorrhage and predict adverse outcomes. *Brain Behav* 12:e2766, 2022. <https://doi.org/10.1002/brb3.2766>
18. Lin H, Shen J, Zhu Y, Zhou L, Wu F, Liu Z, Zhang S, Zhan R: Elevated serum CCL23 levels at admission predict delayed cerebral ischemia and functional outcome after aneurysmal subarachnoid hemorrhage. *J Clin Med* 11:6879, 2022. <https://doi.org/10.3390/jcm11236879>
19. Liu Q, Jiang P, Wu J, Li M, Gao B, Zhang Y, Ning B, Cao Y, Wang S: Intracranial aneurysm rupture score may correlate to the risk of rebleeding before treatment of ruptured intracranial aneurysms. *Neurol Sci* 40:1683-1693, 2019. <https://doi.org/10.1007/s10072-019-03916-1>
20. Lu W, Tong Y, Zhang C, Xiang L, Xiang L, Chen C, Guo L, Shan Y, Li X, Zhao Z, Pan X, Zhao Z, Zou J: A novel visual dynamic nomogram to online predict the risk of unfavorable outcome in elderly aSAH patients after endovascular coiling: A retrospective study. *Front Neurosci* 16:1037895, 2022. <https://doi.org/10.3389/fnins.2022.1037895>
21. Luong CQ, Ngo HM, Hoang HB, Pham DT, Nguyen TA, Tran TA, Nguyen DN, Do SN, Nguyen MH, Vu HD, Vuong HTT, Mai TD, Nguyen AQ, Le KH, Dao PV, Tran TH, Vu LD, Nguyen LQ, Pham TQ, Dong HV, Nguyen HT, Nguyen CV, Nguyen AD: Clinical characteristics and factors relating to poor outcome in patients with aneurysmal subarachnoid hemorrhage in Vietnam: A multicenter prospective cohort study. *PLoS One* 16:e0256150, 2021. <https://doi.org/10.1371/journal.pone.0256150>
22. Mijiti M, Mijiti P, Axier A, Amuti M, Guohua Z, Xiaojiang C, Kadeer K, Xixian W, Geng D, Maimaitili A: Incidence and predictors of angiographic vasospasm, symptomatic vasospasm and cerebral infarction in chinese patients with aneurysmal subarachnoid hemorrhage. *PLoS One* 11:e0168657, 2016. <https://doi.org/10.1371/journal.pone.0168657>
23. Mittal AM, Pease M, McCarthy D, Legarreta A, Belkhir R, Crago EA, Lang MJ, Gross BA: Hunt-hess score at 48 hours improves prognostication in grade 5 aneurysmal subarachnoid hemorrhage. *World Neurosurg* 171:e874-e878, 2023. <https://doi.org/10.1016/j.wneu.2023.01.018>
24. Molyneux A, Kerr R, Stratton I, Sandercock P, Clarke M, Shrimpton J, Holman R: International subarachnoid aneurysm trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: A randomised trial. *Lancet* 360:1267-1274, 2002. [https://doi.org/10.1016/S0140-6736\(02\)11314-6](https://doi.org/10.1016/S0140-6736(02)11314-6)
25. Molyneux AJ, Birks J, Clarke A, Sneade M, Kerr RS: The durability of endovascular coiling versus neurosurgical clipping of ruptured cerebral aneurysms: 18 year follow-up of the UK cohort of the International Subarachnoid Aneurysm Trial (ISAT). *Lancet* 385:691-697, 2015. [https://doi.org/10.1016/S0140-6736\(14\)60975-2](https://doi.org/10.1016/S0140-6736(14)60975-2)
26. Moskowitz SI, Ahrens C, Provencio JJ, Chow M, Rasmussen PA: Prehemorrhage statin use and the risk of vasospasm after aneurysmal subarachnoid hemorrhage. *Surg Neurol* 71:311-317, discussion 317-318, 2009. <https://doi.org/10.1016/j.surneu.2007.12.027>
