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„Strategia postępowania i wyniki leczenia w wybranych grupach niepękniętych tętniaków wewnątrzczaszkowych"

Rozprawa na stopień doktora nauk medycznych i nauk o zdrowiu w dyscyplinie nauki medyczne

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1. Kunert P, **Wójtowicz K**, Żyłkowski J, et al. Flow-diverting devices in the treatment of unruptured ophthalmic segment aneurysms at a mean clinical follow-up of 5 years. Sci Rep. 2021;11(1):9206. doi:10.1038/s41598-021-87498-z.

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2. **Wójtowicz K**, Przepiorka L, Kujawski S, et al. Unruptured Anterior Communicating Artery Aneurysms: Management Strategy and Results of a Single-Center Experience. J Clin Med. 2023;12(14):4619. doi:10.3390/ jcm12144619.

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Spis treści

1. Wykaz stosowanych skrótowców

AComA	ang. *anterior communicating artery* / tętnica łącząca przednia
FDD	ang. *flow diverting device* / stent kierunkujący przepływ
ICA C6	ang. *ophthalmic segment of internal carotid artery* / tętnica szyjna wewnętrzna, odcinek oftalmiczny
PHASES	P – ang. *population* / populacja; H – ang. *hypertension* / nadciśnienie tętnicze; A – ang. *age* / wiek; S – ang. *size of aneurysm* / wymiar tętniaka; E – ang. *earlier SAH from another aneurysm* / uprzedni krwotok z innego tętniaka; S – ang. *site of aneurysm* / lokalizacja tętniaka
UIA	ang. *unruptured intracranial aneurysm* / niepęknięty tętniak wewnątrzczaszkowy
UIATS	ang. *unruptured intracranial aneurysm (UIA) treatment score* / wynik leczenia niepękniętych tętniaków wewnątrzczaszkowych

2. Streszczenie w języku polskim

Wstęp: Niepęknięte tętniaki wewnątrzczaszkowe (ang. *unruptured intracranial aneurysm*, UIA) występują z częstością od 1,8 do 8,8 przypadków na 100 osób, w zależności od źródła oraz przyjętych kryteriów diagnostycznych. Wzrost wykrywalności tętniaków jest wynikiem powszechnego stosowania badań CT i MR. Decyzja o leczeniu tętniaków opiera się na ocenie ryzyka krwotoku oraz ryzyka związanego z interwencją, którą może stanowić mikrochirurgiczne zaklipsowanie lub leczenie wewnątrznaczyniowe. Zwiększona wykrywalność tętniaków oraz rozwój bezpieczniejszych metod leczenia prowadzą do kwalifikacji do leczenia coraz mniejszych tętniaków i starszych pacjentów. Powstały skale do oceny ryzyka krwotoku, m.in. skala PHASES, oraz do wyboru postępowania, skala UIATS, ale istnieje potrzeba przeprowadzania dalszych badań nad ich użytecznością.

Cele: Konieczne są badania oceniające: strategie postępowania z UIA, wyniki leczenia UIA różnymi metodami oraz użyteczność skal oceny ryzyka krwotoku i postępowania z UIA.

Materiał i metodyka: Przeprowadzono cykl retrospektywnych badań, koncentrując się na dwóch podgrupach tętniaków: tętniakach kompleksu tętnicy łączącej przedniej (ang. *anterior communicating artery*, AComA) oraz tętnicy szyjnej wewnętrznej w odcinku oftalmicznym (ang. *ophthalmic segment of internal carotid artery,* ICA C6).

Wyniki: W pierwszej publikacji analizowano skuteczność i bezpieczeństwo stosowania stentów kierunkujących przepływ (ang. *flow diverting device*, FDD) w leczeniu tętniaków ICA C6. Do badania włączono 52 pacjentów z 65 tętniakami. Wyniki wskazują, że 98,1% pacjentów uzyskało zadowalający wynik kliniczny. Skumulowane ryzyko krwotoku z leczonego tętniaka wyniosło 0,33% w ciągu średniego okresu obserwacji trwającego 61 miesięcy przy rocznym ryzyku krwotoku na poziomie 0,07%. Wśród pacjentów bez objawów wzrokowych nie odnotowano pogorszenia widzenia w wyniku leczenia, a u pacjentów z objawowymi tętniakami wyniki były zróżnicowane. Całkowite wyłączenie tętniaka z krążenia nastąpiło w 12,3% przypadków bezpośrednio po zabiegu, a po 6 miesiącach – w 73,4% przypadków. W długoterminowej obserwacji zadowalający

wynik radiologiczny uzyskano w 95,4% przypadków. Komplikacje wystąpiły u 40,4% pacjentów, najczęściej były to powikłania proceduralne, do których doszło u 30,8% pacjentów. Ponadto u 11,5% pacjentów wystąpiły powikłania odległe.

Drugie badanie to analiza strategii postępowania ze 131 tętniakami AComA, koncentrująca się na kwalifikacji do obserwacji lub leczenia, rodzajach leczenia oraz wynikach zastosowanego postępowania. Do obserwacji zakwalifikowano 60 (48,1%) tętniaków, z których 4 się powiększyły. Mediana czasu obserwacji wyniosła 60,9 miesiąca. W tej grupie nie odnotowano krwotoków podpajęczynówkowych. Leczono 69 (53,5%) tętniaków, z czego 33,1% poddano leczeniu wewnątrznaczyniowemu. Komplikacje proceduralne wystąpiły w 17,8% przypadków, w większości bezobjawowe; 93,2% pacjentów zostało wypisanych w stanie jak przy przyjęciu. Śmiertelność w tej grupie wyniosła 4,5%, a ryzyko wystąpienia deficytów neurologicznych – 2,3%. W długoterminowej obserwacji (mediana 7,25 miesiąca) 90% tętniaków zostało wyłączonych z krążenia, w 5% przypadków stwierdzono napływ do szyi tętniaka, a w kolejnych 5% – do worka tętniaka. Rekanalizację stwierdzono w 17,4% przypadków. W długoterminowej obserwacji wystąpił 1 krwotok podpajęczynówkowy z leczonego tętniaka. Leczeniu mikrochirurgicznemu poddano 25 tętniaków. 76% pacjentów zostało wypisanych bez pogorszenia stanu zdrowia, u prawie 1/4 doszło do pogorszenia w następstwie leczenia. Śmiertelność w tej grupie wyniosła 4,8%, a częstość trwałych deficytów neurologicznych – również 4,8%. W długoterminowej obserwacji (mediana 63 miesiące) nie odnotowano krwotoków. Podsumowując, śmiertelność wśród wszystkich pacjentów wyniosła 2,4%, a częstość trwałych deficytów – 1,6%.

W trzecim badaniu porównano rzeczywiste postępowanie ze 129 tętniakami AComA z rekomendacjami wynikającymi ze skali UIATS oraz z oceną ryzyka krwotoku według skali PHASES. Spośród 129 tętniaków 46,5% zakwalifikowano do obserwacji, a 53,5% do leczenia.

Zgodnie ze skalą PHASES większość, 86% UIA cechowało niskie ryzyko krwotoku, podczas gdy 14% charakteryzowało się wysokim ryzykiem. W grupie leczonych tętniaków wartości PHASES były wyższe. Skala UIATS rekomendowała leczenie dla 27% tętniaków, obserwację dla 32%, a dla 37% wynik był niekonkluzywny.

W grupie obserwowanych tętniaków wartość skali PHASES wynosiła od 4 do 9, przy czym nie było tętniaków o wysokim ryzyku krwotoku. Skala UIATS rekomendowała leczenie w przypadku 11% UIA, obserwację dla 51%, a wynik był niekonkluzywny w 38% przypadków. W grupie leczonych tętniaków 26% charakteryzowało się wysokim ryzykiem krwotoku według skali PHASES. Skala UIATS rekomendowała leczenie w przypadku 42% tętniaków, obserwację dla 19%, a wynik był niekonkluzywny dla 39% tętniaków.

Podsumowanie i wnioski:

1. Stenty kierunkujące przepływ mogą zapewnić bardzo wysoki odsetek zadowalających wyników radiologicznych i klinicznych. Niemniej jednak, ze względu na wysokie ryzyko różnego rodzaju powikłań, konieczna jest krytyczna oceny wyników.
2. Zróżnicowane postępowanie z tętniakami AComA, obejmujące obserwację, leczenie mikrochirurgiczne i wewnątrznaczyniowe, zmniejszyło ryzyko krwotoku podpajęczynówkowego do 0,14% w tej podgrupie tętniaków. Nastąpiło to kosztem śmiertelności na poziomie 2,4% oraz wystąpienia trwałych deficytów na poziomie 1,6% w podgrupie tętniaków leczonych. Ryzyko trwałych deficytów neurologicznych i śmiertelności nie może być pomijane, ale dotyczy podgrupy tętniaków wysokiego ryzyka krwotoku.
3. W przypadku ponad 2/3 ocenianych tętniaków AComA wykazano brak zgodności w uzyskanych rekomendacjach pomiędzy skalami PHASES a UIATS. Decyzje co do postępowania nadal zależą w głównej mierze od doświadczenia ośrodka, indywidualnej oceny tętniaka i preferencji pacjenta.

3. Streszczenie w języku angielskim

Introduction: The incidence of unruptured intracranial aneurysms (UIA) is 1.8 to 8.8 per 100 people. This depends on what kind of source we use and the diagnostic criteria we adopt. The higher use of CT and MR results in more frequent intracranial aneurysm identification. The management of aneurysms depends on comparing the hemorrhage risk and intervention risk. The treatment involves microsurgical or endovascular methods. The higher detectability of aneurysms and safer treatment methods provide for the treatment of smaller aneurysms and older patients. Many scales were created to calculate the risk of hemorrhage such as PHASES, or to choose the management such as UIATS, but we need studies to confirm their usefulness.

Purpose: We need studies that analyze the management of UIAs and the result of their treatment with different methods, as well as the usefulness of scales to assess hemorrhage risk and management.

Material and methods: We provide retrospective studies on two aneurysm locations: anterior communicating artery (AComA) and ophthalmic aneurysms (ICA C6).

Results: In the first study, we analyzed the effectiveness and safety of flow divert stents in ICA C6 aneurysm treatment. We analyzed 52 patients with 65 aneurysms. The results showed that 98.1% of patients achieved good outcomes. The overall post-treatment risk of aneurysm rupture was 0.33% during a mean follow-up of 61 months. The annual risk of aneurysm rupture after treatment reached 0.07%. Patients with asymptomatic UIAs had no visual complications immediately after treatment, but with symptomatic UIAs, the results were variable. The complete occlusion was demonstrated in 12.3% of aneurysms but in 73.4% after 6 months. In long-term follow-up, good radiological outcomes were achieved in 95.4 % of aneurysms. Complications occurred in 40.4 % of patients, of which the most frequent were procedural complications, which occurred in 30.8% of patients. Late complications occurred in 11.5% of patients.

In the second study, we analyzed the results of our diverse strategy in AComA UIAs with the additional goal of assessing the risk of treatment and the incidence of hemorrhage. We analyzed 131 patients, of which 45.8% were

assessed for observation, 4 of presented with enlarged aneurysms during follow-up. The median time of observation in this subgroup was 60.9 months. There were no hemorrhages in the observation group. For the treatment, 69 aneurysms (53.5%) were assessed, 33.1% of them were assigned to endovascular treatment. Procedural complications occurred in 17.8% of cases, the majority of them were asymptomatic. 93.2% of patients were discharged in the same state as in admission. The mortality in this group was 4.5%, and the risk of neurologic deficits was 2.3%. In long-term follow-up (median time 7.25 months), 90% of aneurysms were occluded, and in 5 % of the near-complete occlusions (visible neck remnant), the dome remnant rate was 5%. Recanalization of 17.4% of the previously occluded aneurysms was demonstrated. In the long-term follow-up, 1 hemorrhage occurred. For 25 aneurysms microsurgical treatment was used. 76% of patients were discharged without deterioration. Up to 25% deteriorated due to treatment. Morbidity was 4.8% and permanent morbidity was 4.8%. There was no hemorrhage in this group.

In the third study, we compare management recommendations for AComA UIAs, according to UIATS and PHASES, and compare them with each other and to real-life management. Among 129 aneurysms 46.5% were assessed for observation and 53.5% for treatment. According to PHASES, the majority of aneurysms 86% had low risk of hemorrhage and 14 % were high-risk aneurysms. The PHASES scores were significantly higher in the group qualified for treatment. In accordance with UIATS, UIA repair was recommended for 27% of patients and conservative management for 32% of patients, while the recommendation remained not definitive for 37% of individuals. PHASES scores in the group under observation ranged from 4 to 9, and no high-risk aneurysms (according to PHASES interpretation) were identified. In this group, UIATS recommended UIA repair for 11% of patients and conservative management for 51% of patients, while 38% of patients lacked a specific recommendation. PHASES scores in the group of patients who underwent treatment ranged from 4 to 15, with 26% of them having high-risk aneurysms. According to UIATS, UIA repair was recommended for 42% of patients and conservative management for 19% of patients, and recommendations were not definitive for 39%.

Conclusions:

1. Flow-diverting devices may offer a very high proportion of satisfactory radiological and clinical outcomes. However, due to the high rate of different types of complications, critical assessment of their use is essential.
2. Using diversified management of AComA UIAs, which include observation, microsurgery, and embolization, we have decreased the annual risk of SAH to 0.14% at the expense of 2.4% mortality and 1.6% permanent minor deficit rates in the treatment subgroup. The morbidity and mortality in AComA UIAs are compelling, but these refer to a high-risk group with potentially devastating consequences.
3. In two-thirds of cases, we showed a lack of concordance between PHASES and UIATS. Significant discordance in therapeutic suggestions underscores the predominant influence of center experience and individual assessments.

4. Wstęp

Niepęknięte tętniaki wewnątrzczaszkowe występują z częstością od 1,8% do 8,8% w zależności od źródła i przyjętych kryteriów diagnostycznych.[1] Z uwagi na powszechne użycie badań CT i MR rośnie wykrywalność niepękniętych tętniaków.

Podstawą wyboru optymalnego postępowania jest porównanie krótkoterminowego i długoterminowego ryzyka wystąpienia krwotoku oraz ryzyka związanego z interwencją – z mikrochirurgicznym zaklipsowaniem tętniaka lub z leczeniem wewnątrznaczyniowym.

Częstość wystąpienia krwotoku podpajęczynówkowego z tętniaka wynosi od 6 do 10 przypadków w populacji 100 000 osób rocznie. Krwotok z pękniętego tętniaka wiąże się z wysoką śmiertelnością przedszpitalną – na poziomie 26% oraz wewnątrzszpitalną – na poziomie 13%.[2] Poza krwotokiem powiększające się tętniaki mogą powodować objawy w wyniku ucisku na przylegające struktury nerwowe.

Leczenie tętniaków obejmuje metody mikrochirurgiczne i wewnątrznaczyniowe. Pacjenci z tętniakami zakwalifikowanymi do obserwacji wymagają regularnych badań kontrolnych pod kątem oceny powiększania się tętniaka. Zwiększona wykrywalność tętniaków i szybki rozwój nowych metod ich leczenia powodują, że do leczenia kwalifikowane są coraz mniejsze tętniaki oraz coraz starsi pacjenci.[3,4]

Powstały narzędzia w postaci skali do oceny ryzyka wystąpienia krwotoku lub służące do uzyskania rekomendacji dla postępowania.

