Article published online: 2023-09-29

Aneurysmal Subarachnoid Hemorrhage: Is the Time Until Intervention Related to Minor Disabilities in 6 Months?

Yuri Tebelskis[1] Nícollas Nunes Rabelo[1,2] Leonardo Zumerkorn Pipek[1] João Paulo Mota Telles[2] Guilherme Bitencourt Barbosa[3] Natalia Camargo Barbat[3] Antônio Carlos Samaia da Silva Coelho[1] Marcia Harumy Yoshikawa[1] Manoel Jacobsen Teixeira[2] Eberval Gadelha Figueiredo[2]

[1] Faculdade de Medicina, Universidade de São Paulo, São Paulo, SP, Brazil
[2] Department of Neurosurgery, Universidade de São Paulo, São Paulo, SP, Brazil
[3] Faculdade de Medicina do ABC, Centro Universitário Saúde ABC, Santo André, SP, Brazil

Address for correspondence Nicollas Nunes Rabelo, MD, Division of Neurosurgery, School of Medicine-University of São Paulo (FMUSP), Hospital das Clínicas (FMUSP), Rua Dr. Enéas de Carvalho Aguiar, 255, 05403-010, 28 São Paulo, SP, Brazil (e-mail: nicollasrabelo@hotmail.com).

Arq Bras Neurocir 2023;42(3):e195–e199.

Abstract

Background Aneurysmal subarachnoid hemorrhages (aSAHs) account for 5% of all strokes, an appalling number when it comes to the second most common cause of death worldwide. The basis of the treatment is clinical support and either endovascular or surgical intervention. The purpose of the present study is to analyze if the time from the onset of the thunderclap headache until treatment intervention is related to the degree of disability after 6 months.

Methods In the present prospective observational study, data were collected from all patients ($n = 223$) admitted to the hospital with a diagnosis of aSAH. Patients whose data were missing or who missed the follow-up after 6 months were excluded. Then, the number of days from the thunderclap headache until the surgical intervention (Delta T) was obtained. The degree of disability was evaluated using standardized scales, Rankin Scale (RS) and Glasgow Outcome Scale (GOS), at the time of discharge as well as 6 months later. Then, the RS and GOS were correlated with Delta T.

Results An average of 6.8 days was found from the onset of symptoms to the intervention, the average age was 54 years old, 73% were women and 55% were smokers. The mean Glasgow Coma Scale on admission was 13. The mean score on the Hunt and Hess scale was 2.1. From the radiological point of view, the mean size of the aneurysm was 6 mm, and the modified Fisher Scale was 3.1. Of the total number of patients at the end of the study ($n = 78$), 50 underwent microsurgical treatment (63%). Rankin scale at discharge was 1.9 and GOS was 4.5, with no statistically significant change at 6 months. Analyzing the data distribution using linear regression, no statistically significant correlation was found between the time until treatment and

Keywords
- aneurysmal subarachnoid hemorrhage
- disability
- treatment
- outcomes

received
October 31, 2022
accepted
January 24, 2023

DOI https://doi.org/10.1055/s-0043-1775557.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

disability using RS and GOS ($p > 0.05$). The same results were found even analyzing age subgroups (≤ 45 years old, 45 to 55 years old, 55 to 70 years old, and > 70 years old with a p-value > 0.05).

Conclusions The present study suggests that there is no linear correlation between Delta T and disability at 6 months for the population studied. However, more studies are needed to assess whether these findings may be present in other populations, especially with a shorter time from symptoms to intervention, since the greatest risk of rebleeding occurs in the first 3 days after the event.

Introduction

Aneurysmal subarachnoid hemorrhage (aSAH) accounts for 5% of all strokes,[1] which are the second most common cause of death worldwide, accounting for 11% of all deaths, as shown by the Global Burden of Disease (GBD-2017). Although decreasing in fatality,[2,3] the burden associated is high and affects economically active people, especially those < 55 years old, leading to many years lost due to disability (YLD), with variable geographic distribution ranging from 5 to 120 YLD per 100,000 (►**Figure 1**).

The cause of an aSAH is the rupture of a saccular aneurysm. Most of them are acquired and related to known risk factors such as smoking, hypertension, alcohol, and cocaine abuse.[4] Usually, the clinical presentation is characterized by a severe and sudden headache which can be described as the worst ever experienced achieving the peak within one hour (thunderclap headache), often with no other symptoms, but can include neck stiffness, focal symptoms, and loss of consciousness.[5] The standard approach to diagnosis, then, includes a head CT scan and, if negative, a lumbar puncture, achieving 98% of sensitivity, especially valuable to rule out this diagnosis.[6] Once confirmed, it is mandatory to grade the severity of SAH, which can be performed through grading systems such as that proposed by Hunt and Hess in 1968[7] complemented by the Fisher grading of vasospasm based on CT scan.[8]

The treatment aims to prevent complications such as rebleeding; thus, the repair with surgical clipping or endovascular coiling is imperative, recommended to be performed within 24 hours,[9] as a Level B of evidence, as well as clinical stabilization. Even with all efforts, disabilities are not uncommon, and their assessments help to guide the treatment and contribute to the better management of these patients. Hence, the purpose of the present study is to correlate the time from the onset of the symptoms (thunderclap headache) until the treatment (surgical or endovascular) and short and long-term disability using the Rankin Scale[10] (RS) and the Glasgow Outcome Scale (GOS)[11] aiming to evaluate if the impact of the surgical treatment is time-dependent linearly.

Methods

Study Design

The present prospective cohort collected data from all patients admitted to the tertiary care hospital (Hospital das Clínicas da FMUSP) from January 2018 to November 2019 with diagnosed aSAH either from lower complexity centers or from other hospitals of the institution. After initial stabilization, patients were selected for the microsurgical or endovascular treatment depending on imaging and clinical status, and, at discharge, were assessed using the standardized scales RS and GOS. Finally, in a 6-month outpatient consultation, patients were again assessed using the same scales evaluating long-term disability (►**Figure 2**).

Population Data

In the aforementioned period, data were collected from 223 patients. Of those, were included 79 patients in the present study ($n = 79$). A consent form and a full questionnaire were offered for patients to evaluate risk factors, such as smoking, hypertension, diabetes, and drug abuse, as well as previous events of aSAH and onset of the headache.

Exclusion Criteria

Patients with missing data about the time of onset of symptoms or RS or GOS after 6 months were excluded.

Inclusion Criteria

Patients admitted to the Hospital das Clínicas da FMUSP between January 2018 and November 2019 with diagnosed aSAH, who agreed to participate in the study, from both sexes, > 18 years old, with a known time of onset of symptoms, diagnosed aSAH and who completed the 6-month follow-up.

Ethical Standards

The present research project was approved by the Ethics and Research Committee of the Hospital das Clínicas of FMUSP. Online registration CAPPesq: 15226 approved 06/20/2016. Approved on the Brazil platform CAAE number: 61719416.6.0000.0068.

Statistical Analysis

The time from onset of symptoms (considering the thunderclap headache) and the treatment (days) was calculated and called Delta. Linear regression was used to analyze Delta and the standardized RS and GOS in two moments: at discharge and at the 6-month follow-up. Additionally, the same linear regression was used to divide the population of the study into four age subgroups (≤ 45 years old, 45 to 55 years old, 55 to 70 years old, and > 70 years old).

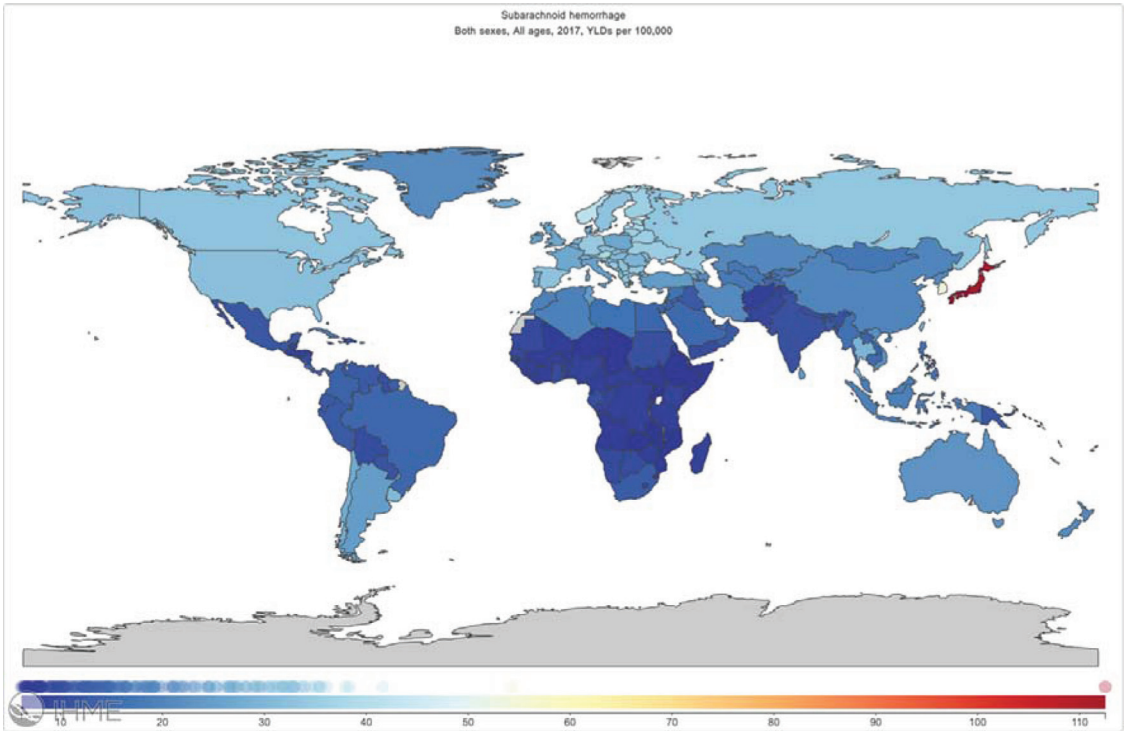

Fig. 1 Geographic distribution of the Years lost due to disability (YLD) caused by subarachnoid hemorrhage. Global Burden of Disease 2017.

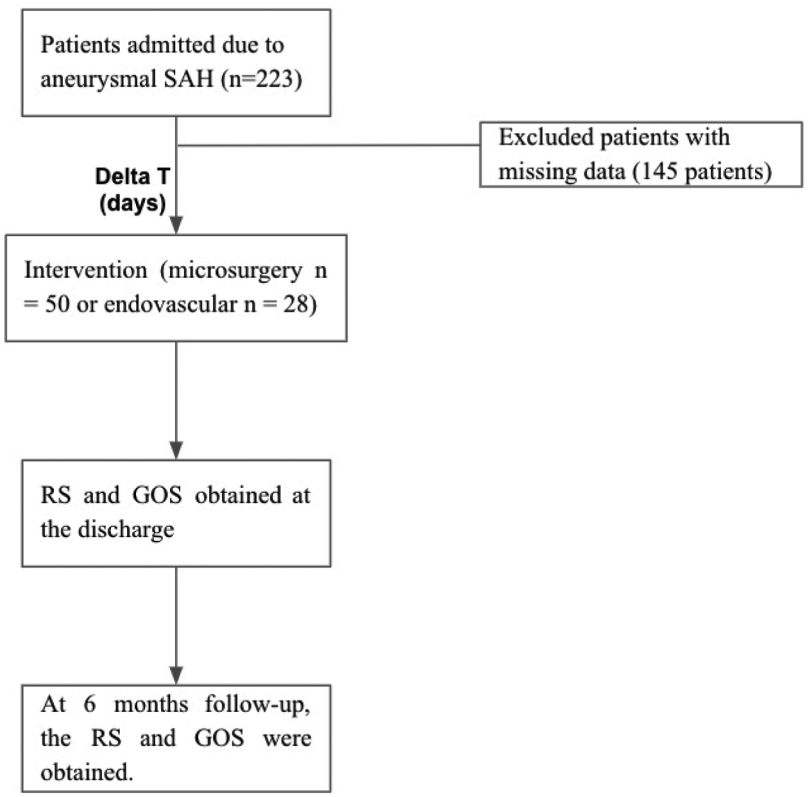

Fig. 2 Selection of patients eligible for the present study.

Results

Of the total of 223 patients included, 145 were excluded due to either missing information or loss to follow-up in 6 months, resulting in 78 patients (►**Figure 2**). The average age was 54, and 73% were women. At admission, the mean Glasgow Coma Scale was 13, and the Hunt and Hess Scale and World Federation Neurological Surgeons Grading (WFNS),

Table 1 Population characteristics of the patients

Population with aSAH (n = 78)	*n*
Epidemiology	
Age (years old)	54
Gender (female)	57 (73%)
Hypertension	53 (68%)
Diabetes	32 (41%)
Smoking	43 (55%)
Alcohol Consumption	18 (23%)
Previous aSAH	12 (15%)
Family History of aSAH (first degree)	4 (5%)
Clinical Features at Admission	
Glasgow Coma Scale (mean)	13
Hunt and Hess Score (mean)	2.1
World Federation of Neurological Surgeons	2.1
Lowered Level of Consciousness	8 (10%)
Syncope	14 (18%)
Meningeal Signs	5 (6.4%)
Motor deficits	30 (38.5%)
Radiologic Features	
Presence of Vasospasm	11 (14%)
Size of Aneurysm (mm)	6.0
More than one aneurysm	13 (16%)
Modified Fisher Grading (mean)	3.1

Abbreviation: aSAH, aneurysmal subarachnoid hemorrhage.

were both 2.1 (►**Table 1**). The average time from the onset of symptoms until intervention was 6.8 days. At discharge, the mean Rankin (RS) was 1.9 and the Glasgow Outcome Score was 4.5. At 6 months, the Rankin Score was 1.8. In the population studied, no correlation was found between the time from onset of symptoms until the treatment and better Rankin Scores, with an adjusted R-squared: 0.023 and $p = 0.09$. Using the same linear regression, but with the population stratified into four subgroups ($\leq$ 45 years old, 45 to 55 years old, 55 to 70 years old, and $>$ 70 years old) obtained similar results, with a *p*-value of 0.38, 0.92, 0.93, and 0.93, respectively.

Additionally, a subgroup analysis was performed, and the patients were divided into four groups based on their ages: $\leq$45 years old, from 45 to 55 years old, from 55 to 70 years old, and $>$ 70 years old. For each group, the same linear regression was used to investigate if there was a different outcome; however, no statistically significant difference was found. (►**Table 2**).

Using the same aforementioned strategy, other subgroup analyses were performed in a more detailed way (►**Table 3**), considering other variables possibly involved on the outcomes,[12] such as gender, days until intervention, size of the aneurysm and previous aSAH and Glasgow Coma Scale at admission, and in none of these a linear correlation between the time until intervention and the disabilities measured by the RS in the 6-month follow-up was found.

Table 2 Age-based subgroup analysis of RS after 6 months and time until intervention

Subgroup (years old)	*p-value*
$\leq$ 45	0.38
45–55	0.92
55–70	0.93
$>$ 70	0.37

Table 3 Detailed subgroup analysis of RS after 6 months and time until intervention

Subgroup	*p-value*
Gender	
Male	0.76
Female	0.57
Time until intervention	
$\leq$ 3 days	0.66
$\geq$ 4 days	0.78
Previous aSAH	
Yes	0.15
No	0.17
Size of the aneurysm	
$\leq$ 5 mm	0.84
$\geq$ 5 mm	0.81
Glasgow Coma Scale at Admission	
15	0.40
13–14	0.67
9–12	0.63
$\leq$ 8	0.27

Abbreviation: aSAH, aneurysmal subarachnoid hemorrhage.

Discussion

It is well-known that the outcomes of an aSAH are complex and depend on a myriad of variables, including characteristics of the patient (comorbidities), the size and location of the aneurysm, the extension of the bleeding,[12] and the time until the transfer to a specialized unit. Accordingly, the Cooperative Aneurysm Study has suggested that the risk of rebleeding achieves a peak during the first 24 hours after the event and subsequently decreases by 1 to 2% per day until the second week. Also, emerging data show that initial rebleeding rates can be of up to 15% in the first 24 hours, which is called ultra-early rebleeding.[13] Thus, after this critical time, the intervention may not be time-dependent for the limitations after 6 months measured by the GOS and the Rankin scales.