27. Mourelou-Fariña M, Pértega S, Galeiras R: A model for prediction of in-hospital mortality in patients with subarachnoid hemorrhage. *Neurocrit Care* 34:508-518, 2021. <https://doi.org/10.1007/s12028-020-01041-y>
28. Neifert SN, Chapman EK, Martini ML, Shuman WH, Schupper AJ, Oermann EK, Mocco J, Macdonald RL: Aneurysmal subarachnoid hemorrhage: The last decade. *Transl Stroke Res* 12:428-446, 2021. <https://doi.org/10.1007/s12975-020-00867-0>

29. Opancina V, Lukic S, Jankovic S, Vojinovic R, Mijailovic M: Risk factors for cerebral vasospasm in patients with aneurysmal subarachnoid hemorrhage. *Open medicine (Warsaw, Poland)* 15:598-604, 2020. <https://doi.org/10.1515/med-2020-0169>
30. Patel S, Parikh A, Okorie ON: Subarachnoid hemorrhage in the emergency department. *Int J Emerg Med* 14:31, 2021. <https://doi.org/10.1186/s12245-021-00353-w>
31. Peng Z, Pang C, Li XJ, Zhang HS, Zhang JT, Zhu Q, Xu HJ, Gao YY, Zhuang Z, Li W, Zhang QR, Lu Y, Hang CH: Peroxiredoxin 2 is a potential objective indicator for severity and the clinical status of subarachnoid hemorrhage patients. *Dis Markers* 2023:5781180, 2023. <https://doi.org/10.1155/2023/5781180>
32. Petridis AK, Kamp MA, Cornelius JF, Beez T, Beseoglu K, Turowski B, Steiger HJ: Aneurysmal subarachnoid hemorrhage. *Dtsch Arztebl Int* 114:226-236, 2017. <https://doi.org/10.3238/arztebl.2017.0226>
33. Picetti E, Barbanera A, Bernucci C, Bertuccio A, Bilotta F, Boccardi EP, Cafiero T, Caricato A, Castioni CA, Cenozato M, Chieriegato A, Citerio G, Gritti P, Lanterna L, Menozzi R, Munari M, Panni P, Rossi S, Stocchetti N, Sturiale C, Zoerle T, Zona G, Rasulo F, Robba C: Early management of patients with aneurysmal subarachnoid hemorrhage in a hospital with neurosurgical/neuroendovascular facilities: A consensus and clinical recommendations of the Italian Society of Anesthesia and Intensive Care (SIAARTI)-part 2. *J Anesth Analg Crit Care* 2:21, 2022. <https://doi.org/10.1186/s44158-022-00049-4>
34. Rinkel GJ, Algra A: Long-term outcomes of patients with aneurysmal subarachnoid haemorrhage. *Lancet Neurol* 10:349-356, 2011. [https://doi.org/10.1016/S1474-4422\(11\)70017-5](https://doi.org/10.1016/S1474-4422(11)70017-5)
35. Samagh N, Bhagat H, Jangra K: Monitoring cerebral vasospasm: How much can we rely on transcranial Doppler. *J Anaesthesiol Clin Pharmacol* 35:12-18, 2019. https://doi.org/10.4103/joacp.JOACP_192_17
36. Shah AH, Snow R, Wendell LC, Thompson BB, Reznik ME, Furie KL, Mahta A: Association of hemoglobin trend and outcomes in aneurysmal subarachnoid hemorrhage: A single center cohort study. *J Clin Neurosci* 107:77-83, 2023. <https://doi.org/10.1016/j.jocn.2022.12.008>
37. Shin KW, Choi S, Oh H, Hwang SY, Park HP: A high immediate postoperative neutrophil-to-albumin ratio is associated with unfavorable clinical outcomes at hospital discharge in patients with aneurysmal subarachnoid hemorrhage. *J Neurosurg Anesthesiol* 2023 (Online ahead of print). <https://doi.org/10.1097/ANA.0000000000000906>
38. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, Bellomo R, Bernard GR, Chiche JD, Cooper-Smith CM, Hotchkiss RS, Levy MM, Marshall JC, Martin GS, Opal SM, Rubenfeld GD, van der Poll T, Vincent JL, Angus DC: The third international consensus definitions for sepsis and septic shock (Sepsis-3). *Jama* 315:801-810, 2016. <https://doi.org/10.1001/jama.2016.0287>
