Initial severity of aneurysmal subarachnoid hemorrhage (SAH): Trend over time

Seung Bin Sung, Young Deok Kim, Seung Pil Ban, Yong Jae Lee, O-Ki Kwon
Department of Neurosurgery, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seoul, Korea

Objective: The trend in the initial severity of aneurysmal subarachnoid hemorrhage (SAH) is unclear. This study aimed to evaluate whether there was an improvement in the initial severity of SAH over time.

Methods: From January 1, 2005, to December 31, 2020, we identified patients who visited the emergency department of our institution with SAH due to intracranial aneurysm rupture. We identified the Hunt Hess (HH) grade and modified Fisher grade of each patient from the medical records, and the Mann-Kendal method was used to estimate the trend of each grade system.

Results: A total of 547 patients with SAH were identified. The mean age of the patients was 59.3 years (standard deviation (SD), 14.6). The mean aneurysm size was 6.9 mm (SD, 4.6 mm). The most frequent aneurysm location was the anterior communicating artery (28.7%). In the Mann-Kendal estimates for the analysis of the trend, there was no statistically significant grade throughout the HH and modified Fisher grades. Similarly, there was no improvement throughout all grades in the modified Fisher grade over time.

Conclusions: The initial severity of SAH due to cerebral aneurysm rupture did not improve over time.

Keywords: Aneurysmal subarachnoid hemorrhage, Severity, Trends

INTRODUCTION

Subarachnoid hemorrhage (SAH) due to rupture of a cerebral aneurysm is a devastating disease because of its high mortality and morbidity. For decades, these outcomes have improved with advances in medical management and aneurysm treatment strategies, including surgical clipping and endovascular coil embolization.

The initial neurological status of patients with SAH is associated with mortality and morbidity. A high Hunt Hess (HH) grade is associated with higher mortality and morbidity than a low HH grade. If the HH grade improves over time, it could contribute to improving the outcomes of SAH.
An improvement in the HH grade could be related to the strategy or stance for the treatment of unruptured intracranial aneurysms. We have a more aggressive stance on aneurysms with presumed risk factors for rupture. These risk factors are related to size, location, features of the aneurysms, and patient characteristics such as age, sex, hypertension, and smoking. The aneurysm size, location, age, and history of hypertension are risk factors for the outcomes of SAH. Thus, aneurysm rupture and SAH outcomes have several common risk factors. In addition, the number of treatments for unruptured intracranial aneurysms is increasing. Therefore, if we treat a sufficient number of unruptured intracranial aneurysms with a high risk of rupture, the mortality and morbidity could be lowered following the improvement of the initial severity.

However, the trend in the HH grade for SAH has not yet been evaluated. Some studies have included information on the initial severity of SAH, but it was roughly described, so it could not be determined whether there was an improvement.

Similarly, the initial amount and extent of SAH could affect outcomes. Cerebral ischemia due to vasospasm is associated with high morbidity and mortality; however, the changes over time are also unclear. Therefore, this study aimed to evaluate whether there was a change in the initial severity of SAH over time.

MATERIALS AND METHODS

We conducted a retrospective observational study to evaluate trends in the initial severity of SAH. The requirement for informed consent was waived because this study was based on retrospective data.

Patients

From January 1, 2005, to December 31, 2020, we identified patients who visited the emergency department of our institution with SAH due to intracranial aneurysm rupture. We excluded patients who had SAH with other etiologies, such as rupture of arteriovenous malformation or arteriovenous fistula (AVF). Patients transferred from other institutions were also excluded because their initial status was not confirmed. Finally, a total number of 547 patients were included in this study.

Assessment of the initial severity

To assess the initial severity, we adapted the HH grade. The HH grade is a grading system for the severity of SAH based on the patients’ clinical status, such as headache and mental status. A higher HH grade is associated with higher mortality. The amount and location of SAH were determined by the modified Fisher grade.

We identified the HH grade and modified Fisher grade of each patient from the medical records and brain imaging studies, such as computed tomography and catheter angiography.

Statistical analysis

Continuous variables were presented as either mean and standard deviation (SD) or median and interquartile range (IQR). Categorical variables are presented as percentages and counts.

To estimate the trend of each grading system, the Mann-Kendal method was used. We defined \( P<0.05 \) as statistically significant. If the \( P \)-value of the Mann-Kendal method was \( <0.05 \), we determined that it had a trend of increasing or decreasing over time.

All statistical analyses were performed using the SAS OnDemand for Academics (SAS Institute, Cary, NC, USA).

RESULTS

The patients’ baseline characteristics and aneurysms are presented in Table 1. Of the 547 patients included in this study, 378 (69.1%) were women. The mean age of the patients was 59.3 years (SD, 14.6). The mean aneurysm size was 6.9 mm (SD, 4.6 mm). The most frequent aneurysm location was the anterior communicating artery (ACOM, 28.7%). The next most frequent locations were the middle cerebral artery bifurcation...
Table 1. Demographics of patients and characteristics of ruptured aneurysms

| Age   | 59.3 years (SD, 14.6) |
|-------|------------------------|
| Sex   |                        |
| Female| 378 (69.1%)            |
| Male  | 169 (30.9%)            |
| Size of ruptured aneurysm | 6.9 mm (SD, 4.6) |
| Location of ruptured aneurysm |          |
| Anterior communicating artery (ACOM) | 157 (28.7%) |
| Middle cerebral artery bifurcation (MCAB) | 121 (22.1%) |
| Posterior communicating artery (PCOM) | 114 (20.8%) |
| Anterior cerebral artery | 29 (5.3%) |
| Paraclinoid | 29 (5.3%) |
| Vertebral artery | 22 (4.0%) |
| Middle cerebral artery | 16 (2.9%) |
| Anterior choroidal artery | 14 (2.6%) |
| Basilar top | 14 (2.6%) |
| Posterior inferior cerebellar artery | 12 (2.2%) |
| Posterior cerebral artery | 5 (0.9%) |
| Superior cerebellar artery | 5 (0.9%) |
| Basilar trunk | 4 (0.7%) |
| Internal carotid artery bifurcation | 4 (0.7%) |
| Anterior inferior cerebellar artery | 1 (0.2%) |

SD, standard deviation

Table 2. Crude distribution and P-value of the Mann-Kendal method in Hunt Hess (HH) grade and modified Fisher grade

| HH grade | Number (%) | P-value |
|----------|------------|---------|
| 1        | 53 (9.7%)  | 0.15    |
| 2        | 190 (34.7%)| 0.06    |
| 3        | 131 (24.0%)| 0.93    |
| 4        | 94 (17.2%) | 0.30    |
| 5        | 79 (14.4%) | 0.52    |

| Modified Fisher grade | Number (%) | P-value |
|-----------------------|------------|---------|
| 1                     | 33 (6.0%)  | 0.89    |
| 2                     | 55 (10.1%) | 0.52    |
| 3                     | 268 (49.0%)| 0.42    |
| 4                     | 191 (34.9%)| 0.79    |

Table 2 shows the overall distribution of the HH grades and modified Fisher grades. The most frequent HH grade was grade 2 (190 patients, 34.7%). The most frequent modified Fisher grade was 3 (268 patients, 49.0%).

Fig. 1 shows the distribution of HH and modified Fisher grades from 2005 to 2020. In the Mann-Kendal estimates for the analysis of the trend, there was no statistically significant difference in grade throughout the HH and modified Fisher grades (Table 2). This suggests that there was no improvement in all HH grades. Similarly, there was no improvement throughout all grades in the modified Fisher grade over time.

Fig. 2 shows the trends in age and aneurysm size between 2005 and 2020. There was no statistically significant trend in age at 15 years (P=0.37) The aneurysm size also showed no significant trend (P=0.2).

DISCUSSION

Throughout this study, we found no improvement in the initial severity of SAH due to intracranial aneurysm rupture. The HH grade and modified Fisher grade showed no trend over 15 years at our institution. However, the trend in the initial severity of SAH is not well known. A previous study showed a change in HH grade over time. However, this was not the primary outcome in that study. Additionally, they did not provide a detailed description. There was no notable change in the initial HH grade over time. Furthermore, favoring the initial status (HH grades 1 and 2) declined from 2010. This suggests that initial severity did not improve over time. This finding is similar to our results.

For decades, the mortality and morbidity of SAH due to aneurysmal rupture have decreased. This is attributed to the evolution of management such as vasospasm and the intensive care unit. Furthermore, the improvement of techniques for surgical clipping and introduction of coil embolization was attributed to lower mortality and morbidity.

The initial neurological status of patients with SAH is also important for the outcomes. The patient's mortality and morbidity with a high HH grade are higher than those with a mild HH grade. Similarly, vasospasm (MCAB, 22.1%) and the posterior communicating artery (PCOM, 20.8%).
affects patient outcomes because cerebral ischemia due to vasospasm is associated with high morbidity and mortality.

Physicians attempt to treat unruptured intracranial aneurysms, which are expected to have a high risk of rupture. The Unruptured Cerebral Aneurysm Study of Japan (UCAS Japan) investigators showed that the risk of aneurysm rupture is associated with the size, location, and features of the aneurysms. Patient characteristics such as age, sex, hypertension, and smoking were also risk factors for aneurysm rupture. Among these risk factors, aneurysm size, location, age, and history of hypertension have been demonstrated as risk factors for SAH outcomes. Therefore, aneurysm rupture

Fig. 1. Distribution of the Hunt Hess grade and modified Fisher grade. (A) Hunt Hess grade. (B) Modified Fisher grade.
and SAH outcomes have several common risk factors. In addition, the number of treatments for unruptured intracranial aneurysms is increasing. Based on these facts, if we treat a sufficient number of unruptured intracranial aneurysms with a high risk of rupture, the mortality and morbidity would be lowered following the improvement of the initial severity.

Kim et al. demonstrated that the incidence of intracranial aneurysms was 52.2/100,000 person-years in Korea. Thus, at least 25,000 new aneurysms develop every year. Considering the population with undiagnosed unruptured intracranial aneurysms, the actual number of new patients could be higher. The number of aneurysm treatments in Korea was approximately 18391 in 2020. This number is insufficient to reduce the incidence of SAH. This suggests that the number of treatments for unruptured intracranial aneurysms may be insufficient to improve the initial severity of SAH.

**Fig. 2.** Distribution of age and aneurysm size in patients with SAH. (A) Age. (B) Size. SAH, subarachnoid hemorrhage
The risk factors related to the initial severity of SAH are not yet well established. Among the various characteristics of aneurysms, aneurysm size is an important risk factor for rupture. Large-sized aneurysms have a higher risk of rupture than do small aneurysms. If aneurysm size is correlated with the initial severity, treatment of the unruptured intracranial aneurysm with consideration of aneurysmal size could improve the initial severity. However, Salary et al. showed that there was no correlation between aneurysmal size and severity. Therefore, the risk factors for the initial severity of SAH might not be associated with the risk factors for rupture, or the initial severity might have an arbitrary behavior that could not be predicted.

The major limitation of our study is that it was based on data from a single institution. This can be criticized for its generality. However, our institution is a tertiary referral center that covers the southern area of the Gyung-Gi Province. The Gyung-Gi province is one of the areas with a large population. If there were a significant difference in the consistency of population or race compared to other provinces, our results could have a severe bias. However, South Korea is a homogeneous nation. We could not assume that the characteristics of the population (the distribution of underlying disease, the incidence of intracranial cerebral aneurysm, or SAH) of other provinces in South Korea showed remarkable differences compared to the southern area of Gyung-Gi province of South Korea. We believe that the results would be similar to ours if we performed a nationwide study on the initial severity of SAH due to cerebral aneurysm rupture. However, it is obvious that this single-center study is a critical weakness.

Our study had several other limitations. This retrospective study design could have caused a hereditary bias. HH grade was not recorded in the medical records of patients with SAH. In this case, we estimated the grades based on the mental status and symptoms of patients in the doctors’ or nurses’ records. There may be a difference between the estimated and actual grades.

CONCLUSIONS

In conclusion, the initial severity of SAH due to the rupture of a cerebral aneurysm did not improve over time.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

REFERENCES

1. Dorhout Mees SM, Molyneux AJ, Kerr RS, Algra A, Rinkel GJ. Timing of aneurysm treatment after subarachnoid hemorrhage: relationship with delayed cerebral ischemia and poor outcome. Stroke. 2012 Aug;43(8):2126-9.

2. Frontera JA, Claassen J, Schmidt JM, Wartenberg KE, Temes R, Connolly ES Jr, et al. Prediction of symptomatic vasospasm after subarachnoid hemorrhage: the modified fisher scale. Neurosurgery. 2006 Jul;59(1):21-7; discussion 21-7.

3. Hunt WE, Hess RM. Surgical risk as related to time of intervention in the repair of intracranial aneurysms. J Neurosurg. 1968 Jan;28(1):14-20.

4. Investigators UJ, Morita A, Kirino T, Hashi K, Aoki N, Fukushima S, et al. The natural course of unruptured cerebral aneurysms in a Japanese cohort. N Engl J Med. 2012 Jun;366(26):2474-82.

5. Jaja BNR, Saposnik G, Lingsma HF, Macdonald E, Thorpe KE, Mamdani M, et al. Development and validation of outcome prediction models for aneurysmal subarachnoid haemorrhage: the SAHIT multinational cohort study. BMJ. 2018 Jan;360:j5745.

6. Kim T, Lee H, Ahn S, Kwon OK, Bang JS, Hwang G, et al. Incidence and risk factors of intracranial aneurysm: a national cohort study in Korea. Int J Stroke. 2016 Oct;11(8):917-27.

7. Korja M, Kivisaari R, Rezai Jahromi B, Lehto H. Natural history of ruptured but untreated intracranial aneurysms. Stroke. 2017 Apr;48(4):1081-4.

8. Lantigua H, Ortega-Gutierrez S, Schmidt JM, Lee K, Badjatia N, Agarwal S, et al. Subarachnoid hemorrhage: who dies, and why? Crit Care. 2015 Aug;19(1):309.

9. Lee HS, Kim YJ, You SH, Jang YG, Rhee WT, Lee SY. The incidence of aneurysmal subarachnoid hemorrhage in...
Youngdong district, Korea. J Korean Neurosurg Soc. 2007 Oct;42(4):258-64.

10. Lee SU, Kim T, Kwon OK, Bang JS, Ban SP, Byoun HS, et al. Trends in the incidence and treatment of cerebrovascular diseases in Korea: Part I. intracranial aneurysm, intracerebral hemorrhage, and arteriovenous malformation. J Korean Neurosurg Soc. 2020 Jan;63(1):56-68.

11. Lo BW, Fukuda H, Nishimura Y, Farrokhyar F, Thabane L, Levine MA. Systematic review of clinical prediction tools and prognostic factors in aneurysmal subarachnoid hemorrhage. Surg Neurol Int. 2015 Aug;6:135.

12. Lovelock CE, Rinkel GJ, Rothwell PM. Time trends in outcome of subarachnoid hemorrhage: population-based study and systematic review. Neurology. 2010 May;74(19):1494-501.

13. Macpherson KJ, Lewsey JD, Jhund PS, Gillies M, Chalmers JW, Redpath A, et al. Trends in incidence and in short term survival following a subarachnoid haemorrhage in Scotland, 1986-2005: a retrospective cohort study. BMC Neurol. 2011 Mar;11:38.

14. Mann HB. Nonparametric tests against trend. Econometrica. 1945;13(3):245-59.

15. Molyneux AJ, Kerr RSC, Yu L-M, Clarke M, Sneade M, Yarnold JA, et al. International subarachnoid aneurysm trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised comparison of effects on survival, dependency, seizures, rebleeding, subgroups, and aneurysm occlusion. Lancet. 2005 Sep;366(9488):809-17.

16. Nanda A, Vannemreddy P. Management of intracranial aneurysms: factors that influence clinical grade and surgical outcome. South Med J. 2003 Mar;96(3):259-63.

17. Qureshi AI, Suarez JI, Bhardwaj A, Yahia AM, Tamargo RJ, Ulatowski JA. Early predictors of outcome in patients receiving hypervolemic and hypertensive therapy for symptomatic vasospasm after subarachnoid hemorrhage. Crit Care Med. 2000 Mar;28(3):824-9.

18. Salary M, Quigley MR, Wilberger JE Jr. Relation among aneurysm size, amount of subarachnoid blood, and clinical outcome. J Neurosurg. 2007 Jul;107(1):13-7.

19. Samuels OB, Sadan O, Feng C, Martin K, Medani K, Mei Y, et al. Aneurysmal subarachnoid hemorrhage: trends, outcomes, and predictions from a 15-year perspective of a single neurocritical care unit. Neurosurgery. 2021 Feb;88(3):574-83.

20. Seo BR, Kim TS, Joo SP, Jang SJ, Lim JS, Oh CW. Incidence rate of aneurysmal SAH in Gwangju city and Jeollanamdo province in 2007. J Korean Neurosurg Soc. 2010 Feb;47(2):124-7.

21. Stegmayr B, Eriksson A, Asplund K. Declining mortality from subarachnoid hemorrhage: changes in incidence and case fatality from 1985 through 2000. Stroke. 2004 Sep;35(9):2059-63.