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An overview of decision-making in cerebrovascular treatment strategies: Part I - unruptured aneurysms

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ABSTRACT

Introduction: Unruptured intracranial aneurysm treatment has evolved over the last two centuries, starting from the introduction of aneurysm ligation and clipping, up until the inception of endovascular treatment and further advancements in both fields.
Research question: The wide variety of aneurysm presentations and possible treatment modalities, complicates the understanding of decision-making for the treatment of a given aneurysm. The goal of this article is to provide an overview of the best available evidence concerning unruptured intracranial aneurysm decision-making and identify insights and hiatuses, as well as providing a scaffold to surpass the subjectiveness of decision-making.
Materials and methods: A literature review was performed for the most impactful articles on decision-making in unruptured intracranial aneurysm treatment, to provide an overview on current practice.
Results: Two groups of decision-altering factors were identified; patient-related and aneurysm-related factors. A summary is presented of the general evidence, and the influence of age, aneurysmal mass-effect, as well as size, morphological aspects and specific anatomical locations on decision-making.
Discussion and conclusion: Decision-making for an unruptured intracranial aneurysm often comes down to combining these different patient- and aneurysm-related factors. In this paper, an evidence-based overview is provided into these different factors which alter management of unruptured saccular aneurysms.

1. Introduction

Over the years, aneurysm treatment changed from carotid artery occlusion, to surgical clipping, the introduction of detachable coils and finally incorporating advanced endovascular methods (stents, flow divertors and intrasaccular flow disruptor) (Lai and O'Neill, 2017; Dandy, 1938; Guglielmi et al., 1991; Lee et al., 2022). This evolution in aneurysm treatment leads to an abundance of choice. Combine this with the large pool of aneurysm presentations, shapes, locations, and sizes, as well as differences in treatment experiences in different centers, and a lot of therapeutic heterogeneity will occur.

This was demonstrated in an agreement study on the decision for a conservative, surgical or endovascular approach for unruptured intracranial aneurysms. A survey with 41 unruptured aneurysm cases was sent to 12 surgeons and 16 radiologists to evaluate their decisions, but remarkably a consensus was only found in only 24% of cases (Darsaut et al., 2014). Even among 233 interventional radiologists, there was heterogeneity for the estimation of complication- and success rates when confronted with 5 different unruptured aneurysm cases (Ospel et al., 2021).

Decision-making for unruptured aneurysms often revolves around a lot of uncertainty and as ruptures from individual aneurysms are rare, an expert opinion is hard to be made based on individual experience alone. Current practice often involves the use of different scoring systems to assess the risk of rupture (PHASES-score), the risk of growth (ELAPSS-score), and the risk of rupture after growth (triple-S prediction model), although some controversy exists around these scoring systems (Greving et al., 2014; Backes et al., 2017; Pagiola et al., 2020; Feng et al., 2021; Sturiale et al., 2021; Van Der Kamp et al., 2021). A consensus-based scoring tool (UIATS-score) was developed to aid in determining whether to treat or remain conservative for a given aneurysm. This

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Abbreviations

ICA	internal carotid artery
ET	endovascular therapy
mRS	modified Rankin Scale
GOS	Glasgow Outcome Scale
RROC	Raymond-Roy occlusion classification
ISUIA	International study for unruptured intracranial aneurysms
CURES	Collaborative unruptured endovascular versus surgery study
ONP	oculomotor nerve palsy
PComm	Posterior communicating artery
FD	Flow diverter
BAC	Balloon-assisted coiling
SAC	Stent-assisted coiling
WNA	wide-neck aneurysm
DNR	dome-neck ratio
WEB	Woven EndoBridge
PICA	posterior inferior cerebellar artery
AComm	Anterior communicating artery
DACA	distal anterior cerebral artery
MCA	middle cerebral artery
RCT	randomized controlled trial
SR	systematic review
CS	case series

utilizes different patient-, aneurysm- and treatment-related factors to weigh conservative and treatment-related risks against each other, but again, this scoring system was met with controversy (Etminan et al., 2015; Hernández-et al., 2021; Ravindra et al., 2017).

The determination of an optimal treatment modality for a particular intracranial aneurysm is a nuanced process, hinged upon a thorough evaluation of diverse patient- and aneurysm-related factors. These considerations play a pivotal role in shaping the decision-making process.

- **Patient-related factors** encompass a spectrum of considerations sourced from the best available general evidence, considering variations in treatment outcomes across different age groups, and addressing the nuanced decision-making scenarios arising from the presence of an aneurysmal mass effect.
- **Aneurysm-related factors** add an additional layer of complexity, taking into consideration parameters such as aneurysm size, morphological features, with special attention to wide-neck aneurysms, and the precise anatomical location of the aneurysm within the cerebral vasculature.

