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*Review Article*

# Analysis of delayed cerebral ischemia incidence after treatment for aneurysmal subarachnoid hemorrhage in young adults: A cohort study

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## ABSTRACT

**Background:** This study aimed to analyze the incidence of delayed cerebral ischemia (DCI) and outcome stratified by age in patients who suffered aneurysmal subarachnoid hemorrhage.

**Methods:** A cohort study with patients from Christ the Redeemer Hospital from 2014 to 2020, with 359 patients separated into 2 groups, 48 of them aged under 40 years and 311 aged 40 years or over.

**Results:** In patients under 40 years of age, DCI was found in 81.3%, while in patients aged 40 or over, it was 61.4%. A relative risk of 1.32 (confidence interval: 1.12–1.55), with $P = 0.013$. After multivariate assessment, patients aged under 40 years were found to have a 27–39% higher risk of presenting DCI.

**Conclusion:** We identified that age under 40 years is a risk factor for the occurrence of DCI.

**Keywords:** Cerebral ischemia, Intracerebral aneurysm, Intracranial vasospasm, Subarachnoid hemorrhage

## INTRODUCTION

Non-traumatic subarachnoid hemorrhage (SAH) is a severe form of stroke characterized by abrupt arterial bleeding into the subarachnoid space. The cause in 80% of cases is the rupture of a brain aneurysm. The general lethality rate of aneurysmal SAH (aSAH) is 32–67%.[1] Furthermore, approximately 30% of survivors will have moderate or severe disability.[3]

The incidence of SAH is controversial and variable in the world literature. Such discrepancies are not only due to ethnic differences but also to the variable degree of efficiency of health and surveillance systems, which can result in diagnostic error and underreporting. According to estimates, women are 1.24 times more likely than men. This difference only occurs in the sixth decade. In general, the etiological factors of aSAH in middle-aged and older adult patients, such as high blood pressure, are not common in patients under 40 years of age.[4,5]

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Furthermore, the rate of aneurysmal rupture increases with age [6], with a peak incidence between the fifth and sixth decade of life.[7] Therefore, the occurrence of aSAH in patients under 40 years old is uncommon. However, it is the form of stroke with the greatest impact on young adults.[8] Neurological consequences can range from mild cognitive decline to severe disability. In this age group, the pathology has important socioeconomic implications by reducing the potentially productive years of a population with a high life expectancy.[4]

In general, the etiological and prognostic factors of aSAH in middle-aged and older adult patients are not common in patients aged under 40 years.[6,7]

Oppong *et al*.[21] found the variable younger age as an independent predictor for the occurrence of vasospasm. Patients under 55 years of age had a significantly higher risk of vasospasm compared to older patients.

Research targeting this population is limited and scarce. Therefore, it is essential to direct our study to enhance public health policy measures that increase the quality of care for this population.

Therefore, the main objective of this study is to analyze the incidence of delayed cerebral ischemia (DCI) from aSAH in adult patients up to 40 years of age, comparing those treated by microsurgery or endovascular surgery with patients in older age groups. Furthermore, the study aims to assess the radiological outcome based on the rate of delayed cerebral ischemia resulting from vasospasm after aneurysmal rupture and to analyze the rate of return to work in discharged patients.

## MATERIALS AND METHODS

A literature review was performed to analyze delayed cerebral ischemia after aSAH from the perspective of the patient's age. In the Pubmed/Medline, Lilacs, Epistemonikos, *Biblioteca Virtual e Saúde,* and Scielo databases, the search was performed using the descriptors: (1) Subarachnoid hemorrhage, (2) cerebral ischemia, (3) intracerebral aneurysm, and (4) age.

Articles published more than 10 years ago, and those without analysis by age were discarded. There was no language limit. The initial selection obtained 167 articles, and subsequently, another 2 were included based on citations in the references of the selected articles. Of these 169 articles, three met the inclusion criteria and were analyzed.

Delayed cerebral ischemia (DCI) was defined as the appearance of new ischemia or infarct in the affected territory observed on computed tomography (CT), which was interpreted by two trained medical students and one neurosurgeon. The examinations were obtained on average 7 days after the aneurysm rupture since control CT is done routinely at the hospital where the study was conducted.[10] Patients who did not have a follow-up CT scan after the onset of vasospasm were excluded from the study. New ischemic areas that appeared in the immediate postoperative period were not considered to be due to vasospasm but rather to complications related to surgery, especially in regions where retractors are commonly used.

### Cohort

A retrospective cohort study was performed following the STROBE method with patients from a reference service in vascular neurosurgery in the state of Rio Grande do Sul, Christ the Redeemer Hospital (*Hospital Cristo Redentor*), in Porto Alegre, Brazil.

Using the Power and Sample Size for Health Researchers online version tool, we calculated a sample size of 148 subjects to test whether there is a difference between the percentages of delayed cerebral ischemia in the groups aged 18–40 years and over 60 years. Considering an increase of 10% for possible losses and refusals, this number was adjusted to 166. For the calculation, we considered a significance level of 5%, a percentage of 30%, a power of 80%, and a relative risk of 1.8.[13]

Initially, all patients admitted to Christ the Redeemer Hospital from January 1, 2014, to December 31, 2020, were selected. Only patients with (a) SAH diagnosis confirmed, either through head CT or lumbar puncture; (b) confirmation of the aneurysmal etiology of SAH performed using tomography angiography of the cerebral vessels (CT Angio) or cerebral angiography; and (c) microsurgical or endovascular treatment for the aneurysm(s).

Of the 365 eligible patients, six were excluded from the sample for not undergoing a control CT scan after the critical period of vasospasm, within 3 weeks after the bleeding event, in order not to underestimate the incidence of ischemic lesions.

After applying the inclusion and exclusion criteria, 359 patients were elected and separated into two groups, 48 of them under 40 years of age and 311 aged 40 years or over.

The collection of demographic, epidemiological, and clinical data occurred through a review of medical records, imaging examinations, and telephone interviews. The informed consent form was presented to the participants. No patient dropped out during the study.

The following variables were collected: age, sex, previous comorbidities, history of smoking or alcohol consumption, family history of aneurysm, day of bleeding with interval until intervention(s), topography of the aneurysm, size (domus and neck) and aneurysm morphology, need for ventricular shunt, clinical picture on admission (Hunt and Hess [HH]), bleeding on initial CT (modified Fisher [Fm] and Fisher [F]), occurrence of intraoperative and postoperative complications, delayed cerebral ischemia, Glasgow Outcome Scale (GOS), index and return to work, and application of the Short-form-12-health-survey questionnaire (SF-12).

### Statistical analysis

Statistical processing of the data was performed using the Statistical Package for the Social Sciences, version 20.0. Comparison between groups (with and without DCI) was performed using Pearson's Chi-square test. The relationship between age and DCI was adjusted for HH, F, and Fm using Poisson multiple regression with robust variance adjustment. It was necessary to perform three different models due to the multicollinearity presented by the three severity scores, verified through the variance inflation factor index. The significance level adopted is $P < 0.05$.

### Ethical procedures

Considering the physical, psychological, moral, intellectual, social, and cultural dimensions of the research participants, the study respected the guidelines and criteria established in Resolution 466/2012 of the National Health Council (BRASIL, 2013), ensuring the legitimacy of the information, privacy, and confidentiality, according to the guidelines of the General Law for the Protection of Personal Data – Law No. 13.709 of August 14, 2018 (BRASIL, 2019), considering ethical precepts throughout the process of constructing the work and publishing the results.

Clarifications and guidance regarding the purpose of the research, as well as authorization from the patient or family member to participate, were provided via telephone.

This project was approved under CAAE number 63666422.2.0000.5530, approval opinion number 6.257.784 of August 24, 2023.

## RESULTS

Selecting the 43.738 patients admitted to the Christ the Redeemer Hospital from 2014 to 2020, 11.963 were from the neurosurgery team. Of those, 800 patients presented SAH and were analyzed. A total of 365 patients were diagnosed with aSAH and received microsurgical or endovascular treatment. Patients who did not undergo a control CT scan after the critical period of vasospasm were excluded from the sample, which is why 359 patients were chosen and separated into two groups, 48 of them under 40 years of age and 311 aged 40 years or over, as shown in Figure 1.

Analyzing our population in terms of sex, women were more affected in a ratio of 3:1, with 262 women (73.2%) and 96 men (26.8%). There was no statistically significant difference in relation to sex in the DCI index, being present in 64.6% of men and 64.1% of women ($P = 0.932$).

Regarding comorbidities, arterial hypertension was most prevalent, present in 54.5% of patients, followed by diabetes mellitus (10.3%), psychiatric diseases (8.4%), and obesity (3.9%). None of these comorbidities demonstrated a statistically significant difference in the DCI index ($P > 0.05$).

We found a smoking rate of 59.7%, with 49.3% being active smokers and 10.4% ex-smokers. The DCI of those who never smoked was 67.6, while ex-smokers and smokers were 61.1 with $P = 0.26$, also demonstrating no statistical significance.

We found 8.7% of patients with a family history of aneurysms. Alcoholism was reported by 9.8% of patients. There was DCI in 77.1% of alcoholics compared to 62.8% of non-drinkers, but without statistical significance ($P = 0.135$). Data are shown in Table 1.

Most of our patients (54.5%) had their treatment, microsurgical or endovascular, within the $5^{th}$ day after the rupture. In 67% of cases, a cerebrospinal fluid drainage system, external ventricular drain, or ventriculoperitoneal drain (VPD) was used. Central nervous system infections were diagnosed in 41.4% of cases.

Among the causes of death, sepsis emerged as the leading factor, accounting for 41.9% of cases, followed by brain death (39.5%), respiratory infections (11.6%), and multiple organ failure (4.7%). Regarding location, 38.3% of patients had aneurysms in the communicating segment of the internal carotid artery, (Pcom), the most common in our sample, followed by the anterior communicating artery (AcomA), with 28.5%. The middle cerebral artery (MCA), was affected in 28.2% of cases, while the ophthalmic segment of the

**Table 1:** Sample characteristics

| Characteristic | |
|---|---|
| Sex | |
| Man | 26.3% |
| Woman | 73.2% |
| Age | |
| <40 years old | 13.4% |
| >40 years old | 86.6% |
| Arterial hypertension | 54.5% |
| Diabetes mellitus | 10.3% |
| Smoking | |
| Active | 49.3% |
| Ex-smokers | 10.4% |
| Alcoholism | 9.8% |
| Family history of aneurysm | 8.7% |

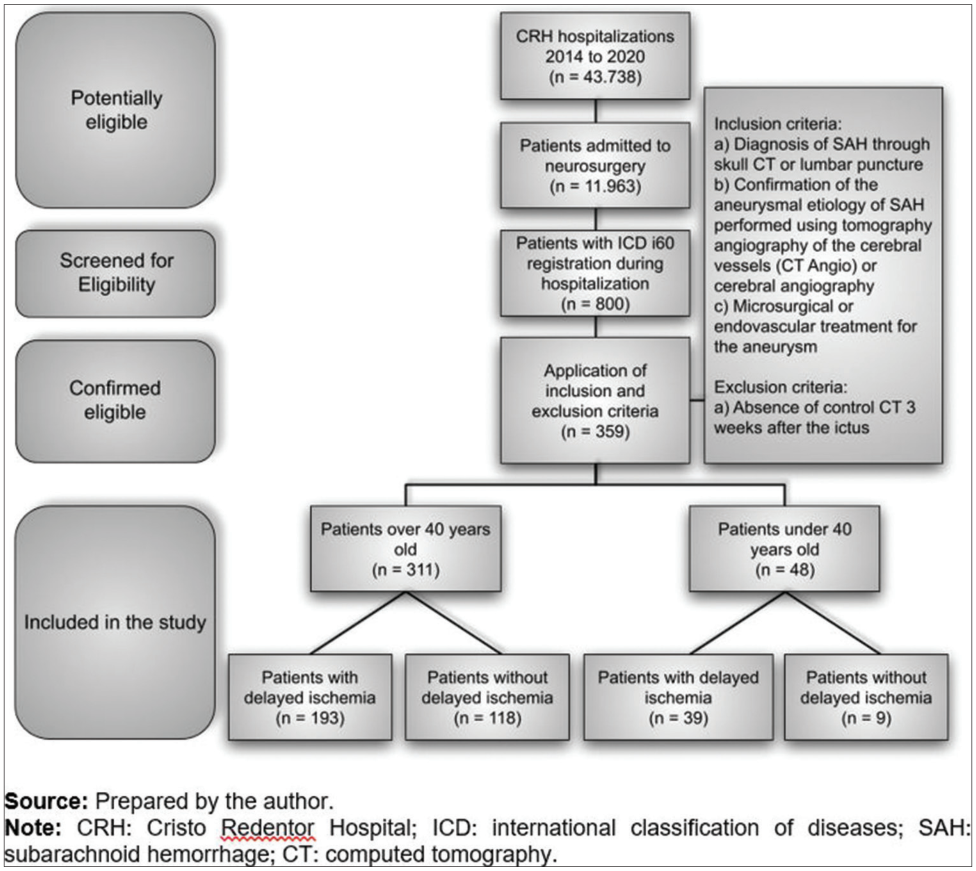


**Figure 1:** Patient selection flowchart.

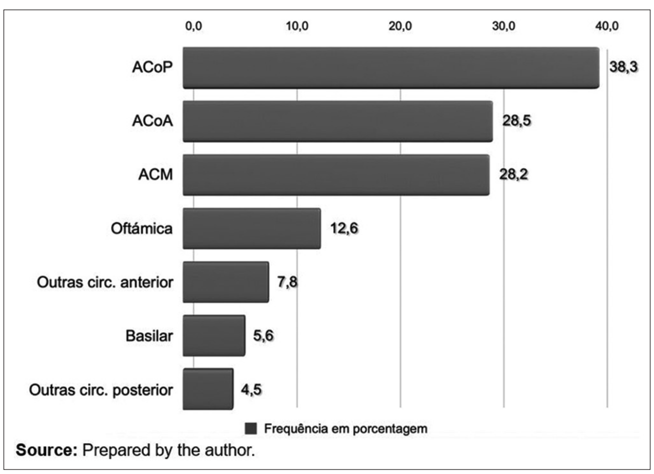


**Figure 2:** Distribution of aneurysms by location.

internal carotid artery was affected in 12.6%. Other locations of the anterior circulation presented aneurysms in 7.8% of patients. The basilar artery presented an aneurysm in 5.6% of patients, and there was an aneurysm in other locations of the posterior circulation in 4.5% of patients [Figure 2].

The HH scale was used to classify patients with SAH according to their clinical condition. In our sample, we had 16.6% of patients with HH 1, 42.2% had HH 2, 28.2% were HH 3, 8.4% were HH 4, and only 4.7% had an HH 5 classification.

Relating the HH variable with the DCI index in Table 2, we evidence a significant association ($P = 0.013$). We also showed a statistically significant linear trend the higher the classification, and the higher the degree of DCI ($P = 0.015$) [Figure 3].

Regarding the severity of bleeding, head CT scans are evaluated and classified using the F and Fm scales. Our sample highlights the close relationship between a higher F and Fm grade with a higher prevalence of DCI [Table 3], both with $P < 0.001$ (Chi-square test for linear trend) [Figure 4].

Of the 48 patients under 40 years of age, 39 had DCI (81.3%). Of the 307 patients aged 40 or over, only 189 showed DCI (61.4%). In this group, DCI was present in 63.6% of patients between 40 and 60 years of age, while over 60 years of age, it was present in 58.5% of patients. The relative risk of DCI in the group under 40 years old found in this sample was 1.32 (CI: 1.12–1.55), with a statistical significance of 0.013 [Table 2].

We analyzed DCI according to the HH scale, separating it into two groups, HH 1 and 2 and HH 3–5, and F's classification

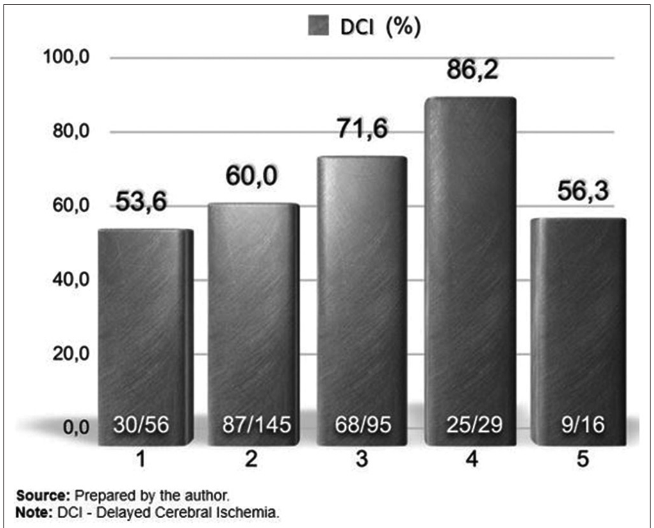


**Figure 3:** Frequency of DCI according to the clinical classification of HH.

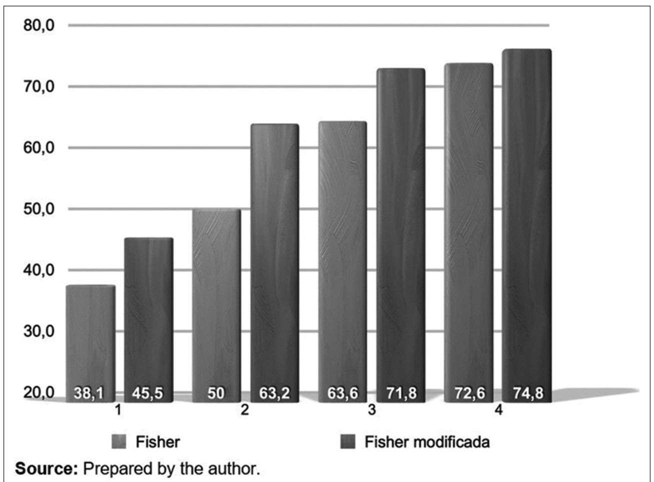


**Figure 4:** DCI in percentage and degree of bleeding using the Fisher and modified Fisher scales (in percentage). DCI: Delayed cerebral ischemia

in a similar way. In the same way, we can evaluate the DCI index by stratifying it according to the HH scale and the Fm classification [Table 3].

Three multivariate analysis models were carried out to clarify the independent relationship between the age variable and DCI when adjusted for the HH, F, and Fm scales individually due to the multicollinearity between these indices [Table 4].

The recovery of the graduates' work capacity was also assessed. In our study, we found a higher frequency of recovery of economic activities in the group under 40 years old, where 50.0% reported returning to work in the same role, while between 40 and 60 and over 60 years old, the value found was 18.5 and 13.9%, respectively.

**Table 2:** Delayed cerebral ischemia (DCI) according to age

| Results | | |
|---|---|---|
| DCI according to age | | |
| <40 years old | 81.3% | RR 1.32 (CI: 1.12 – 1.55) |
| >40 years old | 61.4% | |
| 40-60 incomplete years | 63.6% | |
| >60 years old | 58.5% | |

DCI: Delayed cerebral ischemia, RR: Relative risk, CI: Confidence interval

**Table 3:** Prevalence of DCI by age according to the HH and F or Fm scale combination

| Results | | |
|---|---|---|
| **DCI in<40 years** | **F 1 and 2** | **F 3 and 4** |
| HH 1 and 2 | 75% | 75% |
| HH 3 to 5 | - | 100% |
| **DCI in>40 years** | **F 1 and 2** | **F 3 and 4** |
| HH 1 and 2 | 39.1% | 64.3% |
| HH 3 to 5 | 42.9% | 71.1% |
| **DCI in<40 years** | **Fm 1 and 2** | **Fm 3 and 4** |
| HH 1 and 2 | 68.8% | 84.2% |
| HH 3 to 5 | 100% | 100% |
| **DCI in>40 years** | **Fm 1 and 2** | **Fm 3 and 4** |
| HH 1 and 2 | 43.9% | 68.8% |
| HH 3 to 5 | 58.8% | 72.6% |

HH: Hunt-hess, F: Fisher, Fm: modified Fisher, DCI: Delayed cerebral ischemia

**Table 4:** Multivariable analysis of age in relation to DCI, adjusted for severity índices (HH, F and Fm)

| Multivariate analysis | | | |
|---|---|---|---|
| DCI as dependent variable | | | |
| | RR | CI (95%) | P |
| Age | 1.391 | 1.185-1.632 | < 0.001 |
| Hunt-Hess | 1.296 | 1.111 – 1.512 | = 0.001 |
| Age | 1.277 | 1.085 – 1.503 | = 0.003 |
| Hunt-Hess | 1.517 | 1.153 – 1.996 | = 0.003 |
| Age | 1.328 | 1.135 – 1.554 | <0.001 |
| Hunt-Hess | 1.437 | 1.178 – 1.753 | <0.001 |

HH: Hunt-hess, F: Fisher, Fm: modified Fisher, DCI: Delayed cerebral ischemia, RR: Relative risk, CI: Confidence interval

## DISCUSSION

Two special situations contribute to SAH-related morbidity and mortality: early brain injury and cerebral vasospasm.[23] Early brain injury is considered to occur within 72 hours of aneurysmal rupture and is caused by an acute increase in intracranial pressure with decreased cerebral blood flow, with consequent cerebral edema and inflammation.[14,16,17]

SAH can also cause cerebral vasospasm, a transient and self-limited narrowing of arterial vessels. This phenomenon is associated with delayed cerebral ischemia (DCI).[23] In these cases, in addition to the volume of bleeding, the location of the aneurysm can change the intensity of subsequent events.[24]

The period for its appearance usually begins 3 days after SAH, with a peak incidence on days 6 and 8, and can last for 2–3 weeks. There is a strong association with clinical decline caused by delayed cerebral ischemia in 20–30% of cases.[19]

Cerebral blood flow is affected by SAH through vasospasm, increasing cerebrovascular resistance and affecting autoregulation, increasing susceptibility with transient reductions in cerebral perfusion pressure with risk of hypoflow and ischemia.[25] SAH affects cerebral blood flow mainly through endothelial mechanisms. There is evidence of impairment in endothelium-dependent relaxation and increased production of constricting factors derived from the endothelium.[22]

In Lai's cohort[15] with 328 patients, the assessment using the age criterion had a cutoff point of 55 years. In this case, women in the subgroup under 55 years of age had a higher rate of angiographic vasospasm ($\beta$ = 0.56; 95% confidence interval [CI], 0.19–0.93; $P = 0.003$).

For Oppong *et al.*,[21], in a cohort of 994 patients, younger age was an independent predictor for the occurrence of vasospasm, odds ratio (OR) = 1.03 per year of reduction with 95% CI, 1.01–1.05, and $P < 0.001$. When separated into two groups, patients under 55 years of age had a significantly higher risk of vasospasm compared to older patients. Women had OR = 1.84 with a 95% CI, 1.28–2.67, and $P = 0.001$, while men had OR = 2.63 with a 95% CI, 1.38–5.01, and $P = 0.003$.

On the other hand, when these patients were separated into three groups (under 55 years old, 55–74 years old, and over 74 years old), this study demonstrated an interesting relationship between vasospasm and the female sex factor. While in men, the risk of high vasospasm in the younger group decreased in the second age group, between 55 and 74 years old, with this risk remaining low in the third, in women, the high risk in the young group remained high in the intermediate group and was only reduced in the group of people over 74 years old. Furthermore, women aged 55–74 years had an increased risk of delayed cerebral ischemia, OR = 1.77, with 95% CI, 1.20–2.63, $P = 0.001$, resulting in worsening of functional outcome of these patients.

Analyzing the probability of delayed cerebral ischemia found in de Rooij's *et al.* cohort[3] with 626 patients, using the age factor, the evident increase in risk for younger patients can be noted.

In the selected studies, patients with aSAH under 55 years of age present special characteristics of clinical evolution. Furthermore, Lai[15] showed a high rate of angiographic vasospasm in women under 55 years of age. Even though the objective of that study was to mainly evaluate the female sex factor, its classification into subgroups with an evaluation of the age factor contributes to our research by relating the higher rate of vasospasm to a worse result in the clinical outcome score in this young subgroup. In the largest cohort among the selected studies,[12] Oppong *et al.*[21] defined age as an independent predictor for the occurrence of vasospasm. The drop in the risk of its occurrence is earlier in men, while for women, this effect is evident later.

The average risk of younger patients presenting delayed cerebral ischemia after aSAH is 6.2% higher in the study by de Rooij *et al.*[3] compared to the group over 55 years of age. The risk of delayed cerebral ischemia is also evident, being higher in patients with high Fm grades, as previously mentioned in the study by Claasen[2], and in patients with more severe classification on the World Federation of Neurological Surgeons (WFNS) scale.

This review showed that patients under 55 years of age present differences in clinical evolution compared to older patients. It is important to evaluate such differences because aSAH is the form of stroke with the greatest impact on young adults,[9] with mild neurological consequences, such as cognitive decline, up to severe disability. In young adults, the socioeconomic implications of SAH are also important as they reduce potentially productive years of a population with a high life expectancy.[5] There was the limitation of few studies addressing the analysis of the risk of delayed cerebral ischemia by age group.

In our sample, women were predominant at a frequency of 3:1, with 73.2% women and 26.8% men. Aneurysms predominate in females, and this proportion is reported in the literature.[18]

Regarding comorbidities, systemic arterial hypertension was more prevalent, present in 54.5% of patients. Chronically, elevated blood pressure levels are an important factor in the genesis of aneurysmal rupture. Prospective and retrospective studies show a 2.5–3.5 times greater chance of aneurysm rupture in patients with systemic arterial hypertension.[18]

We found a smoking rate of 59.7%, with 49.3% being active smokers and 10.4% ex-smokers. The chance of aneurysmal rupture is 2–3 times greater than developing aSAH, reaching 6 times when there is a family history of ruptured cerebral aneurysm.[18] In our sample, 8.7% had a family history of aneurysms.

Regarding vasospasm, Lai[15] demonstrated a high rate of angiographic vasospasm in women under 55 years of age. Oppong *et al.*[21] defined age as an independent predictor for the occurrence of vasospasm and reported a drop in the risk of its earlier occurrence in men, while for women, this effect was evident later; however, in our sample, there was no statistically significant difference in relation to sex in the DCI index, being present in 64.6% of men and 64.1% of women ($P = 0.932$).

Regarding the location of the aneurysms, our results present a slight difference in relation to the ISUIA[11] data, where the internal carotid artery was the most frequent location (29.9%), excluding the cavernous segment and Pcom. MCA presented

29.1% of injuries, similar to our result of 28.2%. At AcomA, ISUIA presented 12.3%, while we found 28.2%. The biggest difference was evident in Pcom, where ISUIA found only 8.5%, while our sample showed 38.3%. We emphasize that in that study, we were dealing with unruptured aneurysms.

On the other hand, Forget[20] and international subarachnoid aneurysm trial (ISAT)[21] evaluated ruptured aneurysms. The frequency found by Forget at AcomA was 29%, close to our result of 28.5%. In second place in Forget's study, Pcom presented 19% of aneurysms, while this segment was the most frequently affected in our sample, with 38.3%. Finally, in third place in the Forget and ISAT studies, the MCA affected in 11% of Forget's cases was more frequent in our sample, at 28.2%.

When analyzing DCI stratified by age, in patients under 40 years of age, we found DCI in 81.3%, while in patients aged 40 or over, it was 61.4%, making up a relative risk of DCI in the group under 40 years of 1.32 (CI: 1.12–1.55), with a statistical significance of 0.013 [Table 2].

This probability of increased DCI in young patients was reported in the de Rooij *et al*. cohort[3] with 371 patients, where stratification was created using the WFNS and Fm scale. In the group of patients aged 55 or over, only three of the 16 subgroups presented a high risk for delayed cerebral ischemia, 18.25%, while in those under 55 years of age, five of the 16 subgroups were at high risk, 31.25%. With the same stratification, for those aged 55 years or over, 31.25% were considered low risk, while in patients under 55 years of age, only 6.25% presented low risk [Table 5].

In our cohort, we analyzed DCI according to the HH scale, separating it into two groups, HH 1 and 2 and HH 3–5, and the F classification in a similar way. Likewise, we evaluated the DCI index by stratifying it according to the HH scale and the Fm classification.

It is observed that, in line with de Rooij *et al*.[3] findings, elevated HH scores, F grades, or Fm grades serve as risk factors for the onset of intracranial hemorrhage-related complications. With a more refined evaluation of the age criterion within our cohort, being under 40 years old emerges as a significant standalone risk factor for the occurrence of end-stage renal disease.

Table 4 presents the multivariate evaluation with statistical significance in any of the associations between age and the HH, F, and Fm criteria, proving the importance of this variable as a risk factor for the occurrence of DCI. We concluded that age remained related to DCI even when adjusted, showing a risk that varies from 1.27 to 1.39; that is, at least, those patients under 40 years of age have a 27% higher risk of presenting DCI.

### Study limitations

The initial limitation encountered in conducting this study is the fact that this is a single-center retrospective review. This study is associated with the sample size of patients below the age of 40, as the incidence of aneurysmal rupture tends to increase with age, peaking in the fifth and sixth decades.[7] The data collection started in 2014, representing the earliest year documented in the CRH internal medical records system. Consequently, a comprehensive analysis was conducted, encompassing patients from this starting point until the year immediately preceding the initiation of the study.

**Table 5:** Probability of DCI after SAH for each combination of the four main independent predictors presented at admisson

| WFNS | Thin SAH (Fm 0 to 2) | | Thick SAH (Fm 3 to 4) | | |
|---|---|---|---|---|---|
| | Thin | Thick | Thin | Thick | |
| I | 12% | 17% | 19% | 27% | > 55 years |
| II/III | 15% | 22% | 24% | 33% | |
| IV | 17% | 24% | 26% | 36% | |
| V | 29% | 39% | 42% | 54% | |
| I | 15% | 22% | 24% | 33% | <55 years |
| II/III | 20% | 28% | 30% | 41% | |
| IV | 22% | 30% | 33% | 43% | |
| V | 36% | 47% | 50% | 61% | |

: < 20% Low risk, : 20 – 40% Medium risk, : >40% high risk, SAH: Subarachnoid hemorrhage, WFNS 8 :world federation of neurosurgical surgeons ,CTC: computerized tomography

Furthermore, the analysis based on the application of the SF-12 was of great value but did not reach the expected values to consider statistical validity in comparative analyses, given the limitations found in making telephone contact with patients or family members.

Other limitations include the fact that it is very difficult to separate ischemic changes secondary to DCI from those due to complications related to the management of the aneurysm, so this was not done in the analysis of our cases due to the lack of data in the medical records for such differentiation.

## CONCLUSION

With the data from this study, we identified age under 40 years as a risk factor for the occurrence of DCI, in addition to clinical (HH) or radiological (Fm or F) conditions at hospital admission.

### Ethical approval

The research/study was approved by the Institutional Review Board at CAAE, number 6.257.784, dated August 24, 2023.

### Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

**Use of artificial intelligence (AI)-assisted technology for manuscript preparation**

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

## REFERENCES

1. Ciurea AV, Palade C, Voinescu D, Nica DA. Subarachnoid hemorrhage and cerebral vasospasm - literature review. J Med Life 2013;6:120-5.
2. Claassen J, Bernardini GL, Kreiter K, Bates J, Du YE, Copeland D, *et al*. Effect of cisternal and ventricular blood on risk of delayed cerebral ischemia after subarachnoid hemorrhage: The Fisher scale revisited. Stroke 2001;32:2012-20.
3. De Rooij N, Greving J, Rinkel G, Frjns C, Early prediction of delayed cerebral ischemia after subarachnoid hemorrhage. Development and validation of a rick chart. Stroke 2013;44:1288-94.
4. De Rooij NK, Linn FH, van der Plas JA, Algra A, Rinkel GJ. Incidence of subarachnoid haemorrhage: A systematic review with emphasis on region, age, gender and time trends. J Neurol Neurosurg Psychiatry 2007;78:1365-72.
5. Dietrich HH, Dacey RG. Molecular keys to the problems of cerebral vasospasm. Neurosurgery 2000;46:517-30.
6. Forget TR Jr., Benitez R, Veznedaroglu E, Sharan A, Mitchell W, Silva M, *et al*. A review of size and location of ruptured intracranial aneurysms. Neurosurgery 2001;49:1322-5.
7. Flaherty ML, Haverbusch M, Sekar P, Kissela B, Kleindorfer D, Moomaw CJ, *et al*. Longterm mortality after intracerebral hemorrhage. Neurology 2006;66:1182-6.
8. Hop JW, Rinkel GJ, Algra A, van Gijn J. Case-fatality rates and functional outcome after subarachnoid hemorrhage: A systematic review. Stroke 1997;28:660-4.
9. Huang J, van Gelder JM. The probability of sudden death from rupture of intracranial aneurysms: A meta-analysis. Neurosurgery 2002;51:1101-7.
10. Ikram A, Javaid MA, Ortega-Gutierrez S, Selim M, Kelangi S, Anwar SM, *et al*. Delayed cerebral ischemia after subarachnoid hemorrhage. J Stroke Cerebrovasc Dis 2021;30:106064.
11. International Study of Unruptured Intracranial Aneurysms Investigators. Unruptured intracranial aneurysms-risk of rupture and risks of surgical intervention. N Eng J Med 1998;339:1725-33.
12. Jee TK, Nam TM, Yeon JY, Kim KH, Jeon P, Kim JS, *et al*. Intracranial aneurysms in young adult patients: Surgical and endovascular treatment outcomes. World Neurosurg 2020;136:e214-22.
13. Jennett B, Bond M. Assessment of outcome after severe brain damage. Lancet 1975;1:480-4.
14. Krings T, Geibprasert S, TerBrugge KG. Pathomechanisms and treatment of pediatric aneurysms. Childs Nerv Syst 2010;26:1309-18.
15. Lai PM, Gormley WB, Patel N, Frerichs KU, Aziz-Sultan MA, Du R. Age-dependent radiographic vasospasm and delayed cerebral ischemia in women after aneurysmal subarachnoid hemorrhage. World Neurosurg 2019;130:e230-5.
16. Lawton M. Seven aneurysms: Tenets and techniques for clipping. Germany: Thieme; 2011.
17. Lawton MT, Vates GE. Subarachnoid hemorrhage. N Engl J Med 2017;377:257-66.
18. Machado AB. Neuroanatomia funcional. 2nd ed. São Paulo: Atheneu Editora; 2007.
19. Molyneux A, Kerr R, Stratton I, Sandercock P, Clarke M, Shrimpton J, *et al*. International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: A randomised trial. Lancet 2002;360:1267-74.
20. Ogungbo B. Aneurysmal subarachnoid hemorrhage in young adults. J Neurosurg 2003;98:43-9.
21. Oppong MD, Iannaccone A, Gembruch O, Pierscianek D, Chihi M, Dammann P, *et al*. Vasospasm-related complications after subarachnoid hemorrhage: The role of patients' age and sex. Acta Neurochir (Wien) 2018;160:1393-400.
22. Osborn AG. Diagnostic cerebral angiography. 2nd ed. Philadelphia, PA: Lippincott Williams and Wilkins; 1999.
20. Pontes-Neto OM, Oliveira-Filho J, Valiente R, Friedrich M, Pedreira B, Rodrigues BC, *et al*. Brazilian guidelines for the manegement of intracerebral hemorrhage. Arq Neuropsiquiatr 2009;67:940-50.
24. Qureshi AI, Tuhrim S, Broderick JP, Batjer HH, Hondo H, Hanley DF. Spontaneous intracerebral haemorrhage. N Engl J Med 2001;344:1450-60.
25. Siqueira MG, Souza AA, Vellutini E. Tratado de neurocirurgia. Sao Paulo: Manole; 2016.

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