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# COMPARISON OF MORTALITY AND POSTOPERATIVE COMPLICATIONS IN PATIENTS WITH CLIPPED RUPTURED VS. UNRUPTURED INTRACRANIAL ANEURYSMS

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## ABSTRACT

**Introduction:** Intracranial aneurysm (IA) is a weakening of a cerebral vessel that can lead to rupture and subarachnoid hemorrhage (SAH). Ruptured IAs account for about 85% of SAH cases, with high complication risks. Unruptured intracranial aneurysms (UIAs) are increasingly diagnosed due to advanced imaging techniques, with treatment options including clipping or coiling. The aim of the study was to compare mortality and the incidence of complications in patients after intracranial aneurysm clipping, with a distinction between previously ruptured and unruptured aneurysms.

**Materials and methods:** This retrospective study analyzed patients who underwent cerebral aneurysm clipping between 2022 and 2025 at the Clinical Department of Neurosurgery of the University Clinical Center named after Prof. K. Gibiński, Medical University of Silesia in Katowice, Poland. Data on sex, age, aneurysm location, status (ruptured/unruptured), and complications were collected. Statistical analysis used chi-square and Fisher's exact tests ( $p < 0,05$ ).

**Results:** The study included 61 patients, with 46 females (75,41%) and 15 males (24,59%). Of the aneurysms, 46 (75,41%) were unruptured and 15 (24,59%) ruptured. Postoperative complications occurred in 21 patients (34,43%), including transient paresis, aphasia, and stroke. Three patients (4,92%) died. Chi-square and Fisher's tests showed no statistically significant differences in complications ( $p = 0,08$ ) and mortality ( $p = 0,15$ ) between ruptured and unruptured groups.

**Conclusions:** Postoperative complications were more common in ruptured aneurysms, though no statistical significance was found. The overall mortality rate was low, and no significant difference in mortality was observed between ruptured and unruptured aneurysms.

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## KEYWORDS

Intracranial Aneurysm, Aneurysm Clipping, Postoperative Complications Ruptured Aneurysm

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## Introduction

Intracranial aneurysm (IA) is a specific type of cerebrovascular condition characterized by a localized weakening in the wall of a cerebral artery, which results in a balloon-like bulging or dilation of the affected blood vessel. These aneurysms have the potential to gradually enlarge over time and, in certain circumstances, may rupture, posing a significant risk to the affected individual. It is estimated that ruptured IAs are responsible for approximately 85% of spontaneous subarachnoid hemorrhage (SAH) cases [1], highlighting their clinical importance and the critical need for early detection and management.

The incidence and prevalence of SAH are not uniform across different geographical regions and populations. Epidemiological studies have shown that certain countries, such as Finland and Japan, exhibit notably higher rates of SAH, with estimates of 19.7 and 22.7 cases per 100,000 person-years, respectively, in comparison to the worldwide average of 9.1 cases per 100,000 person-years. These data suggest that genetic, environmental, or lifestyle factors may contribute to regional variations in the occurrence of SAH, although the precise mechanisms underlying these differences remain a topic of ongoing investigation.

The prognosis for patients who suffer from aneurysmal SAH is often unfavorable, and clinical outcomes can vary widely depending on the severity of the hemorrhage, the location and size of the aneurysm, and the timing of therapeutic intervention. Approximately 15–20% of individuals with IA may develop acute hydrocephalus, a condition characterized by the accumulation of cerebrospinal fluid in the ventricles of the brain, which frequently results in severe headaches and other neurological symptoms. In addition, cerebral vasospasm, defined as the pathological constriction of cerebral arteries, can occur between 3 to 12 days following the hemorrhagic event, significantly increasing the risk of ischemic stroke or, in extreme cases, death.

Rebleeding is another major concern in patients with untreated aneurysmal SAH. Current estimates suggest that there is roughly a 19% probability of aneurysm re-rupture within the first two weeks if no surgical or endovascular intervention is undertaken. Moreover, long-term outcomes for these patients are often poor, with 10–20% experiencing significant and permanent neurological disabilities. Unfortunately, approximately one-third of individuals affected by aneurysmal SAH ultimately succumb to the complications associated with the hemorrhage, underscoring the severity and life-threatening nature of this condition [1].

Unruptured intracranial aneurysms (UIAs) are being identified with increasing frequency, largely as a result of significant advancements in non-invasive, high-resolution imaging modalities, such as magnetic resonance angiography (MRA) and computed tomography angiography (CTA). These imaging techniques have greatly improved the ability of clinicians to detect small and asymptomatic aneurysms that would previously have gone unnoticed. According to research conducted by Vlak et al., UIAs are estimated to occur in approximately 3.2% of the general population (95% CI: 1.9%–5.2%) [2,3], indicating that a notable proportion of individuals may harbor aneurysms without any clinical manifestations. This rising detection rate emphasizes the importance of understanding the natural history and potential risks associated with these lesions.

Although unruptured, UIAs are not without risk, as they can potentially rupture, leading to life-threatening complications such as subarachnoid hemorrhage (SAH) and subsequent neurological deficits. Given these significant health risks, timely and effective management is critical. Currently, the two primary therapeutic approaches for UIAs are surgical clipping and endovascular coiling. Surgical clipping has long been regarded as a standard, well-established, and highly effective treatment modality, particularly for aneurysms located in surgically accessible regions. Endovascular coiling, in contrast, represents a minimally invasive alternative, which has gained substantial clinical acceptance since the development and introduction of detachable coils in 1995. Notably, surgical clipping remains the most traditional method for the early treatment of middle cerebral artery aneurysms, and it continues to play a central role in neurosurgical practice, particularly for patients with aneurysms deemed suitable for open surgical intervention [4].

The precise pathophysiological mechanisms that underlie IA rupture remain incompletely understood and are widely considered to be multifactorial. Both aneurysm morphology – including size, shape, and aspect ratio – and hemodynamic factors, such as blood flow patterns and wall shear stress (WSS), have been

implicated as critical contributors to IA formation, growth, and eventual rupture. Despite extensive research efforts, studies examining these morphological and hemodynamic risk factors have frequently produced inconsistent or even contradictory findings, reflecting the complexity of aneurysm biology. For example, Cebal et al. reported a significant association between areas of high wall shear stress (WSS) and the presence of ruptured aneurysms, suggesting that elevated mechanical forces on the aneurysm wall may contribute to its weakening and eventual rupture. Conversely, Xiang et al. identified low WSS regions (LSA) and increased oscillatory shear index (OSI) as potential predictors of rupture risk, highlighting the possibility that both extremes of hemodynamic stress may influence aneurysm stability. These apparent discrepancies may be attributable to variations in individual patient characteristics, aneurysm location, size, or geometry, as well as differences in study methodology and computational modeling approaches [5–8].

Overall, these findings underscore the considerable complexity involved in assessing rupture risk in unruptured intracranial aneurysms (UIAs) and highlight the critical importance of developing personalized risk stratification strategies that carefully account for both morphological and hemodynamic characteristics. A thorough understanding of these factors, including aneurysm size, shape, location, and blood flow dynamics, is essential not only for identifying patients at higher risk of rupture but also for guiding the selection of the most appropriate treatment modalities. Such knowledge is indispensable for optimizing clinical decision-making, minimizing potential complications, and ultimately improving long-term outcomes for patients who harbor unruptured intracranial aneurysms.

The rupture of an intracranial aneurysm constitutes a catastrophic medical event, resulting in aneurysmal subarachnoid hemorrhage (SAH), which is widely recognized as a highly severe and life-threatening cerebrovascular condition. The clinical severity of aneurysmal SAH is commonly assessed using standardized grading systems, most notably the Hunt-Hess scale and the World Federation of Neurological Surgeons (WFNS) scale, which categorize patients into five distinct levels of severity. Patients classified within grades 1 through 3 are generally considered to be in a ‘good grade’ and are typically associated with more favorable neurological outcomes and a higher likelihood of recovery. Conversely, individuals assigned to grades 4 and 5, referred to as ‘poor grade,’ are often at significantly higher risk of severe neurological deficits, prolonged hospitalization, and mortality, reflecting the grave prognosis associated with high-grade SAH.

The pathophysiological consequences of aneurysm rupture are closely linked to disturbances in intracranial homeostasis, alterations in cerebral blood flow, and metabolic disruptions within the brain. These imbalances can precipitate a cascade of secondary injuries, including cerebral ischemia, neuronal damage, and exacerbation of intracranial pressure, all of which contribute to the complexity of post-rupture management. Therapeutic hypothermia has historically been employed in select clinical scenarios as a strategy to reduce metabolic demand, protect neural tissue, and mitigate the deleterious effects of metabolic disturbances. While hypothermia may offer potential benefits, such as reducing neuronal injury and limiting secondary ischemic damage, it also carries inherent risks, including coagulopathy, infection, and cardiovascular complications, necessitating careful patient selection and rigorous monitoring [9].

According to the existing literature, patients with intracranial aneurysms are at risk for a range of complications, which may significantly influence both short- and long-term outcomes. Commonly reported complications include cerebral ischemia, rebleeding or secondary hemorrhage, aneurysm occlusion or incomplete obliteration, prolonged hospitalization, persistent neurological deficits, and, in severe cases, death [2,10–12]. These adverse events underscore the importance of timely and effective intervention, as well as comprehensive postoperative care, in minimizing the morbidity and mortality associated with aneurysmal disease.

Given the critical clinical implications and the need to better understand treatment outcomes, it appears reasonable to undertake a study aimed at comparing the results of patients with ruptured versus unruptured intracranial aneurysms who were treated using the surgical clipping method. Such investigations are essential for evaluating the relative efficacy and safety of clipping in different clinical contexts, assessing risk-benefit ratios, and providing evidence-based guidance for neurosurgical practice. In this context, a study was conducted within a Polish population of patients diagnosed with intracranial aneurysms, focusing specifically on outcomes following surgical clipping. The findings of this investigation, including both clinical and procedural data, are presented and analyzed in the following sections of this paper.

## Materials and methods

The primary aim of this study was to systematically compare both mortality rates and the incidence of postoperative complications in patients who underwent surgical clipping for intracranial aneurysms, with particular attention paid to differentiating outcomes between ruptured and unruptured aneurysms. This investigation sought to provide a clearer understanding of the potential risks and clinical outcomes associated with aneurysm clipping under different preoperative conditions.

This research was designed as a retrospective observational study, encompassing patients who underwent surgical clipping of a cerebral aneurysm over a three-year period, specifically between 2022 and 2025. All patient data were collected from individuals who were hospitalized at the Clinical Department of Neurosurgery of the University Clinical Center named after Prof. K. Gibiński, Medical University of Silesia, located in Katowice, Poland. The study protocol was developed in accordance with standard ethical guidelines for retrospective clinical research, and all data were fully anonymized prior to analysis to ensure the privacy and confidentiality of patient information.

Data collection was performed by reviewing individual patient medical records as well as extracting relevant information from the hospital's electronic medical record systems. A comprehensive set of variables was analyzed to characterize the study population and to evaluate potential risk factors for postoperative complications. These variables included patient sex, chronological age at the time of surgery, anatomical location of the clipped aneurysm, preoperative aneurysm status (ruptured or unruptured), and the occurrence of any postoperative complications, including but not limited to ischemic events, hemorrhagic complications, neurological deficits, or other clinically significant adverse events. Only patients with complete data available for all specified variables and who had undergone aneurysm clipping within the defined study period were included in the final analysis.

All collected data were anonymized and stored in a secure, password-protected database to maintain patient confidentiality. Data management procedures were performed in accordance with institutional guidelines and international standards for clinical research.

Statistical analyses were conducted with a pre-defined significance level of  $p < 0.05$ . Comparative analyses between groups were performed using the chi-square test, under the assumption that the expected values within each group exceeded five. In instances where expected values were lower than five, Fisher's exact test was employed to ensure accurate and reliable statistical inferences. All quantitative results were systematically rounded to two decimal places to maintain clarity and consistency in reporting. The overall approach was intended to provide robust and reproducible insights into the outcomes of surgical clipping for both ruptured and unruptured intracranial aneurysms.

## Results

A total of 61 cases were included in the study population. Among these patients, 46 individuals (75,41%) were female, whereas 15 (24,59%) were male, demonstrating a clear predominance of women in this cohort. The median age of the participants was 60 years, with a mean age of  $56,33 \pm 12,87$  years, indicating a moderately wide age distribution that encompassed both younger and older adult patients. These demographic characteristics are consistent with previously reported trends, which suggest that intracranial aneurysms are more frequently diagnosed in women, particularly in middle-aged and older populations.

Regarding aneurysm status, 46 aneurysms (75,41%) were unruptured, while 15 (24,59%) were classified as ruptured prior to surgical intervention. Of the 15 ruptured aneurysms, 10 occurred in female patients and 5 in male patients, reflecting the overall sex distribution within the study cohort. These findings highlight the clinical importance of monitoring both ruptured and unruptured aneurysms, particularly in female patients who appear to represent the majority of cases.

The anatomical distribution of aneurysms was also analyzed in detail. Two aneurysms (3,28%) were located on the internal carotid artery (ICA), and all of these were unruptured. The majority of aneurysms, 51 cases (83,61%), were situated on the middle cerebral artery (MCA), with 39 (63,93%) unruptured and 12 (19,67%) ruptured. Seven aneurysms (11,48%) were identified on the anterior communicating artery (AComA), of which 4 (6,56%) were unruptured and 3 (4,92%) were ruptured. Finally, a single aneurysm (1,64%) was located on the posterior communicating artery (AComP), and this aneurysm was unruptured. The detailed distribution of aneurysm locations and their rupture statuses is summarized in **Table 1**.

**Table 1.** Distribution of aneurysm locations and rupture status.

Location	Total n (%)	Unruptured n (%)	Ruptured n (%)
Internal Carotid Artery (ICA)	2 (3,28%)	2 (3,28%)	0 (0%)
Middle Cerebral Artery (MCA)	51 (83,61%)	39 (63,93%)	12 (19,67%)
Anterior Communicating Artery (ACoM)	7 (11,48%)	4 (6,56%)	3 (4,92%)
Posterior Communicating Artery (ACoP)	1 (1,64%)	1 (1,64%)	0 (0%)
Total	61 (100%)	46 (75,41%)	15 (24,59%)

Postoperative complications were observed in a total of 21 patients (34,43%) across the study cohort. Of these, 8 patients had previously ruptured aneurysms (13,11%; representing 53,33% of the ruptured aneurysm group), while 13 patients had unruptured aneurysms (21,31%; corresponding to 28,26% of the unruptured aneurysm group). These findings indicate that complications were proportionally more frequent among patients with ruptured aneurysms, which may reflect the increased complexity and higher baseline risk associated with managing aneurysms that have already experienced hemorrhagic events.

The recorded postoperative complications encompassed a variety of clinical presentations, ranging from relatively minor to severe, potentially life-threatening events. Specifically, complications included otolaryngological disorders affecting the sinuses and ears in 1 patient (1,64%), transient neurological deficits such as paresis, aphasia, and dysphasia in 5 patients (8,20%), formation of an epidural fluid collection in 1 patient (1,64%), and deterioration of the general condition necessitating transfer to the intensive care unit without additional concurrent complications in 2 patients (3,28%). Local hemorrhages were observed in 2 patients (3,28%), while subdural hematoma occurred in 1 patient (1,64%) and intracerebral hematoma in 4 patients (6,56%). Ischemic stroke was identified in 2 patients (3,28%), and death occurred in 3 patients (4,92%), highlighting the serious nature of potential post-clipping complications.

In addition to these events, 3 patients from the ruptured aneurysm subgroup required transfer to the intensive care unit due to the severity of their postoperative complications, underscoring the higher risk profile and increased monitoring requirements for this group. The detailed distribution of complications, divided according to ruptured and unruptured aneurysms, is summarized in **Table 2.**, providing a comprehensive overview of the clinical outcomes observed in this study.

**Table 2.** Postoperative complications by aneurysm status.

Postoperative Complication	Number of cases	Ruptured	Unruptured
Otolaryngological disorders (sinuses, ears)	1	0	1
Transient paresis / aphasia / dysphasia	5	0	5
Epidural fluid collection	1	0	1
ICU transfer	2	0	0
Local hemorrhages	2	1	1
Subdural hematoma	1	0	1
Intracerebral hematoma	4	2	2
Ischemic stroke	2	1	1
Death	3	2	1
Total	21	8	13

To evaluate the potential impact of aneurysm status prior to surgery on the subsequent occurrence of postoperative complications following surgical clipping, a chi-square test was conducted. This statistical method was selected because the expected numerical values in each subgroup exceeded 5, meeting the assumptions required for valid application of the chi-square test. The data used for this analysis are summarized in **Table 3.**, which provides a detailed breakdown of complication rates according to aneurysm status, allowing for a clear visual comparison between patients with ruptured and unruptured aneurysms.

**Table 3.** Complications depending on aneurysm status.

Aneurysm Status	Complications	No Complications	Total
Ruptured	8	7	15
Unruptured	13	33	46
Total	21	40	61

The results of the chi-square test indicated no statistically significant difference in the incidence of postoperative complications between patients with ruptured aneurysms and those with unruptured aneurysms ( $\chi^2 = 3,15$ ,  $p = 0,08$ ). This suggests that, within this study cohort, preoperative aneurysm status did not have a measurable or statistically significant effect on the likelihood of experiencing postoperative complications. While numerical differences in complication rates were observed, the statistical analysis confirms that these variations are likely attributable to random chance rather than a true effect of aneurysm status.

Out of the 61 cases included in the study, mortality was observed in only 3 patients (4,92%). Specifically, 1 patient belonged to the unruptured aneurysm group (1,64%; representing 2,17% of all patients with unruptured aneurysms), whereas 2 patients were from the ruptured aneurysm group (3,28%; corresponding to 13,33% of the ruptured aneurysm subgroup). These findings highlight that while overall mortality in this cohort was relatively low, patients with ruptured aneurysms exhibited a proportionally higher risk of death compared to those with unruptured aneurysms, which is consistent with the more severe clinical presentation and higher baseline risk associated with ruptured aneurysms.

To quantitatively assess the relationship between aneurysm status and mortality risk, Fisher's exact test was applied, due to the presence of expected values lower than 5 in the contingency table. This statistical approach was selected to ensure the reliability and validity of the results despite the small sample size in some subgroups. The data utilized for this analysis are summarized in **Table 4.**, which provides a detailed overview of mortality distribution between the two groups.

**Table 4.** Mortality depending on aneurysm status.

Aneurysm Status	Deaths	Survivors	Total
Ruptured	2	13	15
Unruptured	1	45	46
Total	3	58	61

The results of the Fisher's exact test indicated that there was no statistically significant difference in mortality between patients with ruptured and unruptured aneurysms ( $p = 0,15$ ), based on the pre-defined significance threshold of  $p < 0,05$ . Although the observed mortality was higher in the ruptured aneurysm group, the lack of statistical significance suggests that, within this study cohort, aneurysm status alone may not be a decisive predictor of postoperative mortality. Nonetheless, the higher proportion of deaths among patients with ruptured aneurysms emphasizes the need for careful perioperative management, rigorous monitoring, and potentially more intensive postoperative support in this higher-risk subgroup.

### Discussion

The primary objective of this study was to determine the risk of postoperative complications and overall mortality in patients undergoing surgical clipping of intracranial aneurysms, with particular attention paid to the status of the aneurysm prior to surgery, i.e., whether it was ruptured or unruptured. Additionally, this study served as a comprehensive summary and report on the intracranial aneurysm clipping procedures performed at the Clinical Department of Neurosurgery of the University Clinical Center named after Prof. K. Gibiński, Medical University of Silesia in Katowice, over the past three years. By analyzing these cases, the study aimed to provide insight into real-world clinical outcomes, identify potential trends, and contribute to evidence-based recommendations for patient management and surgical decision-making.

Among the 61 cases collected and analyzed, more than three-quarters of the patients were female (46; 75,41%), which is consistent with previous research indicating a higher prevalence of intracranial aneurysms in women [13,14]. This predominance may be partially explained by sex-specific differences in vascular biology, hormonal influences, and variations in risk factor profiles, which have been suggested to contribute to the increased susceptibility of women to aneurysm formation and progression.

The mean age of patients in this cohort was  $56,33 \pm 12,87$  years, a finding that aligns closely with the typical age range reported in the literature for individuals diagnosed with intracranial aneurysms. This observation reflects the fact that aneurysms are most often identified in middle-aged to older adults, a period during which age-related vascular changes, chronic hypertension, atherosclerosis, and other comorbid conditions become increasingly prevalent [15,16]. Such factors are believed to contribute to both the formation and the potential growth of aneurysms over time, underscoring the importance of careful monitoring and timely intervention in these populations.

The total number of cases collected over the three-year study period corresponds to an average of approximately 2 patients per month undergoing aneurysm clipping in the neurosurgery department. This relatively low procedural volume highlights that, although aneurysm clipping is performed on a regular basis at this center, it does not rank among the most frequently performed neurosurgical interventions. The modest case volume underscores the specialized nature of this procedure, which requires a high level of surgical expertise, meticulous planning, and careful perioperative management to minimize complications and optimize patient outcomes. It also reflects the relative rarity of intracranial aneurysms requiring surgical intervention within a defined population, emphasizing the importance of individualized treatment planning and specialized surgical teams in centers performing these operations.

In this study cohort, the vast majority of clipped aneurysms were located on the middle cerebral artery (MCA), which is notable considering that the anterior communicating artery (ACoM) is often reported as the most common location for intracranial aneurysms in epidemiological studies [17]. This finding reinforces the idea that surgical clipping remains the preferred and most effective treatment modality for aneurysms situated in the MCA region. The predominance of MCA aneurysms treated surgically is consistent with existing literature, as these aneurysms are often more accessible for microsurgical intervention due to their superficial anatomical location, favorable branching patterns, and relative proximity to standard surgical corridors [4,18].

These observations support the notion that, despite the evolution and increased adoption of endovascular techniques, surgical clipping continues to play a central role in the management of MCA aneurysms. The anatomical characteristics of these aneurysms, combined with the high rates of complete occlusion and long-term durability achieved through clipping, underscore why this technique remains the gold standard in appropriately selected patients. Furthermore, the study findings highlight the importance of surgical expertise in achieving optimal outcomes, particularly in complex cerebrovascular cases where endovascular approaches may be less effective or technically challenging.

Within the studied group, aneurysm rupture was observed more frequently in male patients, despite the fact that several prior studies have suggested that women may be at higher overall risk of aneurysm rupture [19,20]. This apparent discrepancy may reflect the relatively small sample size of the present study, as well as potential differences in underlying patient characteristics, comorbidities, aneurysm morphology, or hemodynamic factors that were not fully captured in this analysis. It also highlights the complexity and multifactorial nature of aneurysm rupture risk, which may not be determined solely by sex alone but rather by a combination of genetic predisposition, hormonal influences, vascular anatomy, and environmental factors. Consequently, these findings underscore the importance of individualized assessment and careful monitoring of all patients with intracranial aneurysms, regardless of sex, in order to accurately evaluate rupture risk and guide clinical decision-making. The postoperative complications observed in this study were diverse in nature, ranging from neurological deficits to hemorrhagic and systemic events. Among the most commonly observed complications were paresis, aphasia, and dysphasia, which gradually subsided over time and/or appropriate rehabilitation. Additionally, intracerebral and subdural hematomas, as well as ischemic strokes, emphasize the need for meticulous intraoperative hemostasis and vigilant postoperative monitoring, as these are among the most dangerous and frequently occurring complications. The occurrence of complications requiring intensive care unit (ICU) admission, including in patients without concurrent neurological or hemorrhagic symptoms, further highlights the nursing burden that can accompany these procedures.

The complication rate and mortality were notably higher in patients with ruptured aneurysms (53,33% vs. 28,26% for complications; 13,33% vs. 2,17% for mortality), indicating a clear divergence in outcomes. However, statistical analysis did not confirm the significance of these differences. This lack of significance may result from the relatively small sample size, which limits the study's statistical power. Therefore, further research involving larger patient cohorts is needed to validate these preliminary findings and determine whether the trends observed here reach statistical significance in a broader population.

## Conclusions

1. Females predominated in the analyzed group.
2. The majority of aneurysms (75,41%) were unruptured at the time of surgery. The most common location was the middle cerebral artery (MCA), accounting for 83,61% of all aneurysms.
3. Ruptured aneurysms occurred more frequently in men.
4. Postoperative complications occurred in 34,43% of patients. They were more frequent among patients with ruptured aneurysms (53,33% vs. 28,26%), although this difference did not reach statistical significance.
5. The most commonly observed complications included transient neurological symptoms (paresis, aphasia, dysphasia) and intracerebral hemorrhages. The overall mortality rate in the study group was 4,92%.
6. Patients with ruptured aneurysms were more frequently transferred to the intensive care unit due to postoperative complications compared to patients with unruptured aneurysms.
7. No statistically significant difference in mortality was observed between patients with ruptured and unruptured aneurysms.

## Disclosure

### Author's contribution:

All authors contributed to the article.

All authors have read and agreed with the published version of the manuscript.

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