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Treatment strategies of unruptured intracranial aneurysms: A Literature Review

Agnieszka Szema

University Clinical Hospital no. 2 PMU in Szczecin, Powstańców Wielkopolskich 72 St 70-111 Szczecin

aga.szema@gmail.com

<https://orcid.org/0009-0000-5017-3426>

Mikołaj Łabuda

Independent Public Voivodeship Integrated Hospital in Szczecin, ul. Arkońska 4
71-455 Szczecin

labuda.mikolaj@gmail.com

<https://orcid.org/0009-0002-4137-4319>

Karolina Knychalska

University Clinical Hospital no. 2 PMU in Szczecin, Powstańców Wielkopolskich 72 St 70-111 Szczecin

karolinaknychalska@gmail.com

<https://orcid.org/0009-0003-3736-0579>

Teresa Sowińska

University Clinical Hospital no. 2 PMU in Szczecin, Powstańców Wielkopolskich 72 St 70-111 Szczecin

tsowinska@icloud.com

<https://orcid.org/0009-0003-0061-212X>

Adrianna Bogucka

Independent Public Voivodeship Integrated Hospital in Szczecin, ul. Arkońska 4
71-455 Szczecin

adrianna.bogucka@icloud.com

<https://orcid.org/0009-0001-8870-0495>

Jakub Sikora

Profi-Med Medical Center Goleniów Marii Konopnickiej 10A
72-100 Goleniów

esiak10play@gmail.com

<https://orcid.org/0009-0007-9637-0709>

Agata Kotkowiak

Family Medicine Clinic "Podgórna", Podgórna 22 St.
70-205 Szczecin Poland

akotkowiak@gmail.com

<https://orcid.org/0009-0004-4797-6980>

Klaudia Królikowska

University Clinical Hospital no. 2 PMU in Szczecin, Powstańców Wielkopolskich 72 St 70-111 Szczecin

klaudia.1799@wp.pl

<https://orcid.org/0009-0007-7984-4642>

Aleksandra Slojewska

Independent Public Voivodeship Integrated Hospital in Szczecin, ul. Arkońska 4

71-455 Szczecin

o.slojewska@gmail.com

<https://orcid.org/0009-0007-7532-0948>

Oliwia Mentel

University Clinical Hospital no. 2 PMU in Szczecin, Powstańców Wielkopolskich 72 St 70-111 Szczecin

oliwiamentel@gmail.com

<https://orcid.org/0009-0004-4739-0621>

ABSTRACT**Introduction and purpose**

Unruptured intracranial aneurysms (UIAs) are often diagnosed incidentally and become a complex clinical dilemma. The main challenge is to choose between invasive treatment and conservative management, considering the low but difficult to predict risk of rupture. The aim of this review is to present current knowledge and approaches regarding UIA management, highlighting both traditional and emerging strategies.

Description of state of knowledge

Management of UIAs depends on various factors, including aneurysm size, location, morphology, and patient-specific risks. Surgical clipping remains a reasonable method for long-term durability, but more perioperative complications, while endovascular approaches have an advantage due to their less invasive nature, but lower adequate occlusion rate. In selected low-risk patients, conservative monitoring with regular imaging may be appropriate. Advances in computational modeling, artificial intelligence, and hemodynamic analysis are improving our ability to assess rupture risk and tailor treatment plans. However, the lack of universally accepted guidelines continues to complicate decision-making.

Conclusion

UIA management should be individualized, weighing the risks and benefits of each treatment

option. Despite technological progress and improved diagnostic tools, further research and international consensus are needed to establish standardized protocols for clinical practice.

Key words

Unruptured intracranial aneurysm; aneurysm management; endovascular treatment; surgical clipping; PHASE score; ELAPSS score.

INTRODUCTION AND PURPOSE

Intracranial aneurysm (IA) is a vascular defect and may cause dangerous bleeding, such as subarachnoid haemorrhage (SAH). Cerebral aneurysms result from dynamic blood flow in a weakened area of the artery and may lead to an abnormal dilatation of a blood vessel. IAs can be categorised in different ways. Mostly they are classified by size (small with a diameter of <10 mm, large 10-25 mm, giant >25 mm), location (presence in anterior or posterior circulation) or morphology (saccular, fusiform, dissecting).

Unruptured aneurysms are relatively common. An estimated up to 6% of the population has intracranial aneurysm in prospective autopsy and radiological studies [1,2]. An aneurysm rupture is highly dangerous and associated with a 57% mortality rate for anterior circulation and up to 47% for posterior circulation IA within 30 days [3].

Pathogenesis of cerebral aneurysm growth and rupture is still not fully known. Although as risk factors it is considered patient sex, age, genetic background, hypertension, smoking, SAH in the past, family history, alcohol consumption, drug abuse, IA size, location and morphology. After assessing the risk of rupture, it is considered whether to leave it for observation or whether the aneurysm requires treatment. The final choice is also based on the patient's general condition, size, location and type of aneurysm. The available treatment methods are neurosurgery and endovascular therapy. Each method has its own perioperative risks. [4]

The study aims to compare and summarise the current management of intracranial unruptured aneurysms (UIAs). As such, it is intended to serve as a tool for clinicians in selecting the best treatment strategy for such patients, so as to prevent rupture and its consequences.

So far, no strict guidelines have been defined on how to proceed in case of asymptomatic unruptured intracranial aneurysms.

METHODS

A literature research was conducted using the PubMed, Cochrane Library, Medline, Google Scholar and OVID databases with the following keywords: “unruptured intracranial aneurysm”; “aneurysms management”; “endovascular treatment”; “surgical clipping”; “PHASE score”; “ELAPSS score”. The study analyzed guidelines, systematic reviews, and original research articles examining diagnosis, risk factors and treatment of unruptured intracranial aneurysms. It was performed to identify relevant studies between 1995 and 2024.

DESCRIPTION OF THE STATE OF KNOWLEDGE

Estimating the risk of intracranial aneurysms (IAs) rupture and growth is complex, which is why special tools have been developed to support clinicians.

The average risk of rupture is considered to be from 0.3% even up to 15% per 5 years (for lesions smaller than 7 mm is 0.4-0.6%). To more adequately calculate the 5-year rupture risk of IA, there was designed the PHASES score. The method is based on a systematic review of six prospective cohort studies. Data from 8482 patients were analysed and six criteria were selected: population, hypertension, age, size of aneurysm, earlier SAH from another aneurysm, site of aneurysm. However, the PHASES score has its limitations [5].

Widely used scale to predict enlargement of UIAs is ELAPSS (Earlier subarachnoid hemorrhage, aneurysm Location, Age, Population, aneurysm Size and Shape) score.[6] According to the scale patients with a history of SAH, IA localisation in the posterior circulation or posterior communicating artery (PCOM), aged >60 years, of Japanese or Finnish descent, with an aneurysm size >10 mm and an irregular shape are most at risk of increased aneurysm growth. [7] The ELAPSS score has been externally validated and found to be accurately calibrated for the 3-year and 5-year risk of aneurysm growth.

Currently, deep learning (DL) is playing an increasingly important role in the diagnostic process and in the development of treatment strategies. This is also the case with UIAs. AI models are already able to correctly analyse radiological images, make diagnoses and suggest treatments. It is possible the tool will enable us to choose the most suitable treatment for the patient in the future. [8, 9]

Taking into consideration all of the above, we can currently speak of two courses of action.

1. Observation

As knowledge about incidental UIAs and its natural history is not yet fully understood, the decision to only observe or to treat is complicated and needs to be individualised. The wait-and-scan approach is justified for patients with a higher risk associated with surgery than the 5-year risk of aneurysm rupture. [5, 10]

For patients who are unlikely to qualify for preventive vascular or surgical treatment, regardless of the size and location of the aneurysm, it is acceptable to forgo regular follow-up. This group includes patients over the age of 75, with a severely limited life expectancy and advanced multimorbidity. [11]

Whenever a conservative approach is decided upon, the patient is informed about the time interval until the next radiological examination and the re-evaluation of the treatment. The follow-up imaging is recommended in 6 to 12 months after initial diagnosis. If the aneurysm remains stable, it is preferable to repeat the procedure after 2 years. In case of a continuous trend, follow-ups every 5 years can be considered. [1, 12] Patients with tiny UIAs are also candidates for routine imaging, but the guidelines do not have a clear statement on the frequency of follow-up. Based on studies on UIAs of 3 mm or less, it is considered to undergo a radiological examination every 5 years. [13]

The visualisation of a small, newly formed aneurysm in the control scan requires close observation, as there may be an increased risk of it growing and rupturing. Once an aneurysm enlargement is detected, treatment should be reconsidered. Regardless of whether the patient undergoes treatment or not, regular imaging follow-ups should be performed over the long term, as there is a risk of aneurysm recurrence or the formation of a new aneurysm. [14, 15]

For patients with a high ELAPSS score, shorter intervals of imaging may be beneficial. In addition to radiological control, information about risk factors for growth and rupture is crucial. Regular monitoring of blood pressure, abstaining from smoking and limiting certain sports such as weightlifting is recommended for such patients. There are no clear indications for mandatory restriction of physical activity, medication intake, caffeine consumption or disqualification from non-UIA-related surgical treatment. Such actions, on the other hand, can lower the mood and increase anxiety about their condition. [16]

2. Treatment

2.1 Treatment methods

The decision whether to observe or to proceed with treatment depends on many factors. Although there is a risk of leaving an aneurysm untreated, a potential surgical or vascular intervention also carries perioperative complications.

Surgical treatment methods

There are several methods of neurosurgical supply of UIAs, but only one is widely respected and used as the gold standard. Currently, the preferred method is clipping. A clip is surgically placed around the neck of the aneurysm to exclude it from the bloodstream without closing off the surrounding vessels. [17] The considerably less used methods are wrapping or coating the aneurysm. They are not used to treat standard saccular aneurysms, but only in IAs where clipping is barely possible. These cases include aneurysms with major branches arising from the dome, fusiform basilar trunk aneurysm or aneurysm with neck within the cavernous sinus. The method is based on wrapping the aneurysm in fabric such as cotton, muslin, polimer, teflon or fibrin glue to support it and prevent rupture. [18] Multicentre analyses have shown that the course of post-wrapping aneurysm, including the risk of re-bleeding, is practically the same or slightly lower than the natural course. Furthermore, there is a risk of ischaemic stroke, as wrapping materials can stimulate inflammatory reactions and promote artery narrowing. [19]

The meta-analysis of studies published between 2011, and 2017 examined the effects of surgical treatment of UIAs (clipping only) on the 30-day clinical complication risk and case-fatality rate. In 54 studies the pooled complication risk for neurosurgical treatment was 8.34% and the fatality rate was 0.10%. Factors affecting the incidence of perioperative complications include patient age, female sex, taking of anticoagulants or presence of coagulopathy, hypertension, diabetes, congestive heart failure, smoking, aneurysm calcification and location in posterior circulation. [11, 20]

Endovascular treatment methods

Endovascular treatment (ET) of IAa involves minimally invasive procedures performed through a catheter, usually inserted through the femoral artery. ET has made significant progress in recent years, there are now many different methods with different characteristics in use. One of the most common techniques include coiling, where platinum coils are placed into the aneurysm sac to induce thrombosis and occlusion. It is commonly used for smaller aneurysms and those located in easily accessible areas. [21] Flow diverter redirects blood flow away from the aneurysm. Over time, this reduces pressure within the aneurysm, leading to its thrombosis. Those are often used for larger, complex aneurysms, especially in difficult-to-reach locations. [22] Stent-assisted coiling is mostly used for wide-necked aneurysms. Stents may be used to provide support to the coils and prevent coil migration. [23, 24] Technique of Balloon-Assisted Coiling (BAC) is based on inserting inflated balloon catheter at the aneurysm neck to prevent coil migration and stabilize the aneurysm. [25] Intracapsular devices, such as the Woven Endobridge (WEB) device, are relatively new method. Deployment a self-expanding, braided mesh structure inside the aneurysm initiate thrombosis directly in the sac. [26]

A large meta-analysis examining 74 studies of endovascular therapy reported the pooled complication risk was 4.96%, the mortality rate was 0.30%. Female gender, coagulopathy, diabetes, hyperlipidaemia, cardiac comorbidity, wide aneurysm neck, posterior circulation aneurysm, stenting and stent-assisted coiling were associated with complications from endovascular treatment. [11]

2.2 Treatment strategies

Depending on size

Depending on the size of the UIAs, different treatment methods are recommended.

Small aneurysms

Aneurysms with a diameter of less than 5 mm were analysed to determine morbidity and complete occlusion in patients after microsurgery and endovascular treatment. A multi-centre study of 228 small aneurysms found no change in functional outcome after clipping, with permanent neurological morbidity in 2.7% and complete occlusion in 98.2% of patients. [27] A meta-analysis of endovascular treatment cases involving 261 cases of small unruptured aneurysms showed a morbidity and mortality rate of 4% and complete occlusion in 85% of patients. [28] Based on current knowledge about small UIAs, we can conclude that neurosurgical treatment such as clipping is an effective method and should be considered first. This method seems most appropriate for younger patients with a long life expectancy. It is important to emphasize that the management of small aneurysms should be conducted in high-volume medical centers. [29] Despite some research that has been done, presently we can only compare cohort studies. Further comparative studies, preferably randomised, are needed to draw conclusions on this issue.

Large aneurysms

Large aneurysms, i.e. those measuring 10-25 mm, are the most commonly treated aneurysms. The choice of treatment in this case is multifactorial.

Giant aneurysms

Aneurysm with a diameter of more than 25 mm are considered to be giant intracranial aneurysms and challenging to treat, both microsurgical and endovascular. The group studying such variants of IAs concluded that the chances of a good outcome after surgical or endovascular treatment do not differ significantly, so when deciding on treatment, greater attention should be given to the patient's age and the location of the aneurysm. The Giant Intracranial Aneurysm group systematically reviewed 455 cases and found a functional outcome for clipping at 79.7% and for endovascular therapy at 84.9%. However, the choice of endovascular treatment method was significant. Of the balloon-assisted coiling (BAC), stent-assisted coiling (SAC) and flow diverter (FD) methods, SAC and FD achieved the best occlusion rates (73% vs 72%). Nevertheless, the SAC method had the highest complication rate (39%). [30] Based on a smaller study focusing on surgical management, 87% of 140 patients achieved sufficient occlusion, but surgical mortality was up to 13%. [31]

Depending on location

Aneurysms can be located in any vessel. Among intracranial aneurysms, the most common are Anterior Communicating Artery (ACoA), Internal Carotid Artery (ICA), Middle Cerebral Artery (MCA), and then Posterior Communicating Artery (PCA), Basilar Artery (BA), Posterior Inferior Communicating Artery (PICA), Anterior Cerebral Artery (ACA). [32, 33] The location of the UIA is highly significant in regards to the choice of treatment.

Basilar artery aneurysm

About 5% of all intracranial aneurysms are basilar artery aneurysms. Unruptured aneurysms of the mid- and distal basilar artery segments are considered to be the most challenging entities in neurovascular treatment, because of its lack of defined neck, usually giant size or fusiform shape, location in close proximity to critical brainstem structures and perforating arteries. Surgical management is rarely feasible due to limited accessibility and high

procedural risk. No scientific work has been done that would evaluate the results of microsurgical and endovascular treatment in mid- and distal basilar artery segments, much less compare the two techniques. However, we do have records on basilar apex aneurysm management. In a current state of knowledge, the selection of unruptured basilar apex aneurysm treatment is based on the challenging decision of whether the clinical outcome or adequate occlusion is more important in a certain case. Sufficient occlusion can be achieved in 91.7% of patients treated with clipping, but at the expense of poorer clinical outcomes (81.3%). The endovascular method results in 82.6% adequate occlusion, but with better clinical outcomes at 89.8%. [34]

Posterior Cerebral Artery

Endovascular treatment seems to be more important in the treatment of patients with PCA aneurysms. In a study including 685 patients, neurosurgical patients had a significantly higher complication rate (40.1% vs 13.2%). The main complication was a subsequent stroke following parent artery occlusion. The recanalisation rate was worse for the endovascular treatment group. [35]

Posterior inferior communicating artery

Based on the literature to date, it seems that despite a greater chance of achieving complete occlusion rate, unruptured PICA aneurysms should be treated endovascularly, as the studies show a better good functional outcome in these patients. A meta-analysis of saccular PICA aneurysms showed results in patients treated with microsurgical clipping and endovascularly of 85% and 86% as a good outcome and a complete occlusion rate of 89% and 62% for unruptured aneurysms, respectively. [36] A broader analysis from 2016 of 136 cases showed 92.9% and 75.7% of complete occlusion, but rebleeding was reported in 8% vs 4% and long-term morbidity and mortality in 16% and 9%. Nevertheless, a good functional outcome was determined in 91.5% and 93.3% of patients. [37]

Middle Cerebral Artery

Recent research shows that middle cerebral artery (MCA) aneurysms are better to treat surgically than endovascularly. A systematic review of 1552 patients compared open surgery with endovascular techniques including FD, SAC and FD. Clipping had better long-term complete or near complete occlusion rates (95.7%) compared to endovascular (78.1%), lower retreatment rates (1% vs 6%) and less complications (2.9% vs 5.6%). However, ET was correlated with a better rate of good neurological outcomes (97%) in comparison to the surgical group (84%). [38] Study based on randomized controlled trial analysed treatment methods for unruptured MCA aneurysms. A significantly lower rate of treatment failure was demonstrated for surgical treatment compared to endovascular treatment. The incidence of new neurological deficits was comparable in both groups. [39]

Internal Carotid Artery

Internal Carotid Artery aneurysms are rarely the subject of studies. The literature review analyses the results of surgical and endovascular treatment of aneurysms of the orbital area of the internal carotid artery. Among the 147 aneurysms treated endovascularly, 81.6% achieved more than 95% closure on initial angiography, with 1.4% serious complications. In the group of 23 patients who underwent surgical treatment, 26.1% experienced serious complications, including 2 cases of permanent vision loss. [40] Studies of ICA bifurcation aneurysms are underpowered to provide any conclusions. [41]

Anterior Cerebral Artery

The anterior cerebral artery (ACA) study showed that endovascular treatment can be more beneficial for patients, as it has a better clinical outcome and is associated with lower mortality (1% vs. 8.7%). [42] Similarly endovascular treatment of Anterior Communicating Artery (ACoA) has also been shown to be superior to surgical treatment. Comparison of advanced ET options like FD, SAC, intravascular FD with neurosurgery showed better clinical outcomes, less perioperative complications (3% vs 7%), but lower occlusion rate (66% vs 81%). [43] In the small ACoA study, the endovascular retreatment rate was up to 18% compared to 0% for clipping. [44] Among ACA aneurysm, distal anterior cerebral artery

(DACA) plays a significant role. DACA aneurysms are also called pericallosal or A2 aneurysms. These subtypes are fragile and are associated with a higher morbidity than would be expected from their location and radiological appearance. [32, 45] Open surgery for DACA aneurysms provides a better occlusion (89%), while endovascular treatment is present at a rate of 54%. Morbidity and mortality were 11% for the surgical group and 18% for ET patients. Such a rate for endovascular treatment is associated with in-stent thrombosis, and side branch coverage. [46, 47]

In general, neurosurgical treatment of UIAs shows a more favourable outcome in adequate occlusion, but at the risk of increased morbidity and neurological deficits. This makes endovascular treatment seem to be a better first-line treatment. In the case of MCA and DACA aneurysms, however, clipping should be given special consideration, as scientific sources report a greater benefit in this instance.

CONCLUSIONS

The management of unruptured intracranial aneurysms is complex and must be adequate to each patient. Decision-making process involves assessing the risk of aneurysm rupture based on factors such as size, location, patient age, and comorbidities, while also considering the risks associated with treatment options. Surgical clipping remains a reasonable option due to its durability and low recurrence rate, but endovascular techniques like coiling and flow-diverting stents are increasingly favored, especially for high-risk surgical candidates, because they are less invasive. There are also subtypes of aneurysm that some studies suggest are more suitable for neurosurgical treatment. Therefore, each case must be treated individually.

For aneurysms with a low predicted risk of rupture, conservative management with regular imaging follow-up is often the most appropriate course. Recent developments in artificial intelligence and computational modeling show promise in improving rupture risk prediction and guiding clinical decisions. However, despite technological advances, there remains a lack of universally accepted treatment guidelines. Continued research and collaboration are essential to establish standardized protocols that ensure optimal outcomes for patients.

DISCLOSURE

Author's contribution:

- Conceptualization: Agnieszka Szema, Mikołaj Łabuda
- Methodology: Agnieszka Szema, Teresa Sowińska, Agata Kotkowiak
- Software: Agnieszka Szema, Karolina Knychalska
- Check: Karolina Knychalska, Aleksandra Słojewska
- Formal analysis: Karolina Knychalska, Oliwia Mentel, Jakub Sikora
- Investigation: Aleksandra Słojewska, Teresa Sowińska, Oliwia Mentel
- Resources: Agnieszka Szema, Teresa Sowińska
- Data curation: Klaudia Królikowska, Agata Kotkowiak, Adrianna Bogucka
- Writing - rough preparation: Agnieszka Szema, Mikołaj Łabuda,
- Writing - review and editing: Klaudia Królikowska, Aleksandra Słojewska
- Visualization: Jakub Sikora, Karolina Knychalska
- Supervision: Mikołaj Łabuda, Karolina Knychalska, Adrianna Bogucka
- Project administration: Oliwia Mentel, Agnieszka Szema

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