Skala PHASES, szacująca pięcioletnie ryzyko krwotoku z tętniaka, powstała na podstawie analizy sześciu badań z oceną ryzyka krwotoku.[5] Skala rekomendacji UIATS jest modelem opracowanym na drodze konsensusu delhijskiego i jako rezultat analizy wielu czynników obejmuje trzy możliwe rekomendacje: obserwację, leczenie lub brak zdefiniowanej rekomendacji.[6] Z drugiej strony w wielu pracach oceniano użyteczność tych skal we wstecznym przewidywaniu krwotoków w podgrupie pękniętych tętniaków i wykazano, że znaczny odsetek pękniętych tętniaków zostałby oszacowany w tych skalach jako tętniaki o niskim ryzyku krwotoku.[7–10]

Podsumowując powyższe dane odnoszące się do niepękniętych tętniaków wewnątrzczaszkowych: potrzebne są badania, które oceniają strategie postępowania z tętniakami, wyniki leczenia mikrochirurgicznego i wewnątrz-naczyniowego tętniaków, jak również badania oceniające użyteczność skal, które powstały na potrzeby codziennej praktyki przy wyborze sposobu postępowania. Z tego powodu przeprowadzono cykl badań retrospektywnych. Ponieważ badania te nie stanowiły eksperymentów medycznych, zgoda komisji bioetycznej nie była wymagana. Wybrano dwie lokalizacje tętniaków wewnątrzczaszkowych: tętniaki kompleksu tętnicy łączącej przedniej i tętnicy szyjnej wewnętrznej w odcinku oftalmicznym. Tętniaki AComA wzięto pod uwagę ze względu na szczególną lokalizację oraz sąsiadujące perforatory, które zaopatrują funkcjonalnie istotne struktury. Tętniaki ICA C6 uwzględniono w celu oceny skuteczności i bezpieczeństwa stosowania stentów kierunkujących przepływ, które obecnie są dominującym sposobem leczenia tętniaków w tej lokalizacji.

5. Cele pracy

1. Ocena klinicznych i radiologicznych wyników leczenia niepękniętych tętniaków ICA C6 przy użyciu FDD połączona z analizą komplikacji leczenia.

2. Ocena wyników zróżnicowanego postępowania obejmującego obserwację, leczenie wewnątrznaczyniowe i mikrochirurgiczne w podgrupie tętniaków AComA połączona z analizą ryzyka krwotoku, wyników klinicznych i powikłań leczenia.

3. Retrospektywne porównanie rekomendacji uzyskanych według skal PHASES i UIATS oraz ich zestawienie z rzeczywistym postępowaniem dla podgrupy niepękniętych tętniaków AComA.

6. Kopie opublikowanych prac

6.1. Praca 1

1. Kunert P, **Wójtowicz K**, Żyłkowski J, et al. Flow-diverting devices in the treatment of unruptured ophthalmic segment aneurysms at a mean clinical follow-up of 5 years. Sci Rep. 2021;11(1):9206. doi:10.1038/s41598-021-87498-z.

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Flow-diverting devices in the treatment of unruptured ophthalmic segment aneurysms at a mean clinical follow-up of 5 years

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A shift toward the endovascular treatment of ophthalmic segment aneurysms is noticeable. However, it is not clear if the long-term treatment results improve with the development of endovascular methods. The aim of this study was to present the outcomes of the treatment of unruptured ophthalmic aneurysms using flow diverting devices (FDD) with or without coiling. This retrospective study included 52 patients with 65 UIAs treated in 2009–2016. The mean aneurysm size was 8.8 mm. Eight aneurysms were symptomatic. Therapeutic procedures included: 5 failed attempts, 55 first sessions with FDD deployment (bilateral procedures in 3) and 3 retreatment procedures. To cover 55 ICAs, 25 Silk, 26 Pipeline, 9 Fred and 1 Surpass FDD were used. FDD with coiling was applied in 19(29.2%), mainly for symptomatic and larger aneurysms. Mean radiological and clinical follow-up was 12 and 61 months, respectively. Postprocedural deterioration was noted in 3(5.8%) patients, but in long-term the modified Rankin Scale grades 0–2 were achieved in 98.1% of patients. One patient died from the treated aneurysm rupture (annual risk—0.07%). Raymond–Roy occlusion classification class I or II was achieved in 98.5% in the long term, with similar results in both groups. Complications occurred in 40.4% of patients and the most frequent were: imperfect FDD deployment (15%), failed attempt of FDD deployment (9.6%) and late FDD stenosis (9.6%). Flow-diverting devices, with additional coiling in selected cases, may offer a very high proportion of satisfactory outcomes. However, in our experience the high risk of complications remains.

The ophthalmic segment of internal carotid artery (ICA-C6), starts at the distal dural ring and ends just before the posterior communicating artery origin[1]. Aneurysms of ICA-C6 occur with a frequency of approximately 5% of all intracranial aneurysms[2]. Besides the subarachnoid haemorrhage, the clinical presentations include visual deficits[3]. Surgical clipping and different endovascular techniques like coil embolisation, flow diverting device (FDD) deployment and combination of coiling with stenting are current options for the treatment of ICA-C6 aneurysms[4–6]. Permanent morbidity ranges from 0.8 to 38%[4,6–11], and the new visual deficits occur more often after clipping than endovascular treatment[5,11–14]. Flow diverting stents are promising devices for a higher percentage of fully occluded aneurysms as compared to coil embolisation[15].

The aim of this study was to present the clinical and radiological outcomes of endovascular treatment of unruptured ICA-C6 aneurysms using FDDs with or without coiling. Different factors were tested as potential predictors of the most favourable outcome.

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	All aneurysms	Aneurysms treated with FDD (N°46)	Aneurysms treated with FDD + C (N°19)	*p*
Aneurysm				
Mean size (SD)	8.8 mm (5.4)	6.8 mm (3.0)	13.5 mm (7.0)	0.001
Size range	2.2–28 mm	2.2–18 mm	3.3–28 mm	
Aneurysm size ≤ 7 mm	32 (49.2%)	28 (60.9%)	4 (21.1%)	< 0.001
Aneurysm size 7–12 mm	22 (33.8%)	17 (37.0%)	5 (26.3%)	
Aneurysm size 13–24	9 (13.8%)	1 (2.2%)	8 (42.1%)	
Aneurysm size ≥ 25 mm	2 (3.1%)	0	2 (10.5%)	
Neck				
Mean size (SD)	4.7 mm (1.9)	4.3 mm (1.6)	5.9 mm (2.0)	0.004
Size range	1.4–10 mm	1.4–8.8 mm	2.9–10 mm	
Dome-to-neck ratio				
Mean (SD)	1.8 (0.7)	1.7 (0.7)	2.2 (0.7)	0.009
Range	0.7–3.8	0.7–4.1	1.0–3.5	
Symptomatic	8 (12.3%)	3 (6.5%)	5 (26.3%)	0.082

Table 1. Aneurysm characteristics in whole group and subgroups, according to the treatment technique. FDD, flow diverting device alone; FDD+C, flow diverting device with coiling; SD,–standard deviation.

Material and methods

Patients. This retrospective study included 52 patients with 65 unruptured aneurysms (UIA) located on ICA-C6 treated in 2009–2016. The mean patient age was 52.5 years (range: 26–76 years old). Forty-five (86.5%) patients were female. Four (7.7%) patients had a history of subarachnoid haemorrhage (SAH) from another aneurysm. Twenty-seven (51.9%) patients were smokers, 26 (50%) patients had arterial hypertension and 7 (13.5%) had a positive family history of intracranial aneurysms.

All study participants underwent regular, neurosurgical management and treatment. Afterwards, anonymized patient data was retrospectively analyzed by physicians who have access to patients' medical records. The Bioethics Committee of the Medical University of Warsaw (local institutional review board) approved this study and waived the need for informed consent. Moreover, the study has been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki.

The mean radiological follow-up was 12 months (range: 1 to 24 months), and the mean clinical follow-up was 61 months (range: 3 to 111 months). The follow-up data were available for all patients.

Aneurysms. Of 65 aneurysms, 39 (60%) were ophthalmic, 24 (36.9%) superior hypophyseal artery and 2 (3.1%) were dorsal ICA (blister-like) aneurysms. Eleven (21.2%) patients had more than one treated ICA-C6 aneurysm: unilaterally in 8 and bilaterally in 3 cases. The measurements of dome and neck in 2 blister-like aneurysms were feasible therefore they were analysed together with saccular aneurysms. According to the convention[16], 26 (40%) aneurysm necks were small (≤ 4 mm) and 39 (60%) were large (> 4 mm); dome-to-neck ratio was ≤ 2 in 44 (67.7%) aneurysms and > 2 in 21 (32.3%) aneurysms (Table 1).

Symptoms. Eight (12.3%) aneurysms were symptomatic, with multiple symptoms in 4. Visual field deficit was present in 6 patients, acuity decrease in 4, optic nerve atrophy in 1 and oculomotor nerve palsy in 1. The causes of neuroimaging in the remaining patients were headache (N°11; 21.2%), dizziness (N°7; 13.5%), SAH from another aneurysm (N°4; 7.7%) or non-specific complaints (N°22; 42.3%).

Procedures. 52 patients underwent 63 therapeutic procedures for 65 UIAs. Therapeutic procedures included: 5 failed attempts, 55 first sessions with FDD deployment (including 3 patients with bilateral procedures) and 3 retreatment procedures. In total, there were 182 invasive procedures, including 119 DSAs.

Twenty-five Silk, 26 Pipeline, 9 Fred and 1 Surpass FDD were used to cover 55 ICAs in 52 patients. FDD with additional coiling (FDD + C) was performed in 19 (29.2%) cases.

Methods. Data on demographics, medical history, symptoms, aneurysms, treatment, complications and results were recorded from patient files. The follow up data were collected based on files from control hospital stays, ambulatory visits and telephone conversations. Indications for and its technique treatment were discussed by the whole team including neurosurgeons and interventional radiologists. All procedures were performed by 2 interventional radiologists (MJ, JŻ). The clinical and radiological outcomes were assessed by neurosurgeons (KW, PK, JW, KL, AM).

Follow-up Dyna-CT was performed 3 months after the procedure in the last 28 patients of the series. Routinely, the patients underwent the follow-up DSA 6 and 12 months after the procedure. Further imaging was scheduled individually only for patients with incompletely occluded aneurysms. The Raymond–Roy (RROC) and O'Kelly-Marotta (OKM) grading scales were used for aneurysm occlusion assessment[17,18]. The clinical status was established with the use of the modified Rankin Scale (mRS). Formal ophthalmologic evaluation was available

mRS	On admission	On postprocedural day 1	At discharge	In the most recent follow-up	
Clinical outcomes according to the modified Rankin Scale (mRS)					
Grade 0	43 (82.7%)	41 (78.8%)	42 (80.8%)	41 (78.8%)	Satisfactory outcome-51 (98.1%)
Grade 1	8 (15.5%)	8 (15.4%)	8 (15.4%)	9 (17.3%)	
Grade 2	1 (1.9%)	1 (1.9%)	1 (1.9%)	1 (1.9%)	
Grade 3	0	1 (1.9%)	0 (%)	0	Unsatisfactory outcome-1 (1.9%)
Grade 4	0	1 (1.9%)	1 (1.9%)	0	
Grade 5	0	0	0	0	
Grade 6	0	0	0	1 (1.9%)	
	RROC Class I	RROC Class II	RROC Class III		
Radiological outcomes according to the Raymond–Roy occlusion classification					
Immediate post-procedural result					
FDD alone	3 (6.5%)	4 (8.7%)	39 (84.8%)	$p=0.04$	
FDD+C	5 (26.3%)	2 (10.5%)	12 (63.2%)		
All aneurysms	8 (12.3%)	6 (9.2%)	51 (78.5%)		
Results at 6 months follow-up DSA					
FDD alone	35 (76.1%)	4 (8.7%)	7 (15.2%)	p-NS	
FDD+C	12 (66.7%)	2 (11.1%)	4 (22.2%)		
All aneurysms	47 (73.4%)	6 (9.4%)	11 (17.2%)		
Long-term results (the last follow-up DSA)*					
FDD alone	44 (95.7%)	2 (4.3%)	0	p-NS	
FDD+C	18 (94.7%)	0	1 (5.3%)**		
All aneurysms	62 (95.4%)	2 (3.1%)	1 (1.5)**		

Table 2. Clinical and radiological outcomes. NS, not significant.*Include also results of retreatment. **In patient who died, the last DSA performed after SAH revealed a critical distal end stent stenosis and aneurysm remnant (RROC class III, OKM B).

for all patients with symptomatic UIAs. The clinical outcomes were calculated per patient, radiological outcomes per aneurysm, and complication risk per patient, per aneurysm and per procedure.

Statistical methods. Assessment of the differences between groups was done using t-test for numerical and chi-square or Fisher exact test for categorical data. Potential determinants of the outcome were assessed using one and multivariate logistical regression models, using R 3.5.1 statistical software (R: A Language and Environment for Statistical Computing, R Core Team, Vienna, Austria, https://www.R-project.org).

Ethics approval. All study participants underwent regular, neurosurgical management and treatment. Afterwards, anonymized patient data was retrospectively analyzed by physicians who have access to their patients' medical records. For that reason, a signed consent from each patient, or legal representative, was not deemed necessary (Declaration of Helsinki, 25). The Bioethics Committee of the Medical University of Warsaw (local institutional review board) approved this study and waived the need for informed consent.

Results

Clinical outcomes. On admission, 8 (15.5%) patients presented with vision symptoms (mRS grade 1) and 1 (1.9%) with cognitive impairment (mRS grade 2) after SAH in the past (Table 2).

On the postprocedural day one, deterioration was noted in 3 (5.8%) patients including minor deficit in 2 and major in 1. One patient had prolonged cognitive impairment due to thromboembolic complications (mRS grade 4). At the discharge from hospital 51 (98.1%) patients were stable with their mRS scores as before the treatment.

In follow-up, 49 patients were stable and 1 patient with postprocedural cognitive impairment significantly improved. One patient died from the treated aneurysm rupture. One patient deteriorated for a couple of months to mRS grade 3 because of thromboembolic complications at the 6-month follow-up DSA and she eventually improved to mRS grade 1. In the most recent follow-up, 98.1% of patients achieved satisfactory clinical outcome (mRS grades 0–2).

The overall post-treatment risk of aneurysm rupture was 0.33% (1/304 aneurysm-years) during a mean follow-up of 61 months. The annual risk of aneurysm rupture after treatment reached 0.07%. The overall permanent morbidity (mRS> 2) and mortality rate was 1.9%. However, if all minor (also visual) and transient post-procedure deficits were included, then the combined morbidity and mortality was 17.3% (9/52).

Visual symptoms were stable in follow-up in 4 (50%) patients. One (12.5%) patient had transient and two (25%) permanent deterioration after treatment. The vision improved only in one (12.5%) patient. Patients with asymptomatic UIAs had no visual complications immediately after treatment.

Radiological outcomes. Immediate result of the first procedure. The complete occlusion was demonstrated in only 8 (12.3%) aneurysms at the end of the procedure (Table 2). However, the immediate postprocedural results were significantly better when the additional coiling was applied (RROC class I+II; 36.8% for FDD+C vs. 15.2% for FDD; $p=0.04$).

The patient, who died 3 months post-procedure due to SAH from the giant (28 mm), symptomatic aneurysm, underwent FDD+C (Silk and 4 coils) procedure with immediate RROC class III. The last DSA was performed after SAH and revealed critical distal end stent stenosis and aneurysm remnant (RROC class III, OKM B).

Six-month follow-up DSA. The complete aneurysm occlusion was demonstrated in 73.4% (Table 2). The results at the 6-month follow-up were similar in groups with and without coiling (RROC class I+II; 77.8% for FDD+C vs. 84.8% for FDD; *p*—not significant (NS)). At this stage 3 (5.6%) aneurysms with angiographic filling were qualified for retreatment. One stent thrombosis with moderate hemiparesis (mRS grade 3) occurred at the time of follow-up DSA procedure.

Retreatment. Retreatment was needed for 3 (4.6%) residual aneurysms initially treated with FDD in 1 (2.2%), and FDD+C in 2 (10.5%, p-NS). In long-term follow-up all these aneurysms were totally occluded and the patients maintained a good neurological condition (OKM D, mRS 0).

Recanalisation of 1 (1.5%) aneurysm from OKM D to OKM B2 was demonstrated in DynaCT at the 3-month follow-up after treatment of 8 mm aneurysm with FDD+C (Silk and HydroSoft coils). Discontinuation of Clopidogrel administration was recommended and the 6-month follow-up DSA revealed the total aneurysm occlusion without additional treatment.

Long-term radiological outcome. According to the OKM Scale, including the results of retreatment procedures, the most recent DSA showed no aneurysm filling (OKM D) in 62 (95.4%), entry remnant with no stasis (OKM C1) in 2 (3.1%) and subtotal filling with significant stasis (OKM B3) in 1 (1.5%) aneurysm which ruptured. Two aneurysms with entry remnant (OKM C1) were small, with a dome-to-neck ratio < 2, located close to the origin of the ophthalmic artery and were treated with FDD alone. The RROC class I or II was achieved in 98.5% of aneurysms, with insignificant difference between FDD+C and FDD groups (Table 2).

In total, the new FDD thrombosis or stenosis occurred in 5 (9.1%) out of 55 targeted ICAs in follow-up and was symptomatic in 3 (60%) of them. The last accessible follow-up angiograms demonstrated stent occlusion in 2 (3.8%), stenosis in 2 (3.8%) and normalisation of blood flow in 1 patient. The new failures occurred in 4 (16%) of the Silk FDDs and in 1 (4.5%) of the Pipeline FDDs. None of Fred and Surpass FDDs occluded or narrowed.

Ophthalmic artery patency. The follow-up DSA demonstrated the ophthalmic artery occlusion in 6 (10.9%) out of 55 ICAs covered with FDDs. There was no visual deterioration in these patients.

Complications. During 182 invasive procedures, including all DSAs and treatment sessions, 18 (34.6%) patients experienced 29 adverse events. The adverse events included: 3 complications following DSA, 5 failed treatment attempts, 19 procedural complications of completed treatment sessions and 2 access site complications (Table 3).

DSA complications. Three adverse events of diagnostic or follow-up DSA included: asymptomatic FDD thrombosis, asymptomatic cerebral vasospasm and symptomatic ICA dissection.

Procedural complications. Nineteen procedural complications in 14 (26.9%) patients occurred during treatment procedures and included: imperfect FDD expansion (8), incorrect migration of FDD distal end (3), FDD thrombosis (3), ICA dissection (2) and vasospasm (3). The procedural complications occurred in 18.2% (6/33) of patients treated with FDD alone and in 42.1% (8/19) treated with FDD+C ($p=0.1$; the Fisher exact test).

The imperfect FDD expansion (Silk in 7 and Pipeline in 1) was treated with balloon angioplasty. The incorrect FDD (Silk in 1 and Pipeline in 2) migration demanded the device replacement in 1 and implantation of additional FDD in 1. The access site complications occurred in 2 cases and included femoral artery pseudoaneurysm (1) and thrombosis (1). Revision vascular surgery was needed in the latter case.

Additionally, in follow-up a new FDD stenosis developed spontaneously in 4 cases (Silk in 3 and Surpass in 1), which led to SAH in one. To sum up, the early or late complications occurred in 21 (40.4%) patients. Neurological sequelae of all complications were detailed in the chapter "Clinical outcomes" and are summarised in Table 3.

Success rates. Immediate technical success was defined as an accurate deployment of FDD, as it was planned, during the first procedure with no procedural complications. The immediate technical success rate was 70.7% (37/52) per patient and 70.8% (46/65) per aneurysm. The Immediate technical success rate was 76.1% (35/46) in FDD group and 57.9% (11/19) in FDD+C group (p-NS, the Fisher Exact Test).

Six months technical success was defined as an aneurysm occlusion greater than 90% (RROC class I–II) and normal blood flow through the ICA (no stenosis/dissection/occlusion) at the 6-month follow-up DSA. The 6-month technical success rate was 63.6% (35/52) per patient, 70.8% (46/65) per aneurysm, 71.7% (33/46) in the FDD group and 68.4% (13/19) in the FDD+C group (p-NS for FDD vs. FDD+C; the Fisher Exact Test).

Treatment success was defined as a conjunction of the following conditions: an aneurysm occlusion greater than 90% (RROC class I–II), no SAH from targeted aneurysm, mRS grade: 0–2 and no visual deterioration in the most recent follow-up. The treatment success rate was 94.2% (49/52) per patient, 95.4% (62/65) per aneurysm,

	Number	Rate per invasive procedure (DSAs + treatment procedures) (N° 182)	Rate per treatment procedure (N° 63)	Rate per aneurysm (N° 65)	Rate per patient (N° 52)
Failed attempts of FDD deployment	5		7.9% (5/63)	7.7% (5/65)	9.6% (5/52)
Procedural complications	22*	10.4% (19/182)	25.4% (16/63)	30.8% (20/65)	30.8% (16/52)
Intraprocedural ICA dissection	3	1.6% (3/182)	3.2% (2/63)	4.6% (3/65)	5.8% (3/52)
Intraprocedural FDD thrombosis	4	2.2% (4/182)	4.8% (3/63)	4.6% (4/65)	7.7% (4/52)
Imperfect FDD expansion	8		12.7% (8/63)	12.3% (8/65)	15.4% (8/52)
Incorrect FDD distal end migration	3		4.8% (3/63)	4.6% (3/65)	5.7% (3/52)
Cerebral vasospasm	4	2.2% (4/182)	4.8% (3/63)	6.2% (4/65)	7.7% (4/52)
Aneurysms rupture	0				
Intracranial vessel perforation	0				
Intraparenchymal haemorrhage	0				
Access site complications	2	1.1% (2/182)	3.2% (2/63)	3.1% (2/65)	3.8% (2/52)
Late complications					
New FDD thrombosis/stenosis	5***	–	–	7.7%	9.6%
SAH from targeted aneurysm	1	–	–	1.5%	1.9%
Intraparenchymal haemorrhage	0	–	–	–	–
Clinical sequelae (w/o visual complications)					
Transient neurological deficit	2	1.1%	3.2%	3.1%	3.8%
Permanent morbidity	1	0.5%	1.6%	1.5%	1.9%
Mortality	1	–	–	1.5%	1.9%
Overall morbidity and mortality	2	–	–	3.1%	3.8%
Visual complications					
Cranial nerve III palsy	0	–	–	–	–
Permanent visual impairment	2	1.1%	3.2%	3.1%	3.8%
Visual loss	0	–	–	–	–

Table 3. Summary of complications. *Total number of adverse events of all DSAs and treatment procedures. **55 ICAs were covered with FDDs, i.e. bilaterally in 3 cases. ***One late FDD thrombosis, that occurred during the follow-up DSA procedure, was also incorporated in "procedural complications".

97.8% (45/46) in the FDD group and 89.5% (17/19) in the FDD + C group (p-NS for FDD vs. FDD + C, the Fisher Exact Test). However, the most desirable scenario (uneventful treatment procedure, no failed attempts, no retreatment procedures, RROC class I at 6 months DSA, uneventful clinical periprocedural and long-term course) materialised in 47.7% (30/65) of cases only. Potential predictors of the most favourable outcome are presented in Table 4.

Discussion

A shift toward the endovascular treatment of ICA-C6 aneurysms is noticeable[6,9–11]. Endovascular treatment shows some benefits over surgical clipping like a lower risk of visual and other neurologic complications[11,13,14]. However, more than one third of ICA-C6 UIAs are not completely occluded after traditional coiling with or without stenting[8]. That is why FDDs are now increasingly popular, but their effectiveness has to be proven in long-term evaluations. The risk of neurological deterioration immediately after treatment, beyond the visual symptoms, was 6% in our series. A satisfactory clinical outcome was achieved in 98.1% of patients. Permanent morbidity and mortality rates in similar series were: 0–4.5% and 0–1.4%, respectively[7,15,19,20]. The good general outcomes of our series are notably burdened by one catastrophic SAH from a treated aneurysm. Yet, our case of SAH reflects rather a problem of effectiveness of endovascular treatment in giant aneurysms. In this case the additional coiling was used, to promote the intra-aneurysmal thrombosis. However, only RROC class III was achieved. Probably, a denser coil packing should be attempted for such unstable aneurysms, for a more direct protection.

Visual improvement in symptomatic ICA-C6 aneurysms is also a goal of treatment. Indirect decompression with clinical improvement is possible after embolisation, because of a reduction in aneurysm pulsation[9,11,21]. Optimistic literature data indicates that even two thirds of patients may improve their vision after embolisation and three quarters after surgical clipping[4,12,13]. However, many reports do not include objective ophthalmological evaluation. On the contrary, more critical observations demonstrate that vision improvement is rare and at least one third of patients have posttreatment visual dysfunction[22,23]. Our experience on 8 symptomatic UIAs also showed a 25% risk of permanent vision deterioration and a little chance for improvement. Not only our experience indicates that visual symptoms may also appear in delayed period[24]. Nevertheless, the permanent visual impairment after treatment of asymptomatic UIA is unlikely to occur, based on our and other series[13].

Variable	Total N° (%) or mean ± SD	Most desirable scenario /−/ N° (%) or mean ± SD	Most desirable scenario/+/ N° (%) or mean ± SD
Univariate analysis			
Age*			
(y.o.)	52.3 ± 11.7	55.2 ± 11.0	49.0 ± 11.9
Sex			
F	57 (87.7%)	31 (88.6%)	26 (86.7%)
M	8 (12.3%)	4 (11.4%)	4 (13.3%)
Number of treated ICA-C6 UIAs			
Single	41 (63.1%)	21 (60%)	20 (66.7%)
Multiple	24 (36.9%)	14 (40%)	10 (33.3%)
Previous SAH from other aneurysm			
Not	61 (93.8%)	34 (97.1%)	27 (90.0%)
Yes	4 (6.2%)	1 (2.9%)	3 (10.0%)
Side			
Left	36 (55.4%)	19 (54.3%)	17 (56.7%)
Right	29 (44.6%)	16 (45.7%)	13 (43.3%)
Type/location			
ICA-blister like	2 (3.1%)	2 (5.7%)	0 (0.0%)
ICA C6a	39 (60%)	20 (57.1%)	19 (63.3%)
ICA C6b	24 (36.9%)	13 (37.1%)	11 (36.7%)
Aneurysm size			
<7 mm	32 (49.2%)	17 (48.6%)	15 (50.0%)
>7 mm	33 (50.8%)	18 (51.4%)	15 (50.0%)
Aneurysm size (mm)	8.8 ± 5.4	9.3 ± 6.0	8.3 ± 4.8
Neck size (mm)	4.7 ± 1.9	5.1 ± 1.9	4.3 ± 1.8
Dome-to-neck ratio	1.8 ± 0.7	1.8 ± 0.8	1.9 ± 0.7
Symptomatic UIA			
Not	57 (87.7%)	28 (80.0%)	29 (96.7%)
Yes	8 (12.3%)	7 (20.0%)	1 (3.3%)
Smoking			
Not	34 (52.3%)	16 (45.7%)	18 (60.0%)
Yes	31 (47.7%)	19 (54.3%)	12 (40.0%)
Diabetes mellitus			
Not	60 (92.3%)	31 (88.6%)	29 (96.7%)
Yes	5 (7.7%)	4 (11.4%)	1 (3.3%)
Arterial hypertension			
Not	33 (50.8%)	16 (45.7%)	17 (56.7%)
Yes	32 (49.2%)	19 (54.3%)	13 (43.3%)
Type of FDD*			
FRED	11 (16.9%)	2 (5.7%)	9 (30.0%)
PIPELINE	27 (41.5%)	12 (34.3%)	15 (50.0%)
SILK	26 (40%)	21 (60.0%)	5 (16.7%)
SURPASS	1 (1.5%)	0 (0.0%)	1 (3.3%)
Technique of treatment*			
FDD and coiling	19 (29.2%)	14 (40.0%)	5 (16.7%)
FDD alone	46 (70.8%)	21 (60.0%)	25 (83.3%)
Number of FDDs			
1	59 (90.8%)	31 (88.6%)	28 (93.3%)
>1	6 (9.2%)	4 (11.4%)	2 (6.7%)
Variable	**Crude OR (95% CI)**	**Adj. OR (95% CI)**	
Multivariate logistic regression (without treatment-related factors)			
Age (continuous variable)	0.95 (0.91,1)	0.94 (0.89,0.99)	
Dome-to-neck ratio (continuous variable)	1.38 (0.71,2.69)	3.39 (1.23,9.39)	
Symptomatic aneurysm (Yes vs. Not)	0.14 (0.02,1.19)	0.01 (0,0.52)	

Table 4. Uni- and multivariate analysis of potential predictors of the most desirable scenario (RROC class I at 6 months with uneventful treatment and follow-up course). *Age (continuous variable), OR (95% CI): 0.95 (0.91,1); $p=0.038$; Technique of treatment, OR (95% CI): 3.33 (1.03,10.79), $p=0.045$; SILK FDD, OR (95% CI): 0.05 (0.01, 0.33), $p=0.002$, and p-not significant for the rest of tested factors.

The immediate postprocedural complete obliteration rate was 4 times higher for aneurysms treated with FDD and coiling, but the mid- and long-term results were similar in the FDD and FDD + C groups. It indicates that FDDs alone are effective for most ICA-C6 UIAs and the additional coiling may be reasonable in selected cases.

The complete obliteration in 95.4% of aneurysms was finally achieved, as compared to 74.6–89.1% in other series[7,15,19,20,25]. The use of additional coiling in 29% of aneurysms could be the reason for better results in our series. Selection of aneurysms for additional coiling depended mainly upon the size and symptoms. Symptomatic aneurysms (5/8) and those larger than 12 mm (10/11) were qualified mainly for FDD+ C.

The retreatment rate was 4.6% in our series and it ranges from 9 to 30% after coil embolisation and from 0.9 to 6.8% after flow-diversion in other series[4,8,19,20,25]. The revision "stent-in-stent" procedures were safe and fully effective in our patients.

Nowadays, we routinely use Dyna-CT imaging 3 months after FDD deployment. In our experience, the worst delayed complication is in-stent stenosis with persistent inflow to the aneurysm and the main purpose of doing Dyna-CT is to exclude this. The new FDD thrombosis or stenosis occurred in almost 10% of patients and all of them were diagnosed during the first half a year after treatment. Therefore, the close surveillance in this period is needed preferably with less invasive Dyna-CT, as one of adverse events was iatrogenic due to DSA procedure.

Occlusion of the ophthalmic artery was demonstrated in 11%, with no clinical sequalae. In the other series this proportion ranged from 3.6 to 21.6% with questionable clinical significance[3,19,23,26–28].

About 40% of patients experienced complications that, not rarely, were multiple. The most frequent technical complication was imperfect FDD deployment (15% of patients), followed by failed attempts of FDD deployment and late FDD stenosis. Therefore, patients should be informed about the cumulative risk of all invasive procedures and the potentially delayed adverse events.

The procedural complications occurred in 42% of patients in the FDD + C group—more than twice as much as in the FDD group. Also, the immediate technical success rate was 18% lower in the FDD+ C group than in the FDD group. Despite being insignificant, the differences should be pointed out for critical assessment whether the more complex treatment for more complex aneurysms is reasonable.

The treatment success was as high as 95% per aneurysm within a mean follow-up of 5 years. However, the most desirable scenario succeeded in less than half of aneurysms. This indicates that aggressive treatment brings very good final results but is burdened by considerable complication risks.

The multivariate analysis of demographic, clinical and morphometric factors demonstrated that younger age, higher dome-to-neck ratio and asymptomatic aneurysms favour the best outcomes.

Limitations of the study. Four different kinds of FDD had been used according to the needs and local availability. Furthermore, the UIAs treated with FDD alone significantly differed from those treated with FDD and coiling. Therefore our retrospective analysis cannot serve as a comparison of the different devices and techniques. Whether FDD with coiling is more effective than FDDs alone in complex aneurysms has to be proven in prospective trials.

Conclusions

Flow-diverting devices, with the use of additional coiling in selected cases, may offer a very high proportion of satisfactory radiological and clinical outcomes. However, in our experience the high risk of complications of different type and time impose the need for critical assessment and for further improvement of technical capabilities of implanted devices.

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Author contributions

P.K. study concepts and design, interpretation and analysis of data, writing of the manuscript, K.W. data collection, interpretation and analysis of data, writing of the manuscript, J.Ż. data collection, interpretation and analysis of data, writing of the manuscript, M.J. data collection, interpretation and analysis of data, D.R. statistical analysis, J.W. data collection, interpretation and analysis of data K.L. data collection, interpretation and analysis of data A.M. critical revision and final approval of the manuscript.

Competing interests

The authors declare no competing interests.

Additional information

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6.2. Praca 2

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Unruptured Anterior Communicating Artery Aneurysms: Management Strategy and Results of a Single-Center Experience

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Abstract: Although anterior communicating artery (AComA) unruptured intracranial aneurysms (UIAs) comprise one of the largest aneurysm subgroups, their complex adjacent neurovasculature and increased risk of rupture impede optimal management. In the present study, we analyzed the results of our diverse strategy in AComA UIAs with the additional goal of assessing the risk of treatment and the incidence of hemorrhage. We analyzed 131 patients, of which each was assessed by a multidisciplinary neurovascular team and assigned to observation (45.8%), endovascular treatment (34.4%) or microsurgery (19.8%). Median aneurysm sizes were 3, 7.2 and 7.75 mm, respectively. In the observation group, four (7.1%) aneurysms (initially <5 mm) grew over a median time of 63.5 months and were treated endovascularly. We found that fewer patients in the observation group were smokers ($p = 0.021$). The aneurysm size ratio was different between the combined treatment versus the observation group ($p < 0.0001$). Noteworthily, there were no hemorrhages in the observational group. Mortality for all patients with available follow-up was 2.4% (3/124) and permanent morbidity was 1.6% (2/124) over a mean follow-up of 64.2 months. These compelling rates refer to a high-risk group with potentially devastating consequences in which we have decreased the annual risk of hemorrhage to 0.14%.

Keywords: unruptured intracranial aneurysms; microsurgery; endovascular; observation; management; anterior communicating artery; morbidity; mortality

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1. Introduction

The prevalence of unruptured intracranial aneurysms (UIAs) is estimated at 3.2% [1]. The anterior communicating artery (AComA) region stands out from other anatomical locations due to its congestion of functionally important structures, namely, numerous perforators, and relatively frequent prevalence of AComA UIAs. Additionally, AComA UIAs may exhibit twice the risk of rupture than other UIAs with an annual risk of rupture as high as 2.2% [2,3].

Even though AComA aneurysms comprise the biggest subgroup of all UIAs, their optimal management remains unclear. As with any other UIA, each patient needs to be qualified for observation or treatment. Endovascular techniques and microsurgery are standard methods of treatment, though the choice of which of them for patients qualified for treatment is often subjective.

To overcome this lack of unequivocal management guidelines, numerous scales and algorithms have been designed to facilitate the decision-making process [4–6]. In the present study, we analyze the results of our diverse management strategy in patients with AComA UIAs. We additionally set out to assess the risk of treatment including complications, the immediate and long-term outcomes of the endovascular treatment as well as open surgery.

Moreover, we endeavored to measure the incidence of aneurysmal hemorrhage in each of three management option groups.

2. Materials and Methods

This study was designed as a retrospective, single-center, consecutive case series, undertaken in an academic setting from 2011 to 2021. For each patient, the multidisciplinary team—comprising neurological surgeons and neurointerventional radiologists—qualified patients for observation or treatment. Our management strategy changed over time. At the beginning, it was based on the algorithm published by Chalouhi et al. [7]. Over time, we gradually remodeled the assessment of the risk of hemorrhage according to the PHASES and integrated additional tools as well as the UIATS recommendations [4,5]. When needed, the multidisciplinary team chose the treatment modality. In general, endovascular treatment was the preferred modality for patients qualified for treatment, unless the aneurysm configuration made it particularly hazardous, in which case microsurgery was chosen.

We analyzed our long-term clinical follow-up for all groups. In the observational and endovascular groups, we analyzed radiological outcomes, whereas in the endovascular and microsurgical groups, we analyzed clinical outcomes immediately and at discharge. Clinical outcomes were assessed with the modified Rankin scale (mRS). Good outcomes were defined as an mRS score of 0 to 2, and poor outcomes were defined as an mRS score greater than 2. Neurological deficits were divided into minor (mRS 1 to 2) and major (mRS greater than 2). Deterioration was defined as an increase of at least 1 point in the mRS score. Follow-up information was obtained during routine clinic visits or telephone interviews.

2.1. Follow-Up Algorithm

Patients in the observational group were monitored as follows: outpatient clinic visits with a computed tomography angiography (CTA) or magnetic resonance angiography (MRA) at six months and then once a year thereafter.

In the endovascular group, we routinely perform a posttreatment digital subtraction angiography (DSA) approximately 6 months after the endovascular procedure, and in case of a satisfactory result, this is the last radiological study performed. Subsequent DSAs are performed only when necessary (i.e., incomplete occlusion in the first posttreatment DSA, visible remnant, etc.). We use the Raymond–Roy (RROC) grading scale to assess aneurysm occlusion [8]. As a rule in our institution, we waive routine postoperative vascular imaging (DSA, CTA, and MRA) after microsurgery. From 2018, we started routinely using intraoperative indocyanine green videoangiography to confirm the patency of the arteries and closure of the aneurysm. Prior to that, we performed early postoperative CTA in uncertain cases.

2.2. Statistical Analyses

We performed the Shapiro–Wilk and Levene's tests to examine assumptions of data normality and the equality of variances, respectively. We examined the associations between qualitative variables with the chi-squared or Fisher's exact tests. Differences between two groups were evaluated with the Mann–Whitney U or independent *t*-tests, depending on the assumptions met. Differences between more than two groups were evaluated with the Kruskal–Wallis H test or one-way ANOVA, depending on the assumptions met. Post hoc comparisons were made using the Dunn test, and values were adjusted for multiple comparisons. All analyses were performed using R [9], and violin graphs were created with the ggstatsplot library [10]. Effect size (ε) and confidence interval [−95%; 95%] from the ggstatsplot library are reported for the Kruskal–Wallis test result. All analyses were performed with a significance level of $\alpha = 0.05$.

3. Results

During the study period 131 patients were diagnosed with 131 UIAs AComA. Initially, 60 cases (45.8%) were classified to the observation group and 71 cases (54.2%) to the treatment group, of which, 45 cases (63.4%) were qualified to endovascular and 26 cases

(36.6%) to microsurgical treatment (Table 1 and Figure 1). After crossovers, we analyzed 64 patients in the observational group, 44 patients in the endovascular treatment group and 25 patients in the microsurgery group. These numbers exceed the total number of patients diagnosed with UIAs AComA. The reason for that is that patients initially observed—until diagnosed with aneurysmal growth—were included in both the observation group (for the whole observation period) and the endovascular group (after qualification for treatment). The demographics and aneurysmal risk factors for each analyzed group are presented in Table 2.

Table 1. Demographics and aneurysmal characteristics of groups of patients as initially assigned. Abbreviations: IA—intracranial aneurysm, SAH—subarachnoid hemorrhage.

Data	Observation Group No. (%)	Endovascular Group No. (%)	Microsurgical Group No. (%)	p
Initial assignment	60 (45.8%)	45 (34.4%)	26 (19.8%)	
Sex				
male	23 (38.3%)	20 (44.44%)	10 (38.46%)	$p = 0.8$
female	37 (61.7%)	25 (55.56%)	16 (61.54%)	
Age, years				$p = 0.1$
median	65	62	57.5	
patients under 40 years old	5 (8.3%)	4 (8.8%)	3 (11.5%)	$p = 0.9$
Family history of SAH or IAs	5 (8.3%)	5 (11.1%)	4 (15.4%)	$p = 0.8$
Previous SAH from another aneurysm	5 (8.3%)	1 (2.2%)	1 (3.8%)	$p = 0.42$
Hypertension	38 (63.3%)	36 (80%)	23 (88.5%)	$p = 0.06$
Smoking	17 (28.3%)	20 (44.4%)	15 (57.7%)	$p = 0.02$
Initial medical condition (mRS)				
0	56 (93.3%)	43 (95.6%)	23 (92%)	
1	2 (3.3%)	1 (2.2%)	1 (4%)	
2	0	0	1 (4%)	
3	1 (1.7%)	1 (2.2%)	0	
4	1 (1.7%)	0	0	
5	0	0	0	
Aneurysm size, mm				
median	3	7.2	7.75	$p < 0.001$
range	1.4–9	2.7–18.9	3.5–25	
Aneurysm size groups				
<5 mm	49 (81.7%)	6 (13.3%)	3 (11.5%)	
5–7 mm	8 (13.3%)	15 (33.3%)	9 (34.6%)	
>7–12 mm	3 (5%)	20 (44.4%)	9 (34.6%)	
>12–25 mm	0	4 (8.9%)	3 (11.5%)	
>25 mm	0	0	2 (7.7%)	
Aspect ratio > 1.6	10 (16.7%)	27 (60%)	11 (42.3%)	$p < 0.0001$
Size ratio > 3	5 (8.3%)	24 (53.3%)	18 (69.2%)	$p < 0.0001$
Multilobulated	5 (8.3%)	17 (37.8%)	1 (3.8%)	$p < 0.001$
Multiple	22 (36.7%)	19 (42.2%)	10 (38.5%)	$p < 0.9$
Symptomatic aneurysms	0	0	2 (8%): 1 (4%) visual symptom and 1 (4%) seizure	$p < 0.04$

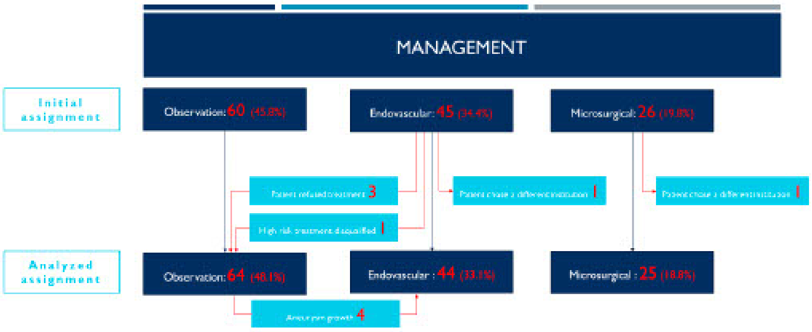

Figure 1. Management of patients with unruptured anterior communicating artery aneurysms as they were initially assigned and then analyzed in our study.

Table 2. Demographics and aneurysmal characteristics of analyzed groups of patients.

Data	Observation Group No. (%)	Endovascular Group No. (%)	Microsurgical Group No. (%)	p
Analyzed assignment *	64 (48.1%)	44 (33.1%)	25 (18.8%)	
Sex				
male	24 (37.5%)	19 (43.2%)	10 (40%)	$p = 0.839$
female	40 (62.5%)	25 (56.8%)	15 (60%)	
Age, years				
median	65.5	62	56	$p = 0.072$
patients under 40 years old	5 (7.8%)	4 (9%)	3 (12%)	
Family history of SAH or IAs	5 (7.8%)	5 (11.4%)	4 (16%)	$p = 0.675$
Previous SAH from another aneurysm	0	0	1 (4%)	$p = 0.606$
Hypertension	42 (65.6%)	34 (77.3%)	23 (92%)	$p = 0.062$
Smoking	17 (26.6%)	19 (43.2%)	14 (56%)	$p = 0.024$
Initial medical condition (mRS)				
0	59 (92.2%)	42 (95.5%)	23 (92%)	
1	2 (3.1%)	2 (4.5%)	1 (4%)	
2	0	0	1 (4%)	
3	2 (3.1%)	0	0	
4	1 (1.6%)	0	0	
5	0	0	0	
Aneurysm size, mm				
median	3	7	8	$p < 0.001$
range	1.4–9	2.7–18.9	3.5–25	
Aneurysm size groups				
<5 mm	49 (76.6%)	6 (13.6%)	2 (8%)	
5–7 mm	10 (15.6%)	16 (36.4%)	6 (36%)	
>7–12 mm	5 (7.8%)	19 (43.2%)	12 (48%)	
>12–25 mm	0	3 (6.8%)	3 (12%)	
>25 mm	0	0	2 (8%)	
Aspect ratio > 1.6	12 (18.75%)	27 (61.4%)	11 (44%)	$p < 0.0001$
Size ratio > 3	8 (12.5%)	22 (50%)	19 (76%)	$p < 0.0001$
Multilobulated	6 (9.4%)	18 (40.9%)	1 (4%)	$p < 0.001$
Multiple aneurysms	23 (35.9%)	20 (45.5%)	9 (36%)	$p = 0.572$
Symptomatic aneurysms	0	0	2 (8%): 1 (4%) visual symptom and 1 (4%) seizure	$p = 0.034$

* Sum of analyzed patients exceeds total number of patients—an explanation is provided in the text. Abbreviations: IA—intracranial aneurysm, SAH—subarachnoid hemorrhage.

3.1. Observation Group

3.1.1. Assignment

Sixty patients were initially qualified for the conservative management specified earlier. Additionally, four patients initially assigned to the endovascular treatment group were moved to the observational group. Three patients refused endovascular treatment. In one case during diagnostic DSA, the risk of an endovascular treatment had been assessed as high, and treatment was not undertaken. For that reason, the analyzed observational group comprised 64 subjects. Significantly fewer patients in the observation group were smokers (chi-square test, $p = 0.021$). The aneurysm size ratio was significantly different between the combined treatment groups versus the observation group (Kruskal–Wallis $p < 0.0001$, $\varepsilon = 0.45$ [0.33; 1]). Post hoc tests showed that the size ratio was significantly smaller in the observational group in comparison to the endovascular and microsurgery groups (both $p < 0.0001$) (Figure 2A).

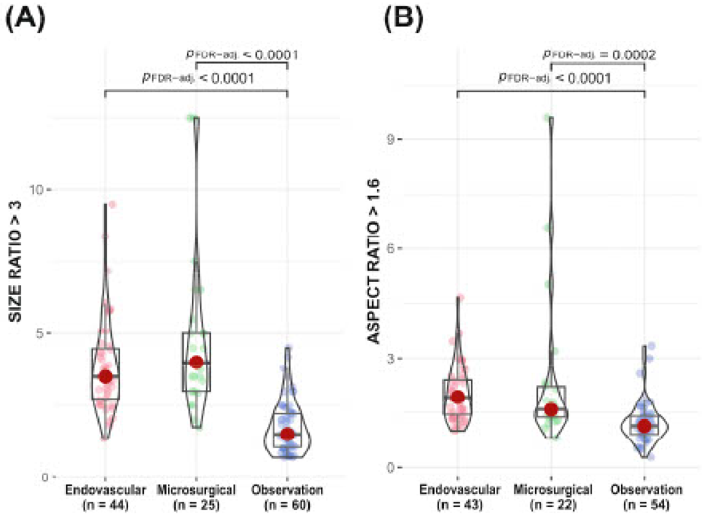

Figure 2. Comparison of size ratio (**A**) and aspect ratio (**B**) between endovascular, microsurgical and observation groups. Red dots and horizontal black lines inside the box indicate median value. Magenta dots in endovascular, green dots in microsurgical and blue in observation groups denote the results of individual patients. The shape of the violin graph indicates the distribution of results.

In addition, the aneurysm aspect ratio was significantly different between examined groups (Kruskal–Wallis $p < 0.0001$, $\varepsilon = 0{,}31$ [0.19; 1]). Post hoc tests showed that the aspect ratio was significantly higher in the endovascular and microsurgery groups than in the observational group ($p < 0.0001$ and $p = 0.0002$, respectively) (Figure 2B).

Subsequently, during the observation period, in four cases (6.25%), we observed aneurysmal growth, and these patients were qualified for endovascular treatment. These aneurysms were not significantly different from the remaining aneurysms in statistical analysis. Of note is that these aneurysms—up till their growth—were included in the observation group analysis. In the observation group, three patients (4.67%) had poor initial neurological condition (mRS 3 or more). These were caused by unrelated conditions such as ischemic stroke (n = 2) and lower extremity peripheral artery disease (n = 1).

3.1.2. Radiological Outcomes

Radiological follow-up data were available for 56 patients (87.5%). During the observation period, four (7.1%) aneurysms grew and were treated endovascularly. The median time to the aneurysm growth was 63.5 months (range: 54–73 months); in each case, the initial aneurysm size was under 5 mm. For the remaining (in other words, stable) 52 (92.9%) aneurysms, the mean radiological follow-up was 60.7 months (range: 5–184). The median follow-up for aneurysms under observation, including aneurysms that eventually grew, was 60.9 (range: 5–184).

3.1.3. Clinical Outcomes

Clinical outcomes were available for 63 patients (98.4%); however, 1 patient was lost to the long-term follow-up. Mean clinical follow-up was 71.5 months (range: 7–187). There were no subarachnoid hemorrhages (SAH) or other symptoms of UIA during this period. Five patients (7.9%) died because of unrelated reasons.