2. Aim and methods

This paper endeavors to offer a comprehensive overview of the most important literature on factors that influence decision-making in the treatment of saccular aneurysms. By synthesizing and critically analyzing existing evidence, the goal is to construct an evidence-based scaffold upon which informed decisions regarding saccular aneurysm treatment can be made in clinical practice. The best available evidence is divided into two parts: Part I focuses on unruptured aneurysms, and Part II addresses ruptured aneurysms.

Key studies were selected based on their impact, relevance, and contribution to the understanding of decision-making in intracranial aneurysms. The literature was gathered from widely recognized sources, including landmark studies, clinical guidelines, expert consensus documents, and pivotal trials. The selection process was guided by the goal of summarizing the essential knowledge required for clinical decision-making. Care should be taken with the interpretation of recent cohort studies, as currently, most centers follow an endovascular-first approach in treating aneurysms. This often results in more complex surgical clipping cases, which inherently will have a higher risk for complications.

This part I overview aimed to highlight the most important considerations for clinicians when evaluating treatment strategies for patients with unruptured and ruptured intracranial aneurysms.

3. Preface

The overarching goal of unruptured intracranial aneurysm treatment is to ensure a **safe** and **effective** therapeutic outcome. Safety hinges on achieving positive clinical results without encountering complications. Clinical outcomes, often evaluated using scales like the modified Rankin Scale (mRS) or the Glasgow Outcome Scale (GOS), distinguish between favorable outcomes (mRS 0–2, GOS 4–5) and adverse outcomes such as death or dependency (mRS 3–6, GOS 1–3) (Gaastra et al., 2022).

The unique challenge in unruptured aneurysm treatment lies in the potential emergence of **new neurological deficits**, especially considering the asymptomatic nature of most patients. These deficits, frequently overlooked by conventional grading systems like mRS and GOS, can lead to enduring daily challenges. To address this, a separate "morbidity" parameter is often used when specific data are unavailable.

Treatment efficacy is assessed by the prevention of post-treatment rupture, often correlated with the degree of aneurysm occlusion. Endovascular cohorts commonly employ the (modified) Raymond-Roy occlusion classification (RROC), distinguishing complete occlusion (grade 1), residual neck filling (grade 2), and any filling within the aneurysm sack (grade 3). Grades 1 and 2 are typically combined to indicate adequate aneurysm occlusion (Darflinger et al., 2016; Pierot et al., 2020a; Roy et al., 2001).

Despite successful initial treatment, the possibility of aneurysm recanalization exists, elevating the risk of hemorrhage. Significant recanalization prompts a decision for retreatment, introducing new risks and complications. The documentation of such retreatments is crucial for a comprehensive understanding of the treatment's long-term effectiveness (Metayer et al., 2021).

4. Patient-related factors influencing decision-making

4.1. Best available general evidence

The decision to treat an unruptured intracranial aneurysm is less clear compared to the ruptured counterparts (where treatment is typically warranted in the vast majority of cases). Decisions are often made based on different scoring systems (PHASES, ELAPSS, Triple-S and UIATS), which guide clinicians in a certain direction.

Copying the results of studies on ruptured aneurysms and applying them to the decision-making process of unruptured aneurysms is inappropriate and may lead to incorrect treatment decisions. For surgical purposes, the surgeon is not confronted with the 'angry brain' after performing a craniotomy in a ruptured aneurysm case, but they can easily identify important surgical landmarks and perform surgery with minimal retraction on the brain itself (Spetzler and Sanai, 2012). The absence of brain-swelling also allows the surgeon to perform more tailored, minimally invasive craniotomies, where there is less cortical exposure (Lan et al., 2017). Intra-procedural rupture of aneurysms is less frequent during clipping of unruptured aneurysms compared to ruptured cases, in contrary to coiling, where the risk is similar (Pierot et al., 2020b; Darkwah et al., 2018). These factors may contribute to

fewer complications when choosing for surgical treatment in unruptured cases and lead to different considerations in decision-making.

Only one randomized controlled trial (RCT) compared clipping and ET for the treatment of unruptured aneurysms, the **CURES** study. This study included 290 unruptured aneurysms, eligible for both clipping and ET. The primary outcome was "treatment failure" at 1 year, defined as a composite endpoint comprising either initial failure of aneurysm treatment, occurrence of an intracranial hemorrhage during follow-up or evidence of a residual or recurrent aneurysm. Treatment failure was seen in 19% of ET-patients compared to 9% in the surgical group. The difference between both groups was mainly due to the superior angiographical results of the clipping-group (93% vs 85% adequate occlusion at 1 year follow-up) and less failure to occlude the aneurysm with the intended treatment modality (1% vs 5%). More neurological deficits were seen after clipping, compared to ET (22% vs 12%), but this didn't result in worse functional outcomes after 1 year. A longer average hospital stay was also seen in clipped patients (6.7 vs 3.8 days) (Darsaut et al., 2023).

A systematic review with 106.433 patients evaluated the 30-day complication- and fatality rates for unruptured aneurysm. ET had a complication-rate of 4.96% and mortality-risk of 0.30%, risk factors for ET-complications were female gender, coagulopathy, diabetes, hyperlipidemia, cardiac morbidity, wide-neck IA, posterior circulation IA and the use of stent-assisted coiling. Surgically treated patients had a complication-rate of 8.34% and a mortality-risk of 0.1%. Risk factors for complications after clipping were advancing age, male gender, coagulopathy, smoking, hypertension, diabetes, congestive heart failure, posterior circulation - and calcified aneurysms (Algra et al., 2019). Following this publication, a risk-stratification score was made for individual aneurysms, the **SAFETEA**-score, which consists of 7 patient- and aneurysmal-related factors. This score can delineate the individual procedure risk for either ET or clipping but remains to be externally validated. This scoring system should not be used to guide decision-making directly, as the data used in this study were from pre-selected patients, which has an intrinsic bias. It does, however, find its place in informing patients of the treatment risk after deciding the intended modality (Algra et al., 2022).

A systematic review with 25 studies and 129.137 patients showed more ischemic complications after clipping, but added that this provided higher complete occlusion rates on short and long-term follow-up (Kang et al., 2020). When looking at the long-term outcomes concerning unruptured aneurysms in 16.622 coiled patients and 13.606 clipped patients, no differences in long-term mortality were seen, but again, there was a higher incidence of ischemic stroke in clipped patients and more retreatments in coiled patients (Krag et al., 2021), an overview is presented in Table 1.

The best available evidence on general principles of aneurysm treatment suggests that clipping is more effective at occluding aneurysms, with similar functional outcomes compared to endovascular treatment. This does come at the expense of a higher complication-rate and extended hospital stay.

4.2. Elderly population

Treating unruptured aneurysms in the elderly population is controversial, as the life expectancy is shorter, and the cumulative risk of rupture is lower compared to younger patients. Considering aneurysm treatment in elderly patients often combines these factors, along with patient expectations and physiology. **Increasing age** causes different vascular alterations, along with multiple comorbidities and general frailty, which all complicate both ET and clipping (Kandregula et al., 2022; O'Neill et al., 2019). Tortuous vessels and intraluminal atherosclerotic plaques may hamper endovascular access and pose a higher risk for thrombo-embolic complications, while surgery faces similar risks with increased difficulty of clipping atherosclerotic aneurysms (Willinsky et al., 2003).

A cohort of elderly Medicare beneficiaries showed more complications after clipping compared to ET (Qureshi et al., 2014). A national database study in the United States showed that clipping was associated with significantly more discharges to short- and long-term facilities, as well as an increased mortality-rate in elderly (Brinjikji et al., 2011; Barker et al., 2004), and significantly more retreatments in the ET-group (Qureshi et al., 2014). The case of cognitive performance after unruptured aneurysm treatment remains undecided in the current literature (Algra et al., 2019). A meta-analysis of ET in unruptured aneurysms in elderly, revealed a permanent morbidity in 5% and 3% new permanent neurological deficits. A good functional outcome was seen in 93% of unruptured aneurysms, with an adequate occlusion in 87% at 1 year. Noteworthy is the relative paucity of advanced endovascular methods in this population, with balloon- and stent-assisted coiling being used in only 5% and 3% of cases (Sturiale et al., 2013).

Overall, evidence suggests ET should be favored in elderly patients, as it comes with fewer complications, less morbidity and mortality, albeit at the cost of an increased retreatment ratio.

Evidence for **younger patient populations** is scarce and limited to case series, often combining data from ruptured and unruptured aneurysms, rendering any conclusions on unruptured aneurysm treatment impossible (Jee et al., 2019).

4.3. Mass effect

The diagnosis of unruptured aneurysms was made due to mass-effect in 5–6% of patients in ISUIA (a large prospective/retrospective cohort) (Wiebers et al., 1998). The two most frequent presentations of aneurysmal mass-effect are oculomotor nerve palsy (ONP) by a posterior communicating artery aneurysm (PComm) and visual disturbances due to compression of the optic nerve by carotid paraclinoid aneurysms.

Twenty-three percent of patients with PComm aneurysms present

Table 1
Overview of patient- and aneurysm related factors influencing treatment decisions in unruptured aneurysms. *Treatment failure was defined as a composite endpoint of either initial failure of aneurysm treatment, occurrence of an intracranial hemorrhage during follow-up or evidence of a residual or recurrent aneurysm. °Less visual morbidity was seen in asymptomatic patients. RCT: randomized controlled trial, SR: systematic review, CS: case series.

Unruptured aneurysms	Favors endovascular	No significant difference	Favors microsurgical	Most relevant evidence	Type of study
General evidence	Neurological deficits	mRSMortality	Less treatment failure*Retreatment	Darsaut et al. (2023)	RCT
	Complications			Algra et al. (2019)	SR
	Hospital stay			Kang et al. (2020)	SR
Elderly population	Complications	Cognitive deficits	Retreatment	Qureshi et al. (2014)	CS
	Lower mortality			Brinjikji et al. (2011)	CS
	Discharge to residential facility			Barker et al. (2004)	CS
ONP PComm aneurysms		Complete recovery	Any improvement	Zheng et al. (2021)	SR
Paraclinoid aneurysms	Less visual morbidity		Visual improvement	Asaid et al. (2017)	SR
	mRS		Occlusion		
Giant aneurysms		mRS		Dengler et al. (2016)	SR

with an ONP, this is due to the parallel course of the oculomotor nerve and **posterior communicating artery** in the interpeduncular cistern (Fig. 1). A sudden onset of (partial) ONP is regarded as a warning sign for impeding rupture and should be treated diligently (Hall et al., 2017). The most recent meta-analysis on this subject included 9 studies and 136 patients with ONP. When looking at complete recovery (resolution of ophthalmoplegia, ptosis, mydriasis, and diplopia), there was no difference between ET and clipping, but any improvement of ONP was seen more frequently in clipped patients. It is important to note that no distinction is made in the degree of partial recovery (a slight ptosis might be less bothersome than diplopia) (Zheng et al., 2021). Other factors associated with a better visual outcome included the preoperative severity of ONP and receiving treatment <7 days (Zhong et al., 2019).

Visual field deficits caused by **paraclinoid aneurysms** were evaluated in a systematic review with 1013 endovascular and 691 microsurgical patients. Asymptomatic patients had more visual morbidity after clipping (10.8% vs 2%), but when visual deficits were present, clipping had significantly more visual recovery (65.2% vs 49.8%) compared to ET. Adequate occlusions were seen in 98.2% and 73.7% in the clipped and ET-groups, although this came at the cost of more death or disability (9.5% vs 2.6%) (Zhong et al., 2019). The use of flow diversion (FD) showed visual improvement in 71% of patients, but a 5% morbidity and 3.9% mortality rate, with further visual deterioration in 4.9% (Kaiser et al., 2022; Silva et al., 2017).

To relieve the mass-effect from an aneurysm, surgical clipping seems to result in better ONP- and angiographical outcomes, although this comes at the cost (at least for paraclinoid aneurysms) of increased visual morbidity and worse functional outcomes.

5. Aneurysm-related factors influencing decision-making

5.1. Size

Small aneurysms are often incidentally found, and guidelines advise to observe them, which has been deemed safe in various observational studies (Wiebers et al., 1998; Gondar et al., 2016; Etminan and Rinkel, 2016). Although some exceptions can be made for de novo aneurysms or highly irregular aneurysms. In the past, it was observed that 13% of subarachnoid hemorrhages occur from IA with <5 mm in diameter (Kassell and Torner, 1983).

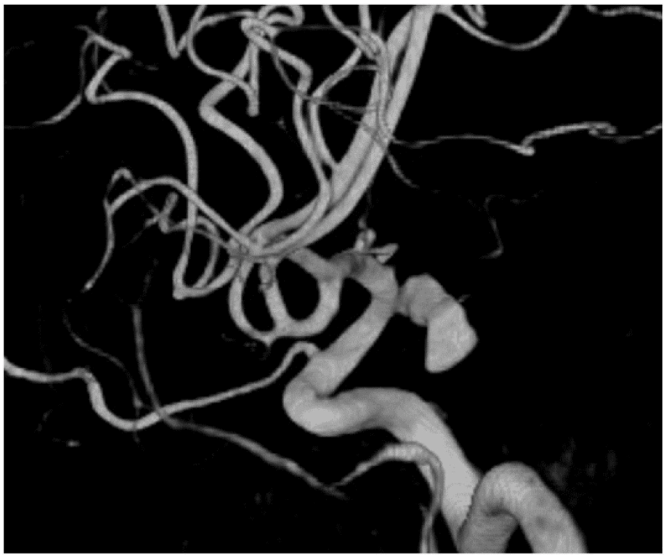

Fig. 1. 3D-reconstruction of digital subtraction angiography images. Injection of the left internal carotid artery, displaying a posterior communicating artery aneurysm with a narrow neck and long fundus.

A multicenter surgical series with 228 small aneurysms reported no changes in functional outcomes after clipping, permanent neurological morbidity was noted in 2.7% and a complete occlusion in 98.2% of patients (Bruneau et al., 2015). A meta-analysis of endovascular studies (261 aneurysms) on small unruptured aneurysms, showed a complete occlusion in 85% with a 6% retreatