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# Factors Associated with Clinical Outcomes in Spontaneous Subarachnoid Hemorrhage

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## ABSTRACT

**Objective:** This study aims at evaluating the factors affecting prognosis in patients with aneurysmal subarachnoid hemorrhage (SAH).

**Methods:** The charts and 6th month outpatient clinic records of the patients who were treated with the diagnosis of SAH between 2016 and 2020 were retrospectively reviewed. Post-discharge clinical status, adaptation to life, and disability status of 44 patients with aneurysmal SAH who were treated with endovascular or microsurgical techniques in our clinic were evaluated with the Glasgow Outcome Scale Extended (GOSE). The relationship between the patient's age, gender, timing of treatment, the location of the aneurysm, the World Federation of Neurological Surgeons (WFNS) scale score, Hunt-Hess scale (HHS) score, Fisher scale score and preoperative evaluations that might affect the GOSE score after discharge were examined.

**Results:** Forty-four patients who met the criteria were included in the study. The mean age of the patients was 49.1±10.3 (minimum-maximum: 29-77). Of those, 54.5% were females while 45.5% were males. Comorbidity was present in 54.5% of the patients. The most common aneurysm was the middle cerebral artery aneurysm with the rate of 27.3%. Of the aneurysmal SAHs, 45.5% were treated with microsurgical clipping and 27.3% with endovascular treatment. A statistically significant correlation was found between GOSE score and timing of treatment days (p=0.014), WFNS (p=0.002) and HHS scores (p<0.001). No statistically significant correlation was found between GOSE score and patient's age (p=0.47) and Fisher scale score (p=0.465).

**Conclusion:** In our study, the effects of early surgery, WFNS, and HHS scores on clinical outcome in cerebral aneurysmatic SAH were shown.

**Keywords:** Spontaneous subarachnoid hematoma, prognosis, clinical outcomes

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## INTRODUCTION

Cerebral aneurysms (CA) occur in 3-5% of the general population (1). Aneurysm rupture causes subarachroid hemorrhage (SAH) and is associated with high mortality and morbidity (2). Its formation and pathophysiology have not been fully defined (3). Current treatment options consist of endovascular treatment and microsurgical clipping. Despite advances in surgical and endovascular techniques, equipment diversity in devices, and the improvements in intensive care units, mortality and morbidity associated with aneurysm rupture remain high (4). Treating ruptured aneurysms is required. The type of treatment is decided according to the choice of patients, the size and site of aneurysm. However, at vascular centers with a high annual number of microsurgical clipping, there is a tendency to perform clipping rather than applying endovascular treatment (5). Although the results of the International Study of Unruptured Intracranial Aneurysms and International Subarachnoid Aneurysm studies point to "coil first" with endovascular surgical intervention, there are ongoing discussions regarding the superiority of endovascular treatment and microsurgical clipping treatment over each other and which one should be preferred (6,7).

The Glasgow outcome scale-extended (GOSE) is used in the treatment of SAH and in the short and long-term follow-ups and results of these treatments, as in other cranial pathologies with brain injury (8,9). Many studies in the literature evaluate clinical outcome with GOSE. Correlation of applied treatment parameters and neurological status with GOSE is examined (8,9). Recently, some studies claimed that early aneurysm treatment achieves better clinical outcomes (8,10). There are also studies showing poor clinical outcomes in patients with WFNS grade IV and V SAH (9). There are few studies comparing GOSE score with preoperative parameters in SAH. No study was found in which all the mentioned parameters were compared with GOSE score.

In this study, we planned to investigate the effects of preoperative parameters and treatments in spontaneous SAH on clinical outcome.

## METHODS

The data of 44 patients who developed SAH due to CA rupture and were admitted to our clinic and were treated between 2016-2020 were analysed retrospectively. The patients with spontaneous SAH who were admitted to our hospital within 72 hours after bleeding were included in the study. The patients with non-spontaneous SAH and those with previous record of neurological diseases (cerebrovascular disease, neurodegenerative diseases, etc.) were excluded from the study. All data of the patients were collected from the hospital database. Data were collected in the following categories: patient age, gender, World Federation of Neurological Surgeons (WFNS) scale score (Table 1) (11), Hunt-Hess scale (HHS) score (Table 2) (12), Fisher scale score (Table 3) (12), the site of aneurysm, the type of treatment performed (microsurgical clipping/endovascular treatment) and the number of days between first bleeding and application of treatment. In addition, the patients' adaptation to life and disability status were evaluated with the (GOSE) score (Table 4) (13) at the 6th month after discharge. Cerebral computed tomography (CT), cerebral CT angiography and Digital Subtraction Angiography (DSA) were performed in all patients after admission to the hospital. Control DSA was also performed in the patients at the 6th month.

