



Clinical Characteristics of Poor-Grade Aneurysmal Subarachnoid Hemorrhage Treatment

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Abstract

Background The initial clinical status after aneurysm rupture, whether primary or secondary, determines the final outcome. The most common cause of patient deterioration is a high Hunt and Hess (HH) score, which correlates closely with a high mortality rate. Poor-grade aneurysmal subarachnoid hemorrhage (SAH) is determined as an HH score 4 or 5. The aim of this study was to evaluate the clinical characteristics of poor graded aneurysmal SAH at our institution.

Patients and Methods During the 5-year period, 415 patients with intracranial aneurysm were admitted to our institution. Patients with poor-grade aneurysmal SAH accounted 31.08% ($n=132$) of the total number of ruptured aneurysms. Interventional treatment was predominantly in the form of surgery, whereas conservative treatment included medication and external ventricular drainage. Final outcome was assessed with a modified Rankin score (mRs). Statistical analysis was performed using SPSS version 23.0 with a significance level set to 5% ($\alpha=0.05$).

Results The majority of patients (57.6%) were in the age range from 51 to 69 years. Twenty-five patients (18.9%) had an HH score of 4, whereas 107 patients (81.1%) had an HH score of 5. Depending on the location, the majority of patients ($n=43$) had an aneurysm on the medial cerebral artery (MCA). The final aneurysm occlusion was performed in 71 patients, of whom 94.36% were treated surgically. A positive outcome (mRs 0–4) was found in 49.25% of patients who underwent primarily surgical, treatment with a mortality of 42.3%. Although the outcome was better in patients with an HH score 4, both groups benefited from surgical treatment.

Keywords

- ▶ outcome
- ▶ poor grade
- ▶ subarachnoid hemorrhage
- ▶ surgery
- ▶ treatment

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Conclusion Poor-grade aneurysmal SAH is a condition of the middle and older age, with most patients with an HH 5 score and deep comatose state. There was better outcome in patients with an HH score of 4 compared to an HH score of 5 and both groups benefited from surgical treatment, which resulted in a positive outcome in almost 50% of surgically treated patients.

Introduction

Intracranial aneurysms are dilations of cerebral arteries caused by hemodynamic and structural changes. Most aneurysms develop spontaneously, while only 1 to 2% are associated with trauma, infection, or tumor.¹⁻⁵ In more than 80% of cases, the cause of subarachnoid hemorrhage (SAH) is rupture of the intracranial aneurysm. Large autopsy series have shown that approximately 5% of the population develops an aneurysm at some stage of life.⁶ According to a large study series, the initial clinical status determines the outcome.² Of all patients with SAH, 3 to 18% of them die at the time of hospitalization as well as 40% of those treated in hospital.⁷

Clinical and neurological status is most commonly determined using the Hunt and Hess (HH) score. The most common causes of patient deterioration is re-hemorrhage or high HH score. HH score as well as aneurysm diameter was directly related to early rehemorrhage.⁸ There is a closed correlation of 75% HH score 5 patients and vasospasm, whereas this is observed in only 2% of patients with an HH score of 1. It is known that mortality is increased in patients with an HH score 5. The incidence of re-hemorrhage is the highest within 24 hours of the hemorrhage, while mortality after re-hemorrhage is up to 75%.^{2,9-13}

Given the high mortality of patients with poor HH score and high rate of hemorrhage, the aim of this study was to evaluate the clinical characteristics and outcome of poor-grade aneurysmal SAH at our institution.

Patients and Methods

We performed a retrospective study that included all patients who were treated in the Department of Neurosurgery, Clinical Center University of Sarajevo, with a diagnosis of aneurysmal subarachnoid hemorrhage from January 1, 2015, to December 31, 2020. This study was approved by our institution ethics committee. Informed consent was taken from legal guardians of patients. All aneurysmal SAH (aSAH) were diagnostic with the CT and CT angiography of the brain or DSA. Demographic and clinical data were collected from the patient's history. The HH scale was used to assess the severity of aSAH, while Fisher's scale was used to measure the amount of blood appearing on the computed tomography (CT). Both scales were documented on admission to the hospital. Inclusion criteria were patients with an HH score 4 or 5, patients older than 18 years, and patients with complete medical documentation.

The term "poor-grade SAH" refers to patients who were classified as score 4 or 5 according to the HH score at the time of admission to the hospital.¹⁴

Based on the admission, Glasgow Coma Score (GCS) patients were divided into three groups: GCS (8–12), GCS (5–8), and deepest coma GCS 3 and 4. The location of the aneurysms was divided into nine groups according to the occurrence in the projection of the Willis circle.

As a treatment modality, interventional treatment was performed in the form of microsurgery or endovascular treatment, depending on the interdisciplinary approach to each patient. All patients with acute hydrocephalus or intraventricular hemorrhage were treated with external ventricular drainage. When patients present with bilateral dilated pupils, impaired blood flow on transcranial Doppler (TCD), massive hematoma in the basal ganglia of the dominant hemisphere or hematoma in the brainstem occur, they are treated conservatively. We defined the final outcome in the form of a modified Rankin score (mRs) at the discharge. Excellent and satisfactory outcome imply positive outcome mRs 0 to 4.

Statistical analysis was performed with GraphPad software. Continuous variables were presented as mean \pm standard deviation (SD), and categorical variables as frequency (percentage). Categorical variables were analyzed using the Fisher exact test and the unpaired *t*-test for parametric values. *p*-Values less than 0.05 were considered statistically significant.

Results

During the study period, 5,615 patients were admitted to our hospital, 415 of whom had a cerebral aneurysm. Poor-grade SAH patients represent 2.35% of the general neurosurgical patients and 31.08% ($n = 132$) of the total number of aneurysms. The youngest patient aged 26 years and the oldest aged 86 years, with an average age of 57.7 years (**► Table 1**).

The most common age group was group 51 to 69 years, which was 57.6%, followed by groups over 70 years and 31 to 50 years, with 24% of patients each. In our cohort, we had 25 patients with an HH score 4 (18.9%), whereas there were 107 patients with an HH score 5 (81.1%). The majority of patients (81.1%) were in Fisher grade 4.

Most patients in this study were in a deep coma (**► Table 1**). According to the aneurysm location, the most common aneurysmal location was middle cerebral artery in (in 33%), followed by anterior communicating artery (in 28%) and internal carotid artery (in 16%) (**► Fig. 1**).

Table 1 Baseline clinical characteristics of patients

| Characteristic | n = 132 |
|-----------------------------|--------------|
| Gender | |
| Male | 44 |
| Female | 88 |
| Age (y) | 57.7 ± 12.25 |
| GCS at admission | |
| GCS 8-12 | 4 |
| GCS 5-8 | 26 |
| GCS 3-4 | 76 |
| Hunt and Hess | |
| Grade IV | 25 |
| Grade V | 107 |
| Fisher grade | |
| Grade I | 2 |
| Grade II | 2 |
| Grade III | 21 |
| Grade IV | 107 |
| Location of aneurysm | |
| anterior circulation | 113 |
| posterior circulation | 19 |
| Treatment modality | |
| endovascular | 4 |
| Microsurgical | 67 |

There is also predominance of aneurysm of the anterior location (85.6% of patients). Of all patients, 71 patients were treated surgically or underwent endovascular treatment (►Table 1). We had 61 (46.2%) conservatively treated patients due to their clinical state. For interventional, primarily surgically treated patients, a positive outcome (mRs 0–4) was found in 49.25% of patients with a mortality of 42.3%. However, excellent outcome (mRs 0–2), was found in 30.38% of surgically treated patients and 19.36% of general poor-grade SAH patients.

Analysis of Treatment

Our study showed that patients aged 51 to 69 years were the most frequently treated; however, there were statistically significant differences in the representation of patients in certain age groups by type of treatment. Patients who were treated conservatively were most often in the older age group of over 70 years ($p = 0.002$). Patients undergoing endovascular treatment were in the age group 31 to 50 years (75.0%), whereas surgically treated patients were mostly in the age group 51 to 69 years (64.2%). In addition, conservatively treated patients were the oldest with a mean age of 62.97 ± 12.31 years, while surgically treated patients had a mean age of 55.64 ± 12.13 years. Statistical analysis using the Mann–Whitney U test for independent samples showed that there was a statistically significant difference in the mean age

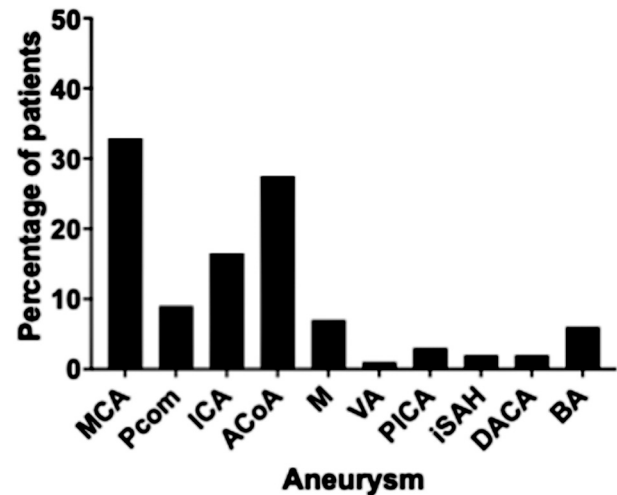


Fig. 1 Location of the source of bleeding in “poor-grade patients”. MCA dominance was found in more than 33% of cases, followed by ACoA aneurysms and ICA complex aneurysms. In case of multiple aneurysms, no significant source of bleeding could be identified with certainty. MCA, middle cerebral artery; Pcom, posterior communicating artery; ICA, internal carotid artery; ACoA, anterior communicating artery; M, multiple aneurysms; VA, vertebral artery; PICA, posterior inferior cerebellar artery; iSAH, idiopathic SAH; DACA, distal anterior cerebral artery; BA, basilar artery.

between treatment types ($p = 0.006$), as well as a negative correlation with higher age group ($p = 0.028–0.003$). There was a statistically significant difference between the choice of treatment type with respect to the patient’s age. It should be noted that most elderly patients are in a deep coma.

According to the state of consciousness, conservatively treated patients were more often in coma 54 (88.5%) compared to surgically treated patients 53 or 74.6% ($p = 0.042$). Comparison of the degree of coma depth according to the GCS scale and the type of treatment showed a statistically significant difference between the type of treatment and the degree of coma depth ($p = 0.0001$). Also, 80.3% ($n = 49$) of conservatively treated patients were in deep coma compared to 46.5% ($n = 33$) treated with final aneurysm intervention (►Fig. 2). Analysis of treatment modality versus aneurysm

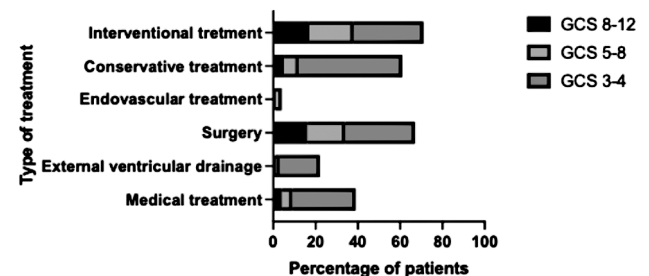


Fig. 2 The relation of the state of consciousness measured by GCS score with a choice of type and group of treatments. A comparison of the degree of coma depth according to the GCS scale and the types and groups of treatment shows that there is a statistically significant difference between the types of treatment according to the depth of coma ($p = 0.0001$).

location revealed no statistically significant difference in final outcome.

As expected, we found the lethal outcome of conservatively treated patients in 94.9% ($n = 37/39$) as well as in those treated with external ventricular drainage without final intervention on the aneurysm (100%). For surgically treated patients, we found a positive outcome in 34.3% ($n = 23$) with lethality in 43.3% of patients ($n = 29$). For the same group of patients, we had a satisfactory outcome in 14.9% ($n = 10$) patients, while a poor outcome was recorded in 7.5% ($n = 5$) patients. Statistical analysis indicates a highly significant difference between treatment types and treatment outcomes.

Outcome of Surgically Treated Patients in Relation to the HH Score

Surgical treatment was mostly performed in HH score 5 patients compared with the HH score 4 group. In general, we found a positive outcome in 47.1% ($n = 8$) of the HH score 4 compared with 30.0% ($n = 15$) of the HH score 5 group. Satisfactory and poor outcomes were found in 11.8% of HH score 4 ($n = 2$) with lethal outcome in 29.4% ($n = 5$) of patients. In HH score 5, we found a satisfactory outcome in 16.0% ($n = 8/50$) patients, while a poor outcome was seen in 6.0% ($n = 3$) patients, with 48% ($n = 24$) have a lethal outcome. There was no statistically significant difference or correlation between HH score and treatment outcome ($p > 0.05$). Although there is a better outcome in HH score 4 patients; both groups have a significant benefit from surgical treatment. The regression model shows that treatment and location have a statistically significant predictive potential for lethal outcome, while age, HH score, GCS, and Fisher grade have no predictive potential (odds ratio [OR] = 2.070 and $p = 0.001$) (► **Table 2**).

Discussion

In this study, we evaluated the clinical characteristics and outcome of poor-grade aneurysmal SAH at our institution. We have found that primarily, surgically treated patients with HH score 4 or 5 have a positive outcome (mRs 0–4) in 49.25% of patients, with a mortality of 42.3%.

The final outcome of treatment of “poor-grade SAH patients” is difficult to predict. Poor clinical grade is also possible as a consequence of intracerebral hematoma, in-

creased intracranial pressure, hydrocephalus, and due to herniation of brain structures.¹⁵ We have found in this study that patients with poor-grade SAH have a positive outcome in terms of mRs (0–4) in 49.25% of the patients who underwent interventional treatment.

Comparing isolated mortality, it was clearly defined as 83% in the earlier era versus 39% in the current era with a slightly higher mortality of our patients of 43.28%, but without the option of endovascular treatment at full capacity. A recent study from 2020 goes a step further in assessing the early aggressive treatment of patients with HH score 5, and those in the deepest degree of coma (GCS 3–5). Although the mortality rate is 65.8%, those who survive are able to live alone or with the help of another person in 85.5% of cases.¹⁰ Our mortality results of the total sample correlate with the above study and are 67%. From a comparative point of view, the best chance of a favorable outcome is exclusively for patients who have been treated surgically, when we decide that the treatment is justified. Thus, some studies show a survival in 38% of patients 1 year after SAH and 73% in the period of 3 months after bleeding.^{16,17} In our study, we recorded similar results for conservatively treated patients, who usually die at early intrahospital stage. We determined similar criteria for the selection of patients to be treated conservatively, with GCS scale that is usually 3 or 4 for such patients.

Moreover, we believe that aneurysms, especially localizations on the MCA, should be urgently treated with the accompanying evacuation of the intracerebral hematoma. If edema is expected or recorded, our surgical strategy is projected toward approach, incision planning, and larger, sometimes decompressive craniotomy. It is important to emphasize that a worse outcome was recorded in patients with presented intracerebral hematoma, whether evacuation of the hematoma was performed or not. However, the choice of decompressive craniectomy shows no long-term benefit.¹⁸

Ellenbogen¹⁵ showed that early aggressive treatment involving EVD, and ultra-early aneurysm intervention results with mortality of 50%. Our results suggest a slightly lower mortality of 43.28% compared with the previous study, and predominantly surgical treatment was performed. In the same study, 26 surviving patients underwent neurophysiological examination, and an excellent outcome was noted in

Table 2 Predictive factors of mortality in regression model

| Predictor | β | SE | Wald | df | Significant | Odds ratio | Lower | Upper |
|---------------------|--------|-------|--------|----|-------------|------------|-------|--------|
| Age | 0.032 | 0.020 | 2.493 | 1 | 0.114 | 1.033 | 0.992 | 1.075 |
| Hunt and Hess score | 1.456 | 1.064 | 1.871 | 1 | 0.171 | 4.287 | 0.532 | 34.518 |
| Glasgow Coma Score | −0.078 | 0.564 | 0.019 | 1 | 0.890 | 0.925 | 0.306 | 2.796 |
| Fisher grade | 0.488 | 0.452 | 1.166 | 1 | 0.280 | 1.628 | 0.672 | 3.946 |
| Treatment | −2.198 | 0.537 | 16.767 | 1 | 0.000 | 0.111 | 0.039 | 0.318 |
| Location | −0.225 | 0.110 | 4.215 | 1 | 0.040 | 0.798 | 0.644 | 0.990 |
| Constant | −3.266 | 4.733 | 0.476 | 1 | 0.490 | 0.038 | | |

Abbreviations: β, beta coefficient; df, degrees of freedom; SE, standard error.

terms of cognitive brain function in surgical versus endovascular treatment.¹⁵ A study conducted on 248 patients with “poor-grade” SAH showed a 24% favorable outcome mostly in WFNS 4 (61%). In our study, most patients were HH score 5, which would correspond to the WFNS score 5. Some authors reported a favorable outcome in 36% of treated and 24% of the total number of patients with WFNS grade 5 in the case of early intervention within 24 hours.¹⁹ Compared with our study, we recorded a statistically significant positive deviation of our results in terms of outcomes in general but also relative to the HH group. The possible bias of the results can be observed in the determination of determining a positive outcome.

A study from India on 2,039 patients shows an increase in favorable treatment outcome to 30% in patients with “poor-grade” SAH patients measured with the GOS with a male/female ratio of 51:49%. Interventional treatment for “poor grade” patients is performed only if patients show neurological recovery.²⁰ In another study, 30% of patients with HH score 4 had a good outcome after surgical occlusion, as opposed to 11% of patients with HH score 5.¹⁵ Zeng et al showed a significant reduction in mortality in surgical versus conservatively treated patients in early-treated patients, within 24 hours. The results of this study are better compared to our positive outcome of our results of 44.17% for HH 4 patients, but significantly worse compared to the 19% of favorable outcome for HH score 5 patients of our study. The Barrow Neurological Institute study from 2018 shows mRs 2 outcome observed in 55% of poor-grade patients on ACM aneurysms.^{21,22}

Depending on the studies and data sources, we can conclude that a favorable outcome can usually be achieved in the range of 30 to 65% of patients. Our results of surgical treatment are close to the average results of recent studies. Still, a positive outcome in terms of mRs (0–4) was observed in 49.25% of the patients who underwent interventional treatment.

Recent studies analyze the influence of location on the outcome of patient outcome. Thus, a 10-year study from the United States with 2,152 aneurysms confirmed that anterior communicating artery (ACoA) complex aneurysms were the dominant location. Similar data were reported in other studies.^{22,23} Another German study showed an increase in the percentage of ACM (27% ACM) aneurysms and a significant decrease in the number of ICA aneurysms.²⁴ Our data reported 33.3% of patients with ACM aneurysms. As a possible cause for the more frequent occurrence of ACM location, in our study, the presence of intracerebral hematoma is very common, which brings the patient to the neurosurgeon earlier. A similar pattern of occurrence was observed in the total number regardless of HH score, in 23.5% of the total 415 aneurysms in the 5-year period. Also, the increase in the percentage of early interventional treatment of incidental on the reduction in the number of ruptured aneurysms in the internal cerebral artery (ICA) is possible.

Male gender and younger age are associated with favorable outcome after poor-grade SAH.⁹ Of all patients, 66.4%

were female, which in consistence with others studies.¹³ Although the percentage of complications and poor outcomes is related to age, the current view is that patients in the geriatric population, including those over 80 years, should be treated surgically, if the quality of life was satisfactory before SAH. Patients up to the age of 60 years of age should definitely be treated.¹⁵ Analyzing the mortality of the elderly population, one study argues in favor of a statistically significantly worse outcome in patients with SAH who are older than 65 years. Nevertheless, a favorable outcome was observed in 31% of treated patients with a dominant PCom localization, and most patient underwent endovascular treatment.²⁵ When comparing our results, we found that mortality as well as the outcomes did not correlate in the negative sense of our results. ACM aneurysms were dominant in our population. Another study from India in the geriatric population with “poor-grade” SAH showed a favorable outcome in terms of GOS in 48% of treated patients if treatment is delayed for 9 to 14 days after bleeding.²⁶ In our study, the geriatric population accounted for one-fifth of the patients. Our study showed that in the elder population, the outcome is significantly worse after 60 years. Our results have shown that mortality is more common in the geriatric population.

Some recent studies suggest delaying treatment of patients with “poor-grade” until the patients recover on the HH scale with a favorable outcome. Early surgery and aggressive medical treatment resulted in better outcomes in 7 to 42.6% of patients.^{27–29} Although some studies emphasize the treatment of aneurysms as an emergency within 72 hours of bleeding,^{21,30} but the ideal timing of the intervention is still not clear. Konczalla et al²⁴ suggest significant survival and favorable outcome for comatose patients defined as mRs 0 to 3 for comatose patients if early and aggressive treatment is initiated. Potential positive outcome factors include younger age, normal pupillary response, development of early hydrocephalus, and positive bilateral corneal reflex. Delaying the treatment of patients with score HH 4 and 5 is no longer justified and that early aggressive treatment, whether endovascular or surgical, is necessary.²⁴

Limitations

The study has several limitations. The study was designed as a retrospective study with subsequent insight into patient histories through the medical records with available data without socio-epidemiological and etiological link. Also, there is no adequate ratio of surgical versus endovascularly treated patients and it is not possible to make comparative results regarding “poor-grade SAH” patients.

Conclusion

In our study, a comprehensive analysis of 132 “poor-grade aneurysmal SAH” patients, most patients presented as HH score 5, and GCS 3 and 4 was performed. For interventional, primarily surgically, treated patients, a positive outcome (mRs 0–4) was found in 49.25% of patients with a mortality

of 42.3% in our study. Although there is a better outcome in patients with HH score 4 compared to score 5, both groups have a benefit from surgical treatment. However, excellent outcome (mRs 0–2) was found in 30.38% of surgically treated patients or 19.36% of general poor grade SAH patients. This study has shown that patients with HH score 4 and 5 should not be surgically abandoned, they need an active treatment to get the best possible results. However, we believe that our study can represent a solid basis for further research.

Authors' Contributions

Adi Ahmetspahić designed the study, collected the data, and contributed to the analysis of the results and the writing of the manuscript. Dragan Janković contributed to the analysis of the results and the writing of the manuscript. Eldin Burazerović contributed to the analysis of the results and the writing of the manuscript, he also supervised the findings of this work. Bekir Rovčanin contributed to the analysis of the results and the writing of the manuscript. Amina Šahbaz collected the data and contributed to the analysis of the results. Esma Hasanagić contributed to the collection of the data and the analysis of the results. Almir Džurlić contributed to the collection of the data and the writing of the manuscript. Nermir Granov contributed to the design of the study and supervised the findings of this work. Alberto Feletti designed the study and supervised the findings of this work. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of Interest

None declared.

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