3.2. Endovascular Treatment

3.2.1. Assignment

The endovascular group primarily included 45 patients. Of these, one patient (2.2%) chose treatment in another institution, and three patients (6.67%) refused endovascular treatment. In the remaining case (2.2%), after a diagnostic DSA, due to the expected high risk of treatment, an endovascular procedure was not initiated. Moreover, four patients (6.7%) from the observational group were diagnosed with aneurysmal growth and qualified for treatment. No significant differences were found in the size, aspect ratio and size ratio between those four patients and the rest of the endovascular group (all $p > 0.05$). Finally, after relocations, 44 patients were treated endovascularly.

The following techniques were used: coiling alone in 59.1% of cases, coiling with stent in 20.5%, coiling with flow-diverting devices in 11.4% and flow-diverting alone in 9.1% of cases. One case (2.3%) required two-staged treatment.

In total, 45 endovascular procedures were performed to treat 44 aneurysms. The intraprocedural complication rate was 17.8% (eight cases), of which 75% (six cases) were asymptomatic. Coil protrusion to the artery occurred in 8.9% of cases (n = 4), after which, stent deployment was required. The rate of vasospasm was 2.2%. The intraprocedural rupture rate for all endovascular procedures was 6.7% (three cases).

3.2.2. Clinical Outcomes

On the first postprocedural day, we observed deterioration in five cases (11.1%). In three of these cases, these were minor; in the other two cases, there were major deficits. Deteriorations were caused by ischemic stroke in two cases, which was confirmed by diffusion-weighted imaging (DWI) magnetic resonance (MR). In two other cases, worsening was caused by an intraprocedural hemorrhage (one was an aneurysmal intraoperative rupture, and the second, more serious, was due to an injury of the A2 segment of anterior cerebral artery). A patient with a major deficit due to an intraprocedural hemorrhage and anterior cerebral artery injury died during hospitalization. There were no intraprocedural complications or ischemia in the postoperative MR in the remaining one patient.

At their discharge from hospital, the neurological status of 41 patients (93.2%) was stable, with their mRS scores as before the treatment; 2 patients (4.5%) were discharged in a worse neurological status due to a new, minor deficit in each case. At discharge from hospital, procedure-related permanent morbidity and mortality rates were 4.5% and 2.3%, respectively. Clinical follow-up data were lost for one patient. Four patients died: one during hospitalization, one due to hemorrhage from the treated aneurysm 57 months after treatment and two due to unrelated reasons. There was one hemorrhage for 186.3 patient years.

3.2.3. Radiological Outcomes

Complete obliteration at the time of treatment was achieved for 38 (86.4%) aneurysms. One patient died shortly after the treatment (see above) and three patients were lost to follow-up. For the remaining 40 patients, the median radiological follow-up was 7.25 months (range: 3–14). The complete occlusion rate was 90%, and the near-complete occlusion (visible neck remnant) rate was 5%, while the dome remnant rate was 5%. Of the two aneurysms with dome remnants, one required retreatment, and the other was left untreated and remained under observation due to a high risk of retreatment. Aneurysms with neck remnants (5%) remained under further observation.

In the statistical analysis, aneurysms with near-complete occlusion and aneurysms with dome remnants were significantly bigger (aneurysm size, mm (median (interquartile range)): 10.9 (2.97) vs. 6.72 (3.09), $p = 0.009$; size ratio > 3:4.66 (1.72) vs. 2.83 (1.33), $p = 0.01$; no significant differences in aspect ratio > 1.6) as compared to the completely occluded aneurysms.

Ultimately, 23 patients (52%) patients had a repeated long-term DSA in a mean follow-up of 37.6 months. Recanalization of four previously occluded aneurysms (17.4%) was demonstrated. These patients exhibited more frequent hypertension (Fisher's exact test $p = 0.03$) and multiple aneurysms (Fisher's exact test $p = 0.04$). In long-term follow-up, two aneurysms with neck remnants had complete occlusion without additional treatment. Additionally, complete occlusion was achieved in the retreatment case.

3.3. *Microsurgical Group*

3.3.1. Assignment

Initially, 26 patients (19.8%) were qualified for elective microsurgery. Of these, 1 patient chose a different institution for treatment, hence, in the final assignment of microsurgery, there were 25 patients. When compared with other groups in our study, these aneurysms caused the mass effect significantly more often (Fisher's exact test $p = 0.04$).

3.3.2. Postoperative Complications

On the postoperative day one, deterioration was noted in seven patients (28%). In one case, the postoperative deficit was temporary. Deteriorations were caused by an ischemic stroke recognizable in CT in six cases (24%). Additionally, one of these patients (4%) had a postoperative epidural hematoma. In the remaining one case (4%), the cause of neurological deterioration was not found. Median aneurysmal size in patients who deteriorated was 7 mm (range: 5–13 mm).

3.3.3. Clinical Outcomes

At discharge from hospital, 19 patients (76%) were stable with their mRS scores as before the treatment. Almost a quarter of patients deteriorated, including five minor deficits (20%) and one major deficit (4%). The patient with a major deficit died one month after the surgery due to medical complications that were a consequence of a neurosurgical treatment.

Long-term clinical follow-up was available for 21 patients (84%), while 4 patients (16%) were lost to long-term follow-up. Mean follow-up was 63 months (range 1–123). Out of six patients (24%) with postoperative deterioration, three patients improved, one patient died (see above), one patient was lost to the follow-up and one patient exhibited permanent deterioration. There was no hemorrhage from the treated aneurysms. Overall mortality for this group was 4.8%, and permanent morbidity (mRS 1) was 4.8%.

3.4. *Overall Results*

Mortality for all patients (observed, treated endovascularly and treated microsurgically) with available follow-up was 2.4% (3/124), and permanent morbidity was 1.6% (2/124) over a mean follow-up of 64.2 months.

4. Discussion

In this study we presented our management strategy with AComA UIAs and analyzed their treatment results. We focused exclusively on AComA aneurysms because their increased risk of rupture makes them distinct from other UIAs [11]. Management of patients with AComA UIAs still poses a considerable challenge. Treatment of UIAs is intended to prevent SAH, but it involves a substantial risk of morbidity and mortality. At the beginning, in our decision-making process, we followed the algorithm published by Chalouhi et al. [7]. Subsequently, we introduced additional tools: PHASES and the UIATS system score. Applying these scales did not simplify the decision-making process; their recommendations often differed. Additionally, in 43.5% of cases, UIATS suggestions were not definitive. According to the most recent European recommendations, the indications for treatment are even more limited [12]. Even though our management was tailored for each individual case, some general trends emerged and will be discussed below.

4.1. Observational Group

Morphological features of aneurysms, such as their size, size ratio and aspect ratio, were significantly smaller in the observational group. Conversely, patients in the treatment group were significantly more often smokers. As a result of our strategy, there were no intracranial hemorrhages or neurological deteriorations caused by aneurysm in the observational group.

4.2. Endovascular Group

In the endovascular group, procedure-related mortality (that was a consequence of the provided treatment) and permanent morbidity were 2.3%. Morbidity in our series is lower, while the mortality is comparable to that from the meta-analysis of the endovascular treatment of AComA aneurysms by Fang et al. in 2014 [13]. In that study, permanent morbidity was 8% (95% CI 3–20%) for AComA UIAs, and the procedure-related mortality was 2% (95% CI 1–9%) for AComA UIAs. The rate of hemorrhage was 2.3% in our series and is comparable to the meta-analysis results by Fang et al. (2%, 95% CI 0–6%) [13]. In that study, the retreatment rate was 3%, compared to 5% in our series.

In our study, the long-term complete and near-complete occlusion rates were 90% and 95%, respectively, which is similar to what Fang et al. found in their meta-analysis, i.e., 90% for both complete and near-complete occlusions.

A systematic analysis by O'Neill et al. presents data separately for coiling and stent-assisted coiling. Good clinical outcomes were achieved in 99.2% and 92.1% for these two treatment modalities, while treatment-related mortality was 0 and 1.1%, respectively [14]. There were no SAHs from the treated aneurysms in either endovascular treatment technique. Retreatment rates were 4.9% and 6.8%, for coiling and stent-assisted coiling, respectively. All these results are similar to those obtained in our series.

4.3. Microsurgical Group

Morbidity and mortality in our microsurgical group were 4.7% and 4.7% respectively. In the review of the literature by Nussbaum, 3.3% of microsurgically treated patients did not achieve a good clinical outcome, while the mortality rate was 0.3% [15]. The mortality rate in our study is higher (4.7%), but it refers to a single patient in a comparatively small group (n = 25). This patient had an aneurysm that was not amenable to endovascular techniques and had a high risk of rupture. Similarly, the majority of microsurgically treated aneurysms had complex anatomy, and endovascular treatment of these aneurysms was evaluated as too risky.

The higher risk of clipping may be related to a decreasing volume of patients treated microsurgically, which imperils the opportunity to develop, improve and sustain high operative abilities.

4.4. Final Comments

The observation of aneurysms did not expose patients to hemorrhage and at the same time avoided the risk of treatment, possibly reducing the mortality and morbidity in the whole group. On the other hand, despite the risk of morbidity of endovascular and microsurgical treatment in our material being 2.3% and 4.7%, respectively, the cumulative morbidity risk for the whole study population was lower, at 1.6%. Ultimately, it appears beneficial to observe AComA UIAs whenever reasonable and—when treatment is warranted—diversify preventive aneurysm repair modalities.

In a meta-analysis of the natural history of AComA UIAs, Mira et al. estimated the annual risk of rupture at 2.2% [2]. Yet, in our study, with 690.15 patient years of follow-up (129 patients and 5.35 years) and one case of SAH, we managed to decrease this number to the 0.14% annual risk of rupture.

Based on our experience, we conjecture that evaluating each AComA UIA in a multidisciplinary team, with a preference to observe whenever possible and reasonable, may be of benefit. Prior to such evaluation a patient should be carefully evaluated using all available UIA scales (PHASES, UIATS, and ISUIA).

4.5. Limitations

Our study is limited by its retrospective nature and small sample size. Additionally, our multidisciplinary team evaluates many patients from outside hospitals. Most of these patients, when qualified for observation, are not followed in our institution, and thus, such patients were not included in our database. As a result, there is an inflated portion of treated patients, relative to the whole study group, whereas the patients in the observational group constitute only a fraction of patients actually surveilled in our outpatient clinics.

Finally, our management strategy changed over time according to updated guidelines and risk calculators and is not homogenous for the evaluated patients.

5. Conclusions

Using diversified management of AComA UIAs, we have decreased the annual risk of SAH to 0.14% at the expense of 2.4% mortality and 1.6% permanent minor deficit rates. Noteworthily, there were no hemorrhages in the observational group. The morbidity and mortality in AComA UIAs are compelling, but these refer to a high-risk group with potentially devastating consequences.

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6.3. Praca 3

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Retrospective Application of Risk Scores to Unruptured Anterior Communicating Artery Aneurysms

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Abstract: Background: Treatment decisions for unruptured intracranial aneurysms (UIAs) pose a challenge for neurosurgeons, prompting the development of clinical scales assessing hemorrhage risk to provide management guidance. This study compares recommendations from the PHASES and UIA treatment scores (UIATS) applied to anterior communicating artery (AComA) UIAs against real-world management. Methods: While UIATS recommends management, for PHASES, an aneurysm with score of 10 or more was considered "high-risk". Analysis involved assessing the concordance in each group alongside comparison to real-word management. Results: Among 129 patients, 46.5% were observed and 53.5% were treated. PHASES scores were significantly higher in the treatment group ($p = 0.00002$), and UIATS recommendations correlated with real-world decisions ($p < 0.001$). We observed no difference in the frequencies of UIATS recommendations between high- and low-risk groups. When comparing the UIATS and PHASES, 33% of high-risk aneurysms received a UIATS conservative management recommendation. In 39% of high-risk aneurysms, the UIATS recommendation was not definitive. Conversely, 27% of low-risk aneurysms obtained a UIATS UIA repair recommendation. Overall, concordance between PHASES and UIATS was 32%. Conclusions: Significant discordance in therapeutic suggestions underscores the predominant influence of center experience and individual assessments. Future studies should refine and validate decision-making strategies, potentially exploring alternative applications or developing tailored scales.

Keywords: unruptured intracranial aneurysm; anterior communicating artery; UIATS; PHASES; concordance

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1. Introduction

With the heightened availability and improved precision of diagnostic imaging, in recent years there has been a notable surge in the detection rate of asymptomatic unruptured intracranial aneurysms (UIAs), particularly among elderly patients [1]. This trend is accompanied by a noteworthy inclination to qualify smaller aneurysms for treatment in older patient cohorts. Presumably, this shift in clinical practice is influenced by the advancing safety profile of aneurysm treatment modalities [2,3].

Nevertheless, navigating the decision of whether to treat a UIA presents a challenging dilemma for neurosurgeons worldwide, as well as remaining an ever-present concern in their daily practice. Consequently, several scales have been developed to assess the risk of hemorrhage and offer treatment recommendations. A number of studies have analyzed the usefulness of these scales in predicting the risk of hemorrhage in populations with ruptured intracranial aneurysms, and they show that a large percentage of ruptured aneurysms would have been assigned as low risk aneurysms pre-rupture [4–7].

In this evolving landscape of UIA management, anterior communicating artery (AComA) UIAs stand out. Their distinctive features include high prevalence, proximity to functionally vital structures, and a speculated increased risk of rupture. The aim of this study is to compare management recommendations for AComA UIAs specifically, evaluate different protocols, and compare them with each other and to real-life management of AComA UIAs in a single institution.

2. Materials and Methods

This study is a retrospective evaluation of patients with AComA UIAs who were observed or treated. These patients, including their follow-ups and complications, have already been extensively described in our previous study [8]. In this paper, we applied PHASES and UIATS in comparison to real-life management at a single institution [9,10].

We analyzed the concordance of these scales in each group and compared them to our management. We analyzed a variety of demographics and aneurysm factors to find the differences between the subgroups of different recommendations. The recommendations from UIATS are categorized as either definitive ('UIA repair', i.e., treatment or 'conservative management', i.e., observation) or non-definitive ('the recommendation is not definitive').

This paper will interchangeably refer to recommendations derived from UIA clinical scales and real-world management. To ensure clarity throughout the text, specific terms will be introduced and utilized consistently. We will refer to the real-world aneurysm cohorts as belonging to either the 'treatment' or 'observation' group. Regarding UIATS recommendations, the terms 'UIA repair' or 'conservative management' will be used, as described in the original paper. For the PHASES scale, which assesses the 5-year hemorrhage risk, a score of 10 or more assigned to the aneurysm was considered high-risk, as proposed by Stumpo et al. [11]. Accordingly, whenever the terms 'high-risk' or 'low-risk' aneurysm are utilized in this paper, they will correspond to the PHASES score interpretation.

Statistical Analysis

We performed the Shapiro-Wilk and Levene's tests to examine the assumptions of data normality and the equality of variances, respectively. We examined the associations between qualitative variables with the Chi-squared and Fisher's exact tests. The Chi-square Goodness of Fit test was used to summarize the discrepancy between observed values and expected values. Differences between the two groups were assessed using either the Mann-Whitney U test or independent *t*-tests, depending on whether assumptions were met. We reported *p*-values both before and after false discovery rate (FDR) correction. Differences between more than two groups were evaluated with the Kruskal-Wallis H test or one-way ANOVA, depending on whether assumptions were met. Post-hoc comparisons were made using the Dunn test, and *p*-values were adjusted for multiple comparisons. All analyses were performed using jamovi, which is a graphical user interface for R and violin graphs, which were created using the ggstatsplot library [12–14]. Effect size (ε) and confidence interval [−95%; 95%] from the ggstatsplot library are reported for Kruskal-Wallis test results. All analyses were performed with a significance level of $\alpha = 0.05$.

To mitigate potential high correlation between PHASES and age, as well as UIATS and age, we avoided including these variables as predictors in the same model. Instead, we independently considered age, PHASES, and UIATS in separate models, allowing a distinct assessment of their contributions to our analyses.

3. Results

In our series of 129 patients with AComA UIAs, 46.5% (60) of patients remained under observation and 53.5% (69) were qualified for treatment.

3.1. PHASES Scores and Real-World Management Decisions

There were 111 (86%) AComA aneurysms classified as low-risk (score < 10) and 18 (14%) classified as high-risk (score ≥ 10), according to the PHASES scores.

The PHASES scores were significantly higher in the group qualified for treatment [median ± interquartile range (IQR) was 8 ± 5 in the treatment group vs. 5 ± 1 in the observation group, $p = 0.00002$, Table 1]. Figure 1 presents the distribution of treated and observed AComA aneurysms according to their PHASES scores.

Table 1. PHASES scores in patients with unruptured anterior communicating artery aneurysms who were under observation or were qualified for treatment.

Group	*n*	PHASES Scores	
		Median	Range
Treatment	69	8	4–15
Observation	60	5	4–9

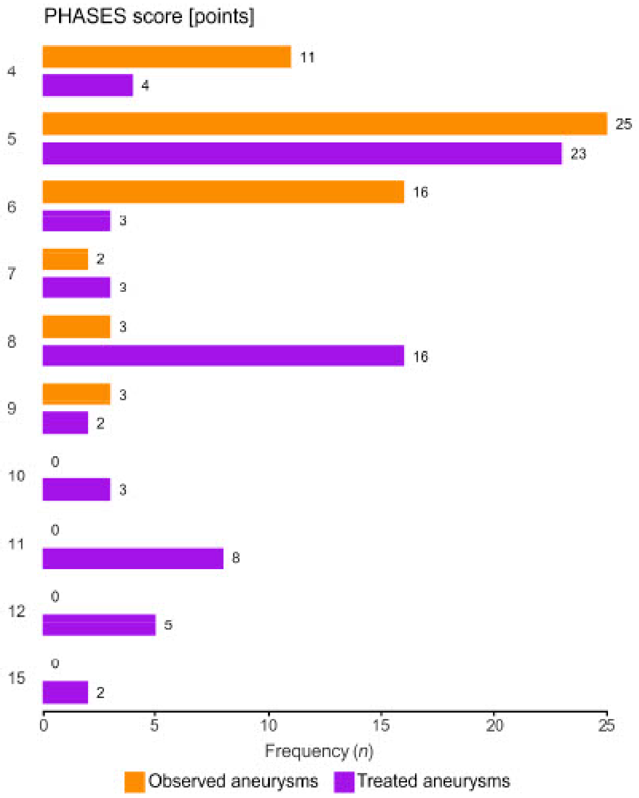

Figure 1. Distribution of PHASES scores across treated and observed unruptured anterior communicating artery aneurysms. Orange—observed aneurysms, violet—treated aneurysms.

3.2. UIATS and Real-World Management Decisions

In accordance with UIATS, UIA repair was recommended for 27% (35) of patients and conservative management for 32% (41) of patients, while the recommendation remained not definitive for 37% (48) of individuals. In five cases, our data was insufficient to calculate UIATS. Patients under observation more frequently received an UIATS conservative management recommendation and, correspondingly, patients who qualified for treatment more frequently received a UIATS UIA repair recommendation (Chi-square test, $p < 0.001$, Table 2). A significant association was identified between UIATS recommendations for UIA repair or conservative management and real-world decisions (Fisher's exact test, $p < 0.001$).

Table 2. UIATS recommendations for patients with unruptured anterior communicating artery aneurysms who were under observation or qualified for treatment. UIA—unruptured intracranial aneurysm.

Group	Recommendation According to UIATS			No Data
	UIA Repair	Conservative Management	Not Definitive	
Observation, $n = 60$	6 (10%)	28 (47%)	21 (35%)	5 (8%)
Treatment, $n = 69$	29 (42%)	13 (19%)	27 (39%)	0

3.3. UIATS Recommendations against PHASES Scores

We observed no difference in the frequencies of UIATS recommendations between high and low-risk groups, as interpreted by PHASES (Table 3, for details please refer to Supplementary Table S1).

Table 3. A comparative analysis of aneurysm evaluations according to PHASES and UIATS recommendations. Aneurysms with PHASES score of 10 and more were classified as high-risk. UIA—unruptured intracranial aneurysm.

PHASES Interpretation of an Aneurysm	Recommendation According to UIATS			Chi-Square Goodness of Fit p-Value
	UIA Repair	Conservative Management	Not Definitive	
Low-risk	30 (28%)	35 (33%)	41 (39%)	0.424
High-risk	5 (28%)	6 (33%)	7 (39%)	0.846

In the entire cohort, PHASES scores were not significantly different in relation to any UIATS recommendation (Chi-squared Kruskal-Wallis = 4.91, $p = 0.086$, Figure 2).

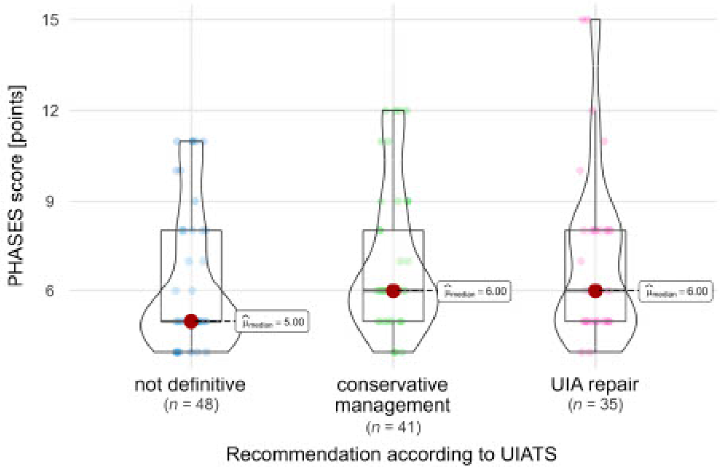

Figure 2. Comparison of PHASES scores in relation to the UIATS recommendation across the whole cohort. A dark red dot denotes the median value, while smaller dots indicate values of individual patients.

In the subgroup of aneurysms with a definitive recommendation, UIATS recommended conservative management for 55% (6) of high-risk and for 54% (35) of low-risk aneurysms, according to PHASES score interpretation. Likewise, in the subgroup with a UIATS definitive recommendation, UIA repair was recommended for 46% (30) of low-risk and for 45% (5) of high-risk aneurysms, as per PHASES score interpretation (chi-squared p-value 0.97).

3.4. Observation Group

PHASES scores in the group of 60 patients under observation ranged from 4 to 9, and no high-risk aneurysms (according to PHASES interpretation) were identified. In this group, UIATS recommended UIA repair for 11% (6) of patients and conservative management for 51% (28) of patients, while 38% (21) of patients lacked a specific recommendation (i.e., the UIATS recommendation was not definitive).

Among patients under observation, PHASES scores were significantly different between subgroups based on UIATS recommendation [Chi-squared Kruskal-Wallis = 6.35, $p = 0.042$, $\varepsilon 2 = 0.12$ (0.02; 1)]. The subgroup with a UIATS conservative management recommendation had significantly higher PHASES scores when compared against patients with 'not definitive' recommendations ($p = 0.035$, Figure 3).

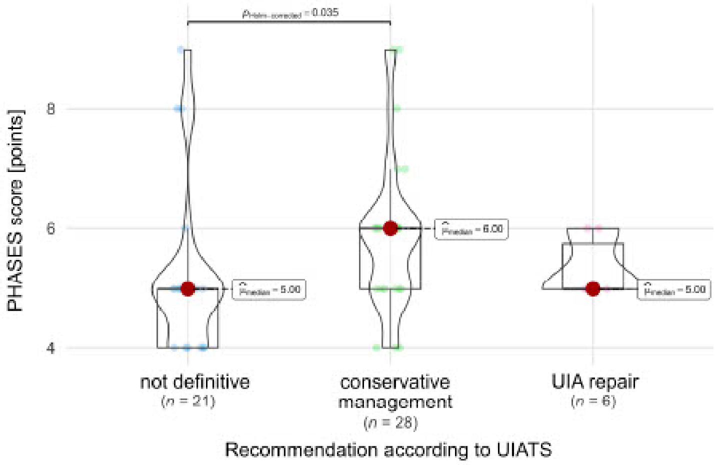

Figure 3. Comparison of PHASES scores in relation to UIATS recommendations in the observation group. A dark red dot denotes the median value, while smaller dots indicate values of individual patients.

We compared patients whom we observed following UIATS recommendations for conservative management against those whom we observed despite UIATS recommending UIA repair. Among the patients under observation in real-life management, we identified a subgroup with a UIATS UIA repair recommendation, displaying distinctive characteristics. Specifically, these patients were significantly younger [median (IQR) age of 51 (48 to 57) years old vs. median (IQR) of 72 (68 to 77) years old], had more frequent previous SAH ($p = 0.025$), a family history of aneurysms and/or a hemorrhage from another aneurysm in the past ($p = 0.016$), were more often active smokers ($p = 0.016$), and had multiple aneurysms significantly more often ($p = 0.021$, Table 4).

3.5. Treatment Group

PHASES scores in the group of patients who underwent treatment ranged from 4 to 15, with 26% (18) of them having high-risk aneurysms (PHASES score of 10 or more). According to UIATS, UIA repair was recommended for 42% (29) of patients and conservative management for 19% (13) of patients, and a recommendation was not definitive for 39% (27). The PHASES scores in these three subgroups of different UIATS recommendations among patients who underwent treatment were significantly different [Chi-squared Kruskal-Wallis = 8.12, p = 0.017, $\varepsilon 2$ = 0.12 (0.04; 1); Figure 4]. Notably, within the treatment group, patients with UIATS conservative management recommendations had significantly higher PHASES scores compared to other treated patients, namely those for whom UIATS recommended UIA repair or did not provide a clear recommendation ('recommendation not definitive').

Table 4. Demographic and aneurysmal information for UIATS recommending unruptured intracranial aneurysm (UIA) repair or conservative management within a group of patients with unruptured anterior communicating artery aneurysms under observation. FDR—false discovery rate, IQR—interquartile range, NA—not applicable, SAH—subarachnoid hemorrhage, UIA—unruptured intracranial aneurysm.

Parameter (Unit)	Recommendation According to UIATS		p-Value	p-Value FDR
	Conservative Management [n (%)/Median (IQR)]	UIA Repair [n (%)/Median (IQR)]		
Patients	28	6		
Age (years)	72 (68 to 77)	51 (48 to 57)	<0.001	0.008
Aneurysm size (mm)	3.94 (2.28 to 6.00)	2.10 (1.55 to 4.00)	0.094	0.12
Previous SAH for another aneurysm	1 (3.6%)	3 (50%)	0.012	0.022
Familial history	0	3 (50%)	0.003	0.014
Active smoking	5 (18%)	5 (83%)	0.005	0.014
Multiple aneurysms	6 (21%)	5 (83%)	0.008	0.019
Aspect ratio > 1.6	1.25 (0.97 to 1.75)	1.27 (0.67 to 1.60)	0.60	0.67
Size ratio > 3	1.88 (1.25 to 2.64)	0.99 (0.78 to 1.77)	0.040	0.06
Low-risk aneurysm *	28	6	NA	NA
High-risk aneurysm *	0	0		

* Evaluated with PHASES interpretation, in which a score of 10 or more assigned to the aneurysm was considered high-risk, while scores under 10 were low-risk.

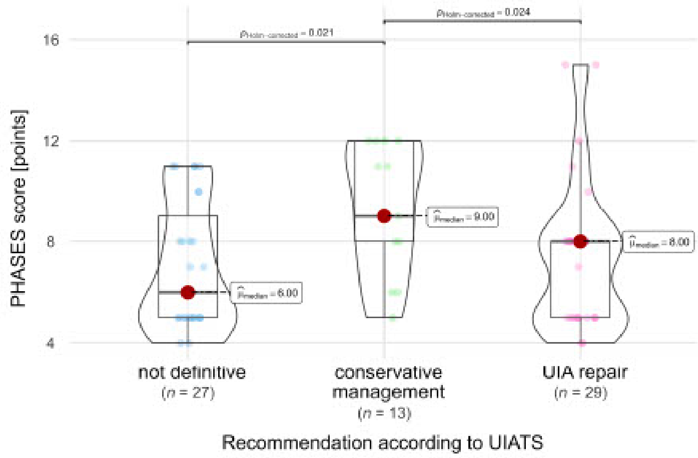

Figure 4. Comparison of PHASES scores in relation to UIATS recommendations in patients who underwent treatment. A dark red dot denotes the median value, while small dots indicate values of individual patients.

We additionally compared the aneurysms within our treatment group, distinguishing between those for which UIATS recommended UIA repair and those for which UIATS recommended conservative management. Patients with UIATS UIA repair recommendation (within the real-world treatment group) were significantly younger [median (IQR) age of 54 (48 to 58) years old vs. median (IQR) of 71 (67 to 75) years old, $p < 0.001$)], were active smokers more frequently (69% vs. 0%, $p < 0.001$), but had lower PHASES scores [median (IQR) of 8 (5 to 8) vs. median (IQR) of 9 (8 to 12), $p = 0.007$], when compared against the patients within the treatment group who received UIATS observation recommendation (Table 5).

Table 5. Demographic and aneurysmal information for UIATS recommending UIA repair or conservative management within groups of patients with unruptured anterior communicating artery aneurysms who underwent treatment. FDR—false discovery rate, IQR—interquartile range, SAH—subarachnoid hemorrhage, UIA—unruptured intracranial aneurysm.

Parameter (Unit)	Recommendation According to UIATS		*p*-Value	*p*-Value FDR
	Conservative Management [*n* (%)/Median (IQR)]	UIA Repair [*n* (%)/Median (IQR)]		
Patients	13	29		
Age (years)	71 (67 to 75)	54 (48 to 58)	<0.001	<0.001
Aneurysm size (mm)	8.2 (7.5 to 10.2)	7.0 (5.5 to 9.0)	0.10	0.16
Previous SAH from another aneurysm	0	2 (6.9%)	>0.99	>0.99
Familial history	0	7 (24%)	0.079	0.16
Active smoking	0	20 (69%)	<0.001	<0.001
Multiple aneurysms	2 (15%)	13 (45%)	0.089	0.16
Multilobulated aneurysms	4 (31%)	9 (31%)	>0.99	>0.99
Aspect ratio > 1.6	1.79 (1.39 to 2.24)	1.56 (1.30 to 2.19)	0.97	>0.99
Size ratio > 3	4.32 (2.82 to 5.26)	3.12 (2.69 to 3.89)	0.059	0.16
Low-risk aneurysm *	7	23	0.16	0.22
High-risk aneurysm *	4	3		

* Evaluated with PHASES interpretation, in which a score of 10 or more assigned to the aneurysm was considered high-risk, while scores under 10 were low-risk.

3.6. Summary of the Results

As a result of our management strategy, we reserved observation only for low-risk AComA UIAs according to the PHASES score interpretation. Even so, concurrently, we treated as many as 46% (51) of low-risk aneurysms. Overall, our management was in concordance with the PHASES score interpretation in 60% of cases.

In 60% (76) of cases, UIATS recommendations were definitive, while the remaining cases were categorized as not definitive. We treated 82% (29) of cases in which UIATS recommended UIA repair and observed 68% (28) of cases for which UIATS recommended conservative management. Overall, our management was in concordance with UIATS recommendations in 46% of cases.

Surprisingly, the concordance of these two scales applied to AComA UIAs was as low as 32% (40). When comparing the UIATS and PHASES evaluations, we found that 33% (6 cases) of high-risk aneurysms (as per PHASES interpretation) received a UIATS conservative management recommendation. In as many as 39% (7) of these high-risk aneurysms, the UIATS recommendation was not definitive. On the other hand, 27% (30) of cases of low-risk aneurysms obtained a UIATS UIA repair recommendation.

In our analysis of AComA UIAs that underwent treatment, an intriguing pattern emerged when evaluating the recommendations from UIATS and PHASES. Notably, a mere 7.2% of treated AComA UIAs received a UIATS UIA repair recommendation while simultaneously being deemed high-risk according to their PHASES interpretation. The majority of treated aneurysms (61%) fell into either the high-risk category based on their PHASES interpretation, or received a UIA repair recommendation from UIATS.

4. Discussion

The AComA complex is a prevalent site for UIAs, constituting up to 33% of cases. A number of studies underscore its elevated risk of rupture, as indicated by a meta-analysis reporting a 2.51 times higher risk for AComA aneurysms compared to those in other anterior circulation sites [15,16]. Moreover, small AComA UIAs have been reported to bear a similar risk of rupture to posterior circulation aneurysms [17]. The conjunction and synergy of these two features established the foundation for distinguishing AComA aneurysms from other locations within the anterior circulation in our studies.

The PHASES score emerged from a collaborative effort among researchers from diverse institutions, originating in a large international study that synthesized data from individual patient records and aneurysm databases [9]. Developed by analyzing various risk factors and their associations with aneurysm rupture, the PHASES score serves as a tool for clinicians to estimate rupture risk in UIAs based on individual patient characteristics [18].

The UIATS recommendations, representing a consensus effort among researchers, were developed through a comprehensive analysis of data from various sources, including individual patient records and aneurysm databases [10]. These guidelines provide clinicians with evidence-based insights for managing UIAs [19].

4.1. UIATS Recommendations

In our investigation, we identified instances where the recommendations provided by UIATS were not clearly delineated. This raises concerns about the suitability of using UIATS in isolation. Notably, patients who were observed in real-life settings more frequently received a UIATS recommendation for conservative management than a recommendation for UIA repair. Nevertheless, 11% of these patients (6) were recommended to undergo UIA repair. This subset of patients, receiving a UIATS UIA repair recommendation and who remained under observation in real life, exhibited distinct characteristics—they were notably younger, had a higher incidence of familial history related to aneurysms or prior hemorrhages from another aneurysm, were more likely to smoke, and presented with multiple aneurysms. Interestingly, the aneurysms in the observation group with a UIATS UIA repair recommendation were very small (median size 2.1 mm), even when compared to those in the subgroup receiving a UIATS conservative management recommendation, although this difference was not statistically significant. This persistent UIA repair recommendation was noteworthy, particularly in light of three points favoring conservative management, which were justified by the aneurysm's complexity arising from a very small diameter (<3 mm).

It is worth noting that, within the treatment group, significantly older patients consistently received UIATS conservative management recommendations. This feature of UIATS, evident in patients who underwent treatment in our real-life scenario, harmonizes with the study by Rutledge et al. [20]. The researchers reported that UIATS tends to underestimate the risk of hemorrhage in older patients. Moreover, older patients are more severely affected by aneurysmal hemorrhage [21,22]. This emphasizes the need for a critical evaluation of UIATS recommendations in older populations, recognizing the potential underestimation of hemorrhage risk and the heightened severity of aneurysmal hemorrhage in this demographic.

4.2. PHASES Scores

Although patients who underwent preventive aneurysm repair had significantly higher PHASES scores, we treated almost half (46%, 51) of patients with low–risk aneurysms (according to PHASES interpretation). An additional analysis of these cases unveiled that the vast majority (96%, 49) harbored at least one type A risk factor, and two-thirds (66.7%, 34) had two type A risk factors, according to Chalouhi et al. [23]. The remaining 4% of patients had one type A risk factor and one type B factor, which advocates for treatment, according to the researcher's algorithm. In our management approach, we did not observe any high-risk aneurysms (as per PHASES interpretation).

4.3. UIATS and PHASES Comparison

As presented in the summary of the results, a notable discordance between PHASES and UIATS persists in AComA UIAs: every third high-risk aneurysm, as per PHASES interpretation, received a UIA repair recommendation according to UIATS. Overall, the concordance of these scales was 32%. It would be reasonable to assume that using more tools should help with daily clinical practice, but our results show that the use of these scales did not make decision-making simpler, instead adding to the confusion on what to do. In certain scenarios, it appears likely that UIATS recommends conservative management for high-risk aneurysms (as per PHASES) due to the consideration of treatment-related risks. Unfortunately, an analogous explanation for why UIATS recommends UIA repair for low-risk aneurysms in certain cases remains elusive.

What is more, we observed two unusual findings - one within the observation group, and another within the treatment group. Firstly, among patients under observation, the subgroup with a UIATS conservative management recommendation had significantly higher PHASES scores compared to patients with a "not definitive" recommendation. The apparent contradiction in this finding may be attributed to the objective of UIATS construction, which considers not only aneurysm characteristics but also the inherent risks of treatment. Such a comprehensive approach may lead to a final recommendation favoring conservative management, despite apparent higher aneurysm risks depicted by relatively higher PHASES scores.

Secondly, within the treatment group, patients with UIATS conservative management recommendations had significantly higher PHASES scores compared to other treated patients, specifically those for whom UIATS recommended UIA repair or did not provide a clear recommendation. This apparent paradox may be simply explained by our management approach, wherein patients with high-risk aneurysms (as per PHASES interpretation) were qualified for treatment, regardless of other associated risks indicated in the UIATS recommendations. In essence, our decision to opt for patient treatment was influenced by the recommendation of only one of the scales.

4.4. Limitations of Aneurysm Scale Use

Scales intended to forecast the risk of aneurysm hemorrhage or offer clinical guidance are not commonly integrated into clinical practice [24]. Additionally, these scales suffer from a notable deficit of prospective evaluation, a crucial element requisite for establishing a robust scientific basis to support their widespread implementation [19]. On the contrary, there are a number of studies that have been critical of using these scales. Ravindra et al. concluded that UIATS recommended the overtreatment of unruptured aneurysms [19]. When analyzing ruptured aneurysms, Rutledge et al. found that applying UIATS to elderly patients would have led to their undertreatment, a problem not observed in younger populations [20]. Furthermore, Hernandez-Duran et al. found that the sensitivity of UIATS in detecting high-risk aneurysms in ruptured aneurysm cases was low [25]. On the contrary, Feghali et al. showed that UIATS demonstrated good concordance with real-world practice [26].

A major shortcoming of UIATS was recently reported by Stumpo et al. [5]. The researchers claimed that UIATS would have failed to recommend UIA repair in 72.6% of patients whose aneurysms eventually ruptured. Additionally, Molenberg et al. reported poor performance of UIATS in predicting aneurysm growth or rupture [27].

4.5. Study Limitations

This study possesses inherent limitations attributed to its retrospective design, a relatively modest sample size, and single-center focus. While the latter introduces a degree of subjectivity to the patient group, management processes, and results evaluation, we contend that this limitation offers unique strengths within the specific context of our investigation.

The homogeneity observed in the evaluated AComA UIAs, coupled with the consistent approach to management decisions (albeit with some adjustments over time) resulting from our single-center methodology, provides a distinctive advantage. This homogeneity facilitates direct comparisons, enabling the derivation of meaningful conclusions—a feat that might prove challenging in a multicenter, retrospective study design with potentially increased variability in patient populations and management practices. The inclusion of numerous centers may introduce additional confounding factors, complicating the interpretation of results.

Furthermore, as previously noted in our earlier publication, a subset of patients from external medical facilities qualified for observation. However, their data are not incorporated into our databases [8]. Consequently, the reported number of patients under observation in this study represents only a fraction of the total AComA UIAs under observation, excluding those managed at external hospitals and outpatient clinics. This omission emphasizes the necessity for cautious generalization of our findings to broader patient populations.

Finally, an important limitation of our study lies in the use of the PHASES score interpretation. Following the approach outlined by Stumpo et al., we categorized aneurysms into high- and low-risk groups, subsequently assigning them to treatment and observation, respectively [11]. It is crucial to acknowledge this methodology when interpreting the results of our investigation. However, the necessity for some degree of generalization, including the use of, at times, arbitrary cutoffs, is recognized to facilitate evaluation in a broader context.

4.6. Final Remarks and Future Directions

Assessing the concordance of aneurysm management with PHASES scores proves challenging, as PHASES scoring primarily estimates the risk of hemorrhage rather than guiding aneurysm management. As per the European Stroke Organisation guidelines, preventive aneurysm repair is recommended for individuals with a 5-year risk of aneurysm rupture, as this surpasses the risks associated with preventive treatment [28]. The impact of implementation of the PHASES score in aneurysm management was evaluated by Hollands et al. [29]. The researchers found that out of two examined centers, one did not change its previous practice, while the other began to qualify less aneurysms for treatment.

In our management, we disqualified high-risk aneurysms from observation, and a substantial number of low-risk aneurysms were treated (as assessed with PHASES interpretation). This finding aligns with the observations of Longnon et al., who reported that PHASES did not identify the majority of patients as being at a high or intermediate risk of rupture [6]. Hilditch et al. reported comparable results [30].

The second noteworthy finding is the divergence in suggestions between PHASES and UIATS in numerous cases. While this initial discrepancy may complicate decision-making, a potential strategy could involve using the PHASES scale to estimate the risk of hemorrhage. Subsequently, if an aneurysm is identified as high risk, the UIATS scale could serve as a more refined tool to strike a balance between the risk of rupture and the risk of treatment. Such a scheme necessitates future prospective evaluation.

Furthermore, prospective multicenter studies, utilizing established frameworks like UIATS and PHASES, are crucial and much needed for advancing our understanding of AComA UIAs. A collaborative, prospective approach in properly designed multicenter studies would enhance the generalizability of findings, capturing diverse patient demographics and management practices. These studies should focus on elucidating natural history and risk factors of UIAs, as well as establishing a consensus on optimal management and the usefulness of clinical scales. Moreover, crucial additional outcomes to consider encompass the real-world morbidity associated with interventions for UIAs and their consequential impact on patients' quality of life. The use of standardized assessment tools ensures a consistent framework, contributing to evidence-based guidelines for improved clinical decision-making.

5. Conclusions

Over two thirds of the evaluations in the AComA UIA group yielded discordant suggestions between PHASES and UIATS assessments. This underscores that therapeutic decisions continue to be primarily influenced by the center's experience, individual assessments, and patient preferences. Recognizing the shortcomings of currently used scales, future prospective studies are needed to refine and validate decision-making strategies for managing UIAs. This may involve exploring alternative applications of current scales and developing new ones tailored to specific patients and aneurysms.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/jcm13030789/s1, Supplementary Table S1. Distribution of the PHASES scores across UIATS recommendations in patients with unruptured anterior communicating artery aneurysms. UIA—unruptured intracranial aneurysm.

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7. Podsumowanie

Praca nr 1

W podgrupie tętniaków ICA C6 dokonano analizy skuteczności i bezpieczeństwa stosowania stentów kierunkujących przepływ. Do analizy włączono 52 pacjentów z 65 tętniakami. W długoterminowej analizie klinicznej u 98,1% pacjentów uzyskano zadowalający wyniki kliniczny. Skumulowane ryzyko krwotoku z leczonego tętniaka wyniosło 0,33% (1/304 tętniakolat) w ciągu średniego okresu obserwacji 61 miesięcy, przy rocznym ryzyku wynoszącym 0,07%. U pacjentów bez objawów wzrokowych nie doszło do pogorszenia widzenia. W grupie pacjentów z objawowymi tętniakami: u 1 doszło do poprawy widzenia, u 1 – do trwałego pogorszenia, u 2 – do przejściowego pogorszenia, a u pozostałych 4 objawy pozostały bez zmian. Całkowite wyłączenie tętniaka z krążenia na koniec przeprowadzonej procedury nastąpiło w 12,3% przypadków. W analizie wykazano, że uzyskanie natychmiastowego wyłączenia tętniaka z krążenia było znacząco wyższe w podgrupie, w której użyto spiral łącznie z FDD, w stosunku do podgrupy, w której użyto samego stentu. Po 6 miesiącach od leczenia wykazano całkowite wyłączenie 73,4% leczonych tętniaków. W analizie wyników radiologicznych po 6 miesiącach nie znaleziono istotnych różnic przy dodatkowym zastosowaniu spiral. W odległej analizie wyników radiologicznych, po zastosowaniu w 3 przypadkach leczenia uzupełniającego, 95,4% tętniaków zostało wyłączonych z krążenia. W 6 (10,9%) przypadkach doszło do zamknięcia tętnicy ocznej, ale bez powikłań wzrokowych. Komplikacje wystąpiły u 40,4% pacjentów, prowadząc w 3,8% przypadków do wystąpienia trwałych deficytów neurologicznych (1,9%) i do śmierci (1,9%). U 26,95% pacjentów były to komplikacje proceduralne obejmujące: nieprawidłowe rozprężenie lub przemieszczenie stentu, rozwarstwienie tętnicy szyjnej, powikłania zatorowe i skurcz naczyniowy. U 11,5% pacjentów wystąpiły komplikacje odległe: powikłania zatorowo-zakrzepowe, zwężenie w stencie oraz krwotok z leczonego tętniaka. W pięciu (9,6%) przypadkach nie powiodła się próba implantacji stentu. U 3 (5,7%) pacjentów powikłania wystąpiły w trakcie diagnostycznej lub kontrolnej angiografii.

Praca nr 2

W podgrupie 131 tętniaków AComA poddano analizie strategie postępowania w kwalifikacji do obserwacji lub leczenia, rodzaju leczenia oraz analizę wyników zastosowanego postępowania. Do obserwacji zakwalifikowano 64 (48,1%) tętniaków, leczono 69, w tym 44 (33,1%) wewnątrznaczyniowo, a 25 (18,8%) operacyjnie. Obserwacja radiologiczna była dostępna dla 87,5% pacjentów, a w jej trakcie 7,1% tętniaków uległo powiększeniu i zostały zakwalifikowane do leczenia. Tętniaki, które się powiększyły, nie różniły się od pozostałych tętniaków w zakresie analizowanych parametrów morfologicznych i populacyjnych. Wymiar tętniaków, które uległy powiększeniu, wyjściowo był mniejszy niż 5 mm. Mediana czasu obserwacji do powiększenia się tętniaka wyniosła 63,5 miesiąca (zakres 54–73 miesiące). W przypadku pozostałych 52 (92,9%) stabilnych tętniaków mediana czasu obserwacji wyniosła 60,7 miesiąca (zakres od 5 do 184). Kliniczna obserwacja była dostępna dla 63 (98,4%) pacjentów. Mediana czasu obserwacji wyniosła 71,5 miesiąca (zakres od 7 do 187 miesięcy). W tym okresie nie stwierdzono krwotoków z obserwowanych tętniaków. W podgrupie 44 pacjentów leczonych wewnątrznaczyniowo: 59,1% tętniaków było leczonych przy użyciu spiral, 20,5% – przy użyciu spiral i stentu podporowego, 11,4% – spiral i FDD, a w 9,1% tętniaków użyto FDD. Jeden tętniak wymagał dwuetapowego leczenia. W celu leczenia 44 tętniaków przeprowadzono 45 procedur. Komplikacje proceduralne wystąpiły w 8 (17,8%) przypadkach, w 6 były one bezobjawowe. Przy wypisie ze szpitala stan neurologiczny 41 (93,2%) pacjentów nie uległ pogorszeniu w stosunku do wyjściowego. Jeden pacjent zmarł w trakcie hospitalizacji w następstwie krwotoku w trakcie leczenia, dwóch pacjentów zostało wypisanych z niewielkim deficytem. Podsumowując, ryzyko śmierci i powikłań wyniosło odpowiednio 4,5% i 2,3% w podgrupie tętniaków leczonych wewnątrznaczyniowo. Wystąpił 1 śmiertelny krwotok z leczonego tętniaka, 57 miesięcy po przeprowadzonym leczeniu (1 krwotok na 186,3 „pacjentolat"). W obserwacji radiologicznej dla 40 pacjentów 90% tętniaków zostało wyłączonych z krążenia. W przypadku 5% uwidoczniono napływ do szyi tętniaka, a w przypadku 5% – do worka tętniaka. Mediana czasu obserwacji radiologicznej wyniosła 7,25 miesiąca (zakres od 3 do 14 miesięcy). Tętniaki, w przypadku których nie uzyskano całkowitego wyłączenia z krążenia, były znacząco większe.

W odległej kontroli radiologicznej wykonanej u 23 (52%) pacjentów stwierdzono rekanalizację 4 (17,4%) wyłączonych z krążenia tętniaków.

W podgrupie 25 tętniaków leczonych mikrochirurgicznie 19 (76%) pacjentów zostało wypisanych w stanie jak przy przyjęciu. U prawie 1/4 pacjentów doszło do pogorszenia. W 5 przypadkach wystąpił niewielki, a w 1 przypadku ciężki deficyt neurologiczny. Pacjent z ciężkim deficytem zmarł w trakcie hospitalizacji.