39. Steiner T, Juvela S, Unterberg A, Jung C, Forsting M, Rinkel G: European Stroke Organization guidelines for the management of intracranial aneurysms and subarachnoid haemorrhage. *Cerebrovascular Dis* 35:93-112, 2013. <https://doi.org/10.1159/000346087>
40. Suzuki Y, Oinaka H, Nakajima H, Nampei M, Kawakita F, Miura Y, Yasuda R, Toma N, Suzuki H, p SG: Plasma fibulin-5 levels as an independent predictor of a poor outcome after an aneurysmal subarachnoid hemorrhage. *Int J Mol Sci* 23:15184, 2022. <https://doi.org/10.3390/ijms232315184>
41. Turan N, Heider RA, Zaharieva D, Ahmad FU, Barrow DL, Pradilla G: Sex differences in the formation of intracranial aneurysms and incidence and outcome of subarachnoid hemorrhage: Review of experimental and human studies. *Transl Stroke Res* 7:12-19, 2016. <https://doi.org/10.1007/s12975-015-0434-6>
42. Udy AA, Vlastic C, Saxby ER, Cohen J, Delaney A, Flower O, Anstey M, Bellomo R, Cooper DJ, Pilcher DV: Subarachnoid hemorrhage patients admitted to intensive care in australia and new zealand: A multicenter cohort analysis of in-hospital mortality over 15 years. *Crit Care Med* 45:e138-e145, 2017. <https://doi.org/10.1097/CCM.0000000000002059>
43. van Donkelaar CE, Bakker NA, Birks J, Veeger NJ, Metzemaekers JD, Molyneux AJ, Groen RJ, van Dijk JMCJS: Prediction of outcome after aneurysmal subarachnoid hemorrhage. *Stroke* 50:837-844, 2019. <https://doi.org/10.1161/STROKEAHA.118.023902>
44. van Gijn J, Rinkel GJ: Subarachnoid haemorrhage: Diagnosis, causes and management. *Brain* 124:249-278, 2001. <https://doi.org/10.1093/brain/124.2.249>
45. Vychopen M, Lampmann T, Asoglu H, Guresir A, Vatter H, Wach J, Guresir E: Non-convulsive status epilepticus in aneurysmal subarachnoid hemorrhage: A prognostic parameter. *Brain Sci* 13:184, 2023. <https://doi.org/10.3390/brainsci13020184>
46. Weller J, Lampmann T, Asoglu H, Schneider M, Ehrentauf SF, Lehmann F, Güresir E, Dorn F, Petzold GC, Vatter H, Zimmermann J: Additive prognostic impact of the cerebrospinal fluid arginine/ornithine ratio to established clinical scores in aneurysmal subarachnoid hemorrhage. *Front Neurol* 14:1156505, 2023. <https://doi.org/10.3389/fneur.2023.1156505>
47. Yin L, Ma CY, Li ZK, Wang DD, Bai CM: Predictors analysis of symptomatic cerebral vasospasm after subarachnoid hemorrhage. *Acta Neurochir Suppl* 110:175-178, 2011. https://doi.org/10.1007/978-3-7091-0356-2_32
48. Yousef K, Crago E, Kuo CW, Horowitz M, Hravnak M: Predictors of delayed cerebral ischemia after aneurysmal subarachnoid hemorrhage: A cardiac focus. *Neurocritical Care* 13:366-372, 2010. <https://doi.org/10.1007/s12028-010-9408-4>
49. Zeineddine HA, Divito A, McBride DW, Pandit P, Capone S, Dawes BH, Chen CJ, Grotta JC, Blackburn SL: Subarachnoid blood clearance and aneurysmal subarachnoid hemorrhage outcomes: A retrospective review. *Neurocrit Care* 39:172-179, 2023. <https://doi.org/10.1007/s12028-023-01729-x>