Conclusion

The present article suggests that there was no linear correlation between time until intervention and better outcomes using the Rankin scale or the GOS. Besides that, it is worth saying that emerging clinical therapies involving intensive care minimizing complications should be encouraged and incorporated.

Further studies are needed to understand what impacts best the life after aSAH.

Disclosure
The authors have no personal, financial, or institutional interest in any of the drugs, materials or devices described in the present article.

Financial
The authors have no financial support to report.

Conflict of Interests
The authors have no conflict of interests to declare.

References

1 Etminan N, Chang H-S, Hackenberg K, et al. Worldwide Incidence of Aneurysmal Subarachnoid Hemorrhage According to Region, Time Period, Blood Pressure, and Smoking Prevalence in the Population: A Systematic Review and Meta-analysis. JAMA Neurol 2019;76(05):588–597. Doi: 10.1001/jamaneurol.2019.0006
2 Mackey J, Khoury JC, Alwell K, et al. Stable incidence but declining case-fatality rates of subarachnoid hemorrhage in a population. Neurology 2016;87(21):2192–2197. Doi: 10.1212/WNL.0000000000003353
3 Nieuwkamp DJ, Setz LE, Algra A, Linn FHH, de Rooij NK, Rinkel GJE. Changes in case fatality of aneurysmal subarachnoid haemorrhage over time, according to age, sex, and region: a meta-analysis. Lancet Neurol 2009;8(07):635–642. Doi: 10.1016/S1474-4422(09)70126-7
4 Feigin VL, Rinkel GJE, Lawes CMM, et al. Risk factors for subarachnoid hemorrhage: an updated systematic review of epidemiological studies. Stroke 2005;36(12):2773–2780. Doi: 10.1161/01.STR.0000190838.02954.e8
5 Perry JJ, Stiell IG, Sivilotti MLA, et al. Clinical decision rules to rule out subarachnoid hemorrhage for acute headache. JAMA 2013;310(12):1248–1255. Doi: 10.1001/jama.2013.278018
6 Perry JJ, Spacek A, Forbes M, et al. Is the combination of negative computed tomography result and negative lumbar puncture result sufficient to rule out subarachnoid hemorrhage? Ann Emerg Med 2008;51(06):707–713. Doi: 10.1016/j.annemergmed.2007.10.025
7 Hunt WE, Hess RM. Surgical risk as related to time of intervention in the repair of intracranial aneurysms. J Neurosurg 1968;28(01):14–20. Doi: 10.3171/jns.1968.28.1.0014
8 Fisher CM, Kistler JP, Davis JM. Relation of cerebral vasospasm to subarachnoid hemorrhage visualized by computerized tomographic scanning. Neurosurgery 1980;6(01):1–9. Doi: 10.1227/00006123-198001000-00001
9 Connolly ESJ Jr, Rabinstein AA, Carhuapoma JR, et al; American Heart Association Stroke Council Council on Cardiovascular Radiology and Intervention Council on Cardiovascular Nursing Council on Cardiovascular Surgery and Anesthesia Council on Clinical Cardiology. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/american Stroke Association. Stroke 2012;43(06):1711–1737. Doi: 10.1161/STR.0b013e3182587839
10 van Swieten JC, Koudstaal PJ, Visser MC, Schouten HJ, van Gijn J. Interobserver agreement for the assessment of handicap in stroke patients. Stroke 1988;19(05):604–607. Doi: 10.1161/01.str.19.5.604
11 Jennett B, Bond M. Assessment of outcome after severe brain damage. Lancet 1975;1(7905):480–484. Doi: 10.1016/s0140-6736(75)92830-5
12 Cross DT III, Tirschwell DL, Clark MA, et al. Mortality rates after subarachnoid hemorrhage: variations according to hospital case volume in 18 states. J Neurosurg 2003;99(05):810–817
13 Hillman J, Fridriksson S, Nilsson O, Yu Z, Saveland H, Jakobsson KE. Immediate administration of tranexamic acid and reduced incidence of early rebleeding after aneurysmal subarachnoid hemorrhage: a prospective randomized study. J Neurosurg 2002;97(04):771–778