The patients were treated by a single surgeon experienced in vascular surgery. They were operated with micro-Doppler and neuromonitoring.

Single or multiple aneurysm clips (Sugita®, Mizuho, Tokyo, Japan) were used during surgery. Endovascular treatment was performed by experienced senior neuroradiologists. Diagnostic or therapeutic angiography was performed with a routine femoral approach using biplane angio-graphic system with a flat panel detector (Toshiba Infinix, Toshiba Medical, Nasu, Japan). Lesions were treated with coils (Boston Scientific Corp., Natick, MA, USA) and stent (Neuroform® Stent System, Boston Scientific Corp., Natick, MA, USA).

All procedures were carried out in accordance with the 1964 Helsinki declaration. Written informed consent for scientific

**Table 1. World Federation of Neurological Surgeons scale**

| Grade | Glasgow coma scale score | Motor deficit |
|---|---|---|
| I | 15 | Absent |
| II | 13-14 | Absent |
| III | 13-14 | Present |
| IV | 7-12 | Present or absent |
| V | 3-6 | Present or absent |

**Table 2. Hunt-Hess scale**

| Grade | Criteria |
|---|---|
| I | Asymptomatic, or minimal headache, nuchal rigidity |
| II | Moderate to severe headache, no neurological deficit except for cranial nerve palsy |
| II | Drowsiness, confusion, mild focal deficit |
| IV | Stupor, moderate to severe hemiparesis, early decerebrate posturing |
| V | Deep coma, decerebrate posturing, moribund |

**Table 3. Fisher scale**

| Grade | CT scan |
|---|---|
| 1 | No blood visualized |
| 2 | A diffuse deposition or thin layer with all vertical layers of blood (interhemispheric fissure, insular cistern, ambient cistern) less than 1 mm thick |
| 3 | Localized clots and/or vertical layers of blood 1 mm or greater in thickness |
| 4 | Diffuse or no subarachnoid blood, but with intracerebral or intraventricular clots |

CT: computed tomography

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**Table 4. Glasgow outcome scale-extended**

| Category | Name | Definition |
|---|---|---|
| 1 | Death | |
| 2 | Persistent vegetative state | Unresponsive and speechless |
| 3 | Sever disability Lower | Requires frequent help of someone to be around at home most of the time every day |
| 4 | Sever disability Upper | Can be left alone >8 h during the day, but unable to travel and/or go shopping without assistance |
| 5 | Moderate disability Lower | Unable to work or only in sheltered workshop |
| 6 | Moderate disability Upper | Reduced work capacity; resumes <50% of the pre-injury level of social and leisure activities |
| 7 | Good recovery Lower | Minor problems that affect daily life; resumes >50% of the pre-injury level of social and leisure activities |
| 8 | Good recovery Upper | No current problems related to the brain injury that affect daily life |

**Table 5. Description of study participants**

| | Characteristics | |
|---|---|---|
| Age | $\bar{x}\pm s$ | 49.1±10.3 |
| Gender | Female, n (%) | 24 (54.5) |
| | Male, n (%) | 20 (45.5) |
| Co-morbidities | Yes, n (%) | 24 (54.5) |
| | No, n (%) | 20 (45.5) |
| Hypertension | Yes, n (%) | 20 (45.5) |
| | No, n (%) | 24 (54.5) |
| Asthma | Yes, n (%) | 4 (9.1) |
| | No, n (%) | 40 (90.9) |
| Other co-morbidities | Yes, n (%) | 10 (22.7) |
| | No, n (%) | 34 (77.3) |

**Table 6. WFNS scale, HHS and Fisher scale scores**

| | Score | n (%) |
|---|---|---|
| **WFNS scale** | 1 | 18 (40.9) |
| | 2 | 10 (22.7) |
| | 3 | 8 (18.2) |
| | 4 | 5 (11.4) |
| | 5 | 3 (6.8) |
| **Fisher scale** | 1 | 3 (6.8) |
| | 2 | 8 (18.2) |
| | 3 | 17 (38.6) |
| | 4 | 16 (36.4) |
| **HHS** | 1 | 18 (40.9) |
| | 2 | 10 (22.7) |
| | 3 | 8 (18.2) |
| | 4 | 5 (11.4) |
| | 5 | 3 (6.8) |

WFNS: World Federation of Neurological Surgeons, HHS: Hunt-Hess scale

purposes and clinical data collection were obtained from patients according to institutional protocol. Ethical approval was obtained from the local ethics committee (approval no: 319, date: 22.09.2021).

### Statistical Analysis

The Statistical Package for Social Sciences (SPSS) 25.0 was used for statistical analysis (SPSS Inc.; Chicago, IL, USA). The Kolmogorov-Smirnov test was used to examine the normal distribution. According to results of normality analyses, the data was not normally distributed. The descriptive statistical methods (frequency, percentage, mean, standard deviation) were used to evaluate the demographic data. Pearson's chi-square test was used to compare the qualitative data. The Spearman correlation analysis was used for analysing the association of the quantitative data. The results were evaluated at a confidence interval of 95% and a significance level of $p<0.05$.

## RESULTS

The total number of patients who were admitted to the clinic with the diagnosis of CA and underwent treatment between 2016 and 2020 was 44. The characteristic features of the patients are given in Table 5. Their mean age was 49.1±10.3 (minimum-maximum: 29-77). Of them 54.5% were females while 45.5% were males. Comorbidity was present in 54.5% of the patients. The three most common comorbidities were hypertension (HT) (45.5%), asthma and chronic obstructive pulmonary disease. WFNS scale, HHS and Fisher scale scores of the patients are shown in Table 6. The most common values for each scale were as follows: For WFNS scale score "Grade 1" in18 (40.9%) patients, for HHS score "1" in 18 (40.9%) patients, and for Fisher score "3" in 17 (38.6%) patients.

The angiography results of the patients with SAH were as follows: Twelve (27.3%) had middle cerebral artery (MCA) aneurysm, 8 (18.2%) anterior communicating artery (AcoA) aneurysm, 4 (9.1%) internal carotid artery aneurysm, 3 (6.8%) posterior communicating artery aneurysm, 2 (4.5%) distal anterior cerebral artery aneurysm, 2 (4.5%) posterior inferior cerebellar artery aneurysm, 1 (2.3%)

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basilar artery type aneurysm (Figure 1). Twelve (27.3%) patients were angiography negative. Except for these 12 patients, 20 (45.5%) patients were treated with microsurgical clipping and 12 (27.3%) patients with endovascular treatment, making the total number of treated patients 32. The mean number of days between bleeding and application of microsurgical clipping or endovascular treatment after SAH was 1.2, with the first day and the fifth day of bleeding representing the minimum and maximum values, respectively.

The study found a statistically significant negative correlation between GOSE score and timing of treatment (p=0.014) and a moderate significant negative correlation between GOSE and WFNS scale (p=0.002) and HHS scores (p<0.001) (Table 7). The overall mortality rate of the patients at the 6-month follow-up was 11.3%.

## DISCUSSION

Nearly half of the SAH cases are caused by CA (14). Studies on predicting the prognosis of patients after SAH and the risk factors that affect the treatment outcome are still pending (15). In our current study, a negative correlation was found between WFNS scale and HHS scores, which were the preoperative evaluation scales, the GOSE score, and the timing of treatment applied.

**Table 7. Relationship of clinical parameters with GOSE**

| | GOSE | |
|---|---|---|
| | r | p-value* |
| Surgery day | -0.390 | 0.014 |
| WFNS | -0.477 | 0.002 |
| HHS | -0.566 | <0.001 |
| Age | 0.119 | 0.47 |
| Fisher scale | -0.120 | 0.465 |

*Spearman correlation, GOSE: Glasgow outcome scale-extended, WFNS: World Federation of Neurological Surgeons, HHS: Hunt-Hess scale

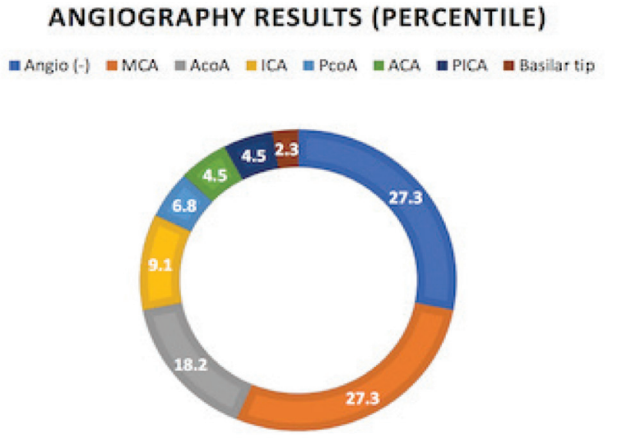


**Figure 1.** Angiography results (percentile)

*MCA: middle cerebral artery, AcoA: anterior communicating artery, ICA: internal carotid artery, PcoA: posterior communicating artery, ACA: anterior cerebral artery, PICA: posterior inferior cerebellar artery*

In this study, 27.3% of the 44 patients with SAH were found to have negative angiogram. When compared with the literature this rate is high. In the literature, angiogram negative SAHs constitute approximately 10-20% of spontaneous SAHs (16,17). It also has the same negative clinical outcomes as aneurysmal SAH (16,17). In line with the literature, GOSE scores of patients with angiogram negative SAH and aneurysmal SAH are similar. It is thought that the frequency of angiogram negative SAHs has increased, and this may be related to the widespread use of antiplatelet drugs (18).

Complications after SAH (vasospasm, ischemic neurological deficit, and brain infarction) are closely related to age and gender (19). While the incidence of complications is lower in elderly patients, they occur more commonly among the younger patients (20). It has been stated that 30-39 age group has higher risk whereas 60-69 age group has significantly lower risk (19). In addition, there are studies showing that the females are at higher risk of experiencing SAH and its complications (19,21). Our study, however, found no significant gender (p=0.395) or age (p=0.119) related difference among our patients in terms of risks. Although the studies in the literature generally state that age and gender are important risk factors, there are also articles with findings concurring that of our study (22).

HT is accepted as a risk factor for aneurysm formation and rupture (23). Laboratory studies have shown that a link exists between cerebral aneurysm and HT (24). Our study also found that HT was the most important morbidity accompanying SAH.

The most common site for aneurysm was MCA. In the literature, however, the most common site for aneurysm is ACoA which is the type of aneurysm with the highest rate of mortality and morbidity (3). The mortality rate we found in our study (11.7%) was unaffected by the site of aneurysm. We think that this differentiation may be related to the sample size of our study (n=44).

Discussions on the timing of surgery continue and varying views have been put forward about this issue thus far (25-27). However, in our study, we found a statistically significant relationship between the timing of surgery and GOSE score (p=0.014): The earlier the surgery was performed, the higher the patient's GOSE values and the lower the mortality and morbidity were.

A strongly negative correlation was found between the HHS and GOSE scores of the patients (p<0.001). As HHS score increased, survival rate decreased significantly. We think that it gives a very significant information about the prognosis. Past studies also support our findings (27-30). For example, studies conducted with 100 patients with SAH in 2001, with 3567 patients with SAH in 2007, with 720 patients with SAH in 2020, as well as some other studies conducted with many patients revealed the relationship between HHS score and prognosis (31-33). Like HHS score, WFNS scale score was also found to have a statistically significant relationship with GOSE score (p=0.002). As WFNS scale score increased, GOSE score decreased. A look at the literature shows that the findings about WFNS scale score and patient prognosis are compatible with our results (31-36).

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In the literature comparing clinical outcome and preoperative parameters, fewer parameters were examined than in our study. We determined that all parameters such as age, gender, day of surgery, HHS, WFNS Scale and Fisher scale scores, and aneurysm localization were not considered.

In our study, it was seen that the findings related to age and gender were not compatible with the literature. Findings on the day of surgery and WFNS scale score were consistent with the literature. Findings on HHS and Fisher scale scores supported the literature.

### Study Limitations

The limitations of the study were that it was conducted in a single center, it was retrospective, and the number of patients was low. The low number of patients caused underpowered statistical analysis. Consequently, further comparative, long-term studies with larger patient groups are necessary to confirm these findings.

## CONCLUSION

We suggest that WFNS scale and HHS scores of patients with aneurysmal SAH and timing of treatment provide important information about their GOSE scores and thereby the prognosis. Age, gender, comorbidities of the patients and the site of aneurysm did not make a significant contribution to the prognosis of the patients. Identifying and analysing the risk factors in studies with larger sample sizes will contribute to the literature. Conducting the study with a larger patient series will yield more reliable results.

**Ethics Committee Approval:** Ethical approval was obtained from the University of Health Sciences Turkey, Gaziosmanpaşa Training and Research Hospital Clinical Research Ethics Committee (approval no: 319, date: 22.09.2021).

**Informed Consent:** Written informed consent for scientific purposes and clinical data collection were obtained from patients according to institutional protocol.

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