Dla 21 (84%) pacjentów była dostępna długoterminowa ocena kliniczna z medianą 63 (zakres od 1 do 123) miesięcy. Nie obserwowano w tym okresie krwotoków z leczonych tętniaków. Podsumowując, śmiertelność w tej grupie wyniosła 4,8% i częstość trwałych deficytów również 4,8%.

Podsumowując wyniki w całej analizowanej grupie: śmiertelność wyniosła 2,4%, częstość trwałych deficytów neurologicznych – 1,6%, a roczne ryzyko krwotoku podpajęczynówkowego – 0,14%.

Praca nr 3

W trzeciej pracy dla podgrupy 129 tętniaków AComA porównano realnie zastosowane postępowanie (obserwację albo leczenie) z rekomendacjami uzyskanymi na podstawie dwóch skal. Wybrano dwie skale: skalę PHASES, oceniającą ryzyko krwotoku, i UIATS, która podaje następujące rekomendacje: obserwacja, leczenie lub wynik niekonkluzywny. W podgrupie 129 tętniaków 46,5% zakwalifikowano do obserwacji, a 53,5% do leczenia. Według skali PHASES znaczna część tętniaków (86%) została oceniona jako tętniaki niskiego ryzyka (wynik w skali PHASES poniżej 10), a 14% tętniaków – jako tętniaki wysokiego ryzyka (wynik w skali 10 i powyżej). W podgrupie tętniaków leczonych wartości w skali PHASES były znacząco wyższe. W skali UIATS rekomendację leczenia uzyskano dla 27% pacjentów, a obserwacji dla 32%. W przypadku 37% pacjentów nie uzyskano zdefiniowanej rekomendacji. Znaleziono statystycznie istotny związek pomiędzy rekomendacją uzyskaną w klasyfikacji UIATS a decyzjami podjętymi w rzeczywistości. Nie stwierdzono natomiast istotnej zależności pomiędzy rekomendacjami UIATS a interpretacjami uzyskanymi w skali PHASES. W podgrupie tętniaków obserwowanych punktacja w skali PHASES wyniosła od 4 do 9. W tej podgrupie nie było tętniaków wysokiego ryzyka według tej skali. Skala UIATS w tej podgrupie obserwowanych tętniaków rekomendowała leczenie dla 11%, obserwację dla 51%, a dla 38% wynik był niekonkluzywny. Pacjenci z rekomendacją leczenia byli znacząco młodsi, częściej mieli w wywiadach krwotok podpajęczynówkowy i rodzinne występowanie tętniaków, częściej palili i mieli mnogie tętniaki. W podgrupie tętniaków leczonych uzyskano wyniki w skali PHASES od 4 do 15, ale tylko 26% tętniaków w tej podgrupie zostało ocenionych jako tętniaki wysokiego ryzyka według PHASES (PHASES ≥ 10). W skali UIATS w tej podgrupie dla 42% pacjentów uzyskano rekomendację leczenia, dla 19% – obserwacji, a dla 39% brak było zdefiniowanej rekomendacji. W podgrupie leczonych tętniaków pacjenci, którzy uzyskali rekomendację obserwacji, mieli znacząco wyższe punktacje w skali PHASES w porównaniu z tymi, którzy uzyskali rekomendację leczenia lub dla których rekomendacja nie była zdefiniowana.

Podsumowując, w rzeczywistości obserwacji poddawano tylko tętniaki interpretowane jako niskiego ryzyka według PHASES. Leczono zaś 46% tętniaków niskiego ryzyka według PHASES. Zgodność naszego postępowania ze skalą PHASES wyniosła 60%.

W 60% przypadków rekomendacje według UIATS były zdefiniowane. Leczono 82% przypadków, dla których uzyskano rekomendację leczenia według UIATS, i obserwowano 68% przypadków, dla których uzyskano rekomendację obserwacji według tej skali. Nasze postępowanie było zgodne z rekomendacjami UIATS w 46% przypadków.

Zaskakujące było to, że zgodność między dwiema skalami była niska i wyniosła jedynie 32%. Porównując te dwie skale: 33% tętniaków wysokiego ryzyka według PHASES uzyskało rekomendację obserwacji. Aż dla 39% tętniaków wysokiego ryzyka nie uzyskano w UIATS zdefiniowanej rekomendacji. Z drugiej strony 27% tętniaków niskiego ryzyka według PHASES otrzymało rekomendację leczenia w UIATS. W naszej analizie tylko 7,2% leczonych tętniaków uzyskało jednocześnie rekomendację leczenia według UIATS i status tętniaka wysokiego ryzyka według PHASES. Z drugiej strony większość leczonych tętniaków (61%) uzyskała rekomendację leczenia w co najmniej jednej skali.

8. Wnioski

1. Zastosowanie stentów kierunkujących przepływ w leczeniu tętniaków tętnicy szyjnej wewnętrznej w odcinku ocznym przynosi bardzo wysoki odsetek zadowalających wyników radiologicznych i klinicznych. Wysokie ryzyko różnego rodzaju powikłań wymaga krytycznej oceny wczesnych i odległych następstw tych procedur, dalszego doskonalenia samych urządzeń i metod ich implantacji.

2. Zróżnicowane postępowanie z niepękniętymi tętniakami tętnicy łączącej przedniej pozwala utrzymać roczne ryzyko krwotoku podpajęczynówkowego na poziomie 0,14%. Brak krwotoków w grupie obserwacyjnej podkreśla znaczenie postępowania wyczekującego jako optymalnej strategii dla dużej grupy pacjentów. Ogólna śmiertelność wynosząca 2,4% oraz częstość trwałych deficytów na poziomie 1,6% wynikały z powikłań leczenia. Ryzyko deficytu neurologicznego i śmierci w podgrupie leczonych tętniaków tętnicy łączącej przedniej jest nieuniknione, ale odnosi się ono do grupy wysokiego ryzyka tętniaków z potencjalnie katastrofalnymi konsekwencjami w następstwie krwotoku.

3. Dla ponad dwóch trzecich ocen w podgrupie tętniaków tętnicy łączącej przedniej uzyskano niezgodne sugestie pomiędzy skalami PHASES a UIATS. Podkreśla to, że na decyzje terapeutyczne nadal główny wpływ mają doświadczenie ośrodka, indywidualne cechy tętniaka, dane kliniczne pacjenta oraz jego preferencje. Ze względu na ograniczenia obecnie stosowanych skal konieczne są badania prospektywne w celu doskonalenia i walidacji strategii podejmowania decyzji dotyczących niepękniętych tętniaków. Może to obejmować rozwój nowych alternatywnych skal, dopasowanych na przykład do specyficznej lokalizacji tętniaków.

9. Oświadczenia współautorów publikacji

Warszawa, 15.11.2024

Prof. Dr hab. Przemysław Kunert

OŚWIADCZENIE

Jako współautor pracy pt. Flow-diverting devices in the treatment of unruptured ophthalmic segment aneurysms at a mean clinical follow-up of 5 years oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi udział w: przygotowaniu koncepcji i metodyki, interpetacji wyników i nadzoru pracy.

Mój udział procentowy w przygotowaniu publikacji określam jako 30%.

Wkład Katarzyny Przepiórki w powstawanie publikacji określam jako 30%,

(imię i nazwisko kandydata do stopnia)

obejmował on: przygotowanie koncepcji i metodyki pracy, zbiór danych oraz interpretację wyników

(merytoryczny opis wkładu kandydata do stopnia w powstanie publikacji) *

Jednocześnie wyrażam zgodę na wykorzystanie w/w pracy jako część rozprawy doktorskiej lekarza Katarzyny Przepiórki.

(imię i nazwisko kandydata do stopnia)

KIEROWNIK
Oddziału Klinicznego Neurochirurgii
Centralny Szpital Kliniczny UCK WUM

....
Prof. dr hab. n. med. Przemysław Kunert
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 15.11.2024

Dr Jarosław Żyłkowski

OŚWIADCZENIE

Jako współautor pracy pt. Flow-diverting devices in the treatment of unruptured ophthalmic segment aneurysms at a mean clinical follow-up of 5 years oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi udział w interpretacji wyników.
Mój udział procentowy w przygotowaniu publikacji określam jako 7,5%.
Wkład Katarzyny Przepiórki w powstawanie publikacji określam jako 30%,
(imię i nazwisko kandydata do stopnia)
obejmował on: przygotowanie koncepcji i metodyki pracy, zbiór danych oraz interpretację wyników
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(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 15.11.2024

Dr Maciej Jaworski

OŚWIADCZENIE

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Mój udział procentowy w przygotowaniu publikacji określam jako 7%.

Wkład Katarzyny Przepiórki w powstawanie publikacji określam jako 30%,

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Maciej Jaworski

....

(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 17.11.2024

Daniel Rabczenko

OŚWIADCZENIE

Jako współautor pracy pt. Flow-diverting devices in the treatment of unruptured ophthalmic segment aneurysms at a mean clinical follow-up of 5 years oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi udział w interpretacji wyników.

Mój udział procentowy w przygotowaniu publikacji określam jako 7,5%.

Wkład Katarzyny Przepiórki w powstawanie publikacji określam jako 30%,

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(imię i nazwisko kandydata do stopnia)

Dokument podpisany
przez Daniel Rabczenko
Data: 2024.11.17
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(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 15.11.2024

Jakub Wojciechowski

OŚWIADCZENIE

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Mój udział procentowy w przygotowaniu publikacji określam jako 6%.
Wkład Katarzyny Przepiórki w powstawanie publikacji określam jako 30%,
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Jakub Wojciechowski
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Warszawa, 15.11.2024

Kamil Leśniewski

OŚWIADCZENIE

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Mój udział procentowy w przygotowaniu publikacji określam jako 6%.

Wkład Katarzyny Przepiórki w powstawanie publikacji określam jako 30%,

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Kamil Leśniewski

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(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 15.11.2024

Prof. Dr hab. Andrzej Marchel

OŚWIADCZENIE

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Mój udział procentowy w przygotowaniu publikacji określam jako 6%.

Wkład Katarzyny Przepiórki w powstawanie publikacji określam jako 30%,

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(imię i nazwisko kandydata do stopnia)

Andrzej Marchel

....

(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 15.11.2024

Łukasz Przepiórka

OŚWIADCZENIE

Jako współautor pracy pt. Unruptured Anterior Communicating Artery Aneurysms: Management Strategy and Results of a Single-Center Experience oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi udział w interpretacji wyników.
Mój udział procentowy w przygotowaniu publikacji określam jako 25%.
Wkład Katarzyny Przepiórki w powstawanie publikacji określam jako 34%,
(imię i nazwisko kandydata do stopnia)
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Łukasz Przepiórka
....
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 15.11.2024

Dr Sławomir Kujawski

OŚWIADCZENIE

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Mój udział procentowy w przygotowaniu publikacji określam jako 15%.

Wkład Katarzyny Przepiórki w powstawanie publikacji określam jako 34%,

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(imię i nazwisko kandydata do stopnia)

Kujawski

....

(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 15.11.2024

Prof. Dr hab. Andrzej Marchel

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Mój udział procentowy w przygotowaniu publikacji określam jako 6%.

Wkład Katarzyny Przepiórki w powstawanie publikacji określam jako 34%,

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Andrzej Marchel

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Mój udział procentowy w przygotowaniu publikacji określam jako 20%.

Wkład Katarzyny Przepiórki w powstawanie publikacji określam jako 34%,

(imię i nazwisko kandydata do stopnia)

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(merytoryczny opis wkładu kandydata do stopnia w powstanie publikacji) *

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Warszawa, 15.11.2024

Łukasz Przepiórka

OŚWIADCZENIE

Jako współautor pracy pt. Retrospective Application of Risk Scores to Unruptured Anterior Communicating Artery Aneurysms oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi udział w interpretacji wyników.

Mój udział procentowy w przygotowaniu publikacji określam jako 20%.

Wkład Katarzyny Przepiórki w powstawanie publikacji określam jako 30%,

(imię i nazwisko kandydata do stopnia)

obejmował on: przygotowanie koncepcji i metodyki pracy, zbiór danych oraz interpretację wyników

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(imię i nazwisko kandydata do stopnia)

Łukasz Przepiórka

....

(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 15.11.2024

Dr Sławomir Kujawski

OŚWIADCZENIE

Jako współautor pracy pt. Retrospective Application of Risk Scores to Unruptured Anterior Communicating Artery Aneurysms oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi udział w interpretacji wyników.

Mój udział procentowy w przygotowaniu publikacji określam jako 15%.

Wkład Katarzyny Przepiórki w powstawanie publikacji określam jako 30%,

(imię i nazwisko kandydata do stopnia)

obejmował on: przygotowanie koncepcji i metodyki pracy, zbiór danych oraz interpretację wyników

(merytoryczny opis wkładu kandydata do stopnia w powstanie publikacji) *

Jednocześnie wyrażam zgodę na wykorzystanie w/w pracy jako część rozprawy doktorskiej lekarza Katarzyny Przepiórki.

(imię i nazwisko kandydata do stopnia)

Kujawski

....

(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 15.11.2024

Dr hab. Edyta Maj

OŚWIADCZENIE

Jako współautor pracy pt. Retrospective Application of Risk Scores to Unruptured Anterior Communicating Artery Aneurysms oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi udział w interpretacji wyników.

Mój udział procentowy w przygotowaniu publikacji określam jako 8%.

Wkład Katarzyny Przepiórki w powstawanie publikacji określam jako 30%,
(imię i nazwisko kandydata do stopnia)
obejmował on: przygotowanie koncepcji i metodyki pracy, zbiór danych oraz interpretację wyników
(merytoryczny opis wkładu kandydata do stopnia w powstanie publikacji) *

Jednocześnie wyrażam zgodę na wykorzystanie w/w pracy jako część rozprawy doktorskiej lekarza Katarzyny Przepiórki.
(imię i nazwisko kandydata do stopnia)

Edyta Maj
(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 15.11.2024

Prof. Dr hab. Andrzej Marchel

OŚWIADCZENIE

Jako współautor pracy pt. Retrospective Application of Risk Scores to Unruptured Anterior Communicating Artery Aneurysms oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi udział w: przygotowaniu koncepcji i nadzoru pracy.

Mój udział procentowy w przygotowaniu publikacji określam jako 7%.

Wkład Katarzyny Przepiórki w powstawanie publikacji określam jako 30%,

(imię i nazwisko kandydata do stopnia)

obejmował on: przygotowanie koncepcji i metodyki pracy, zbiór danych oraz interpretację wyników

(merytoryczny opis wkładu kandydata do stopnia w powstanie publikacji) *

Jednocześnie wyrażam zgodę na wykorzystanie w/w pracy jako część rozprawy doktorskiej lekarza Katarzyny Przepiórki.

(imię i nazwisko kandydata do stopnia)

....

(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 15.11.2024

Prof. Dr hab. Przemysław Kunert

OŚWIADCZENIE

Jako współautor pracy pt. Retrospective Application of Risk Scores to Unruptured Anterior Communicating Artery Aneurysms oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi udział w: przygotowaniu koncepcji i metodyki, interpetacji wyników i nadzoru pracy.

Mój udział procentowy w przygotowaniu publikacji określam jako 20%.

Wkład Katarzyny Przepiórki w powstawanie publikacji określam jako 30%,

(imię i nazwisko kandydata do stopnia)

obejmował on: przygotowanie koncepcji i metodyki pracy, zbiór danych oraz interpretację wyników

(merytoryczny opis wkładu kandydata do stopnia w powstanie publikacji) *

Jednocześnie wyrażam zgodę na wykorzystanie w/w pracy jako część rozprawy doktorskiej lekarza Katarzyny Przepiórki.

(imię i nazwisko kandydata do stopnia)

KIEROWNIK KLINIKI Neurochirurgii Oddziału Klinicznego Centralny Szpital Kliniczny UCK WUM

Prof. dr hab. n. med. Przemysław Kunert

....

(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

10. Piśmiennictwo do rozdziałów w języku polskim

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5. Greving, J. P. *et al.* Development of the PHASES score for prediction of risk of rupture of intracranial aneurysms: a pooled analysis of six prospective cohort studies. *Lancet Neurol.* **13**, 59–66 (2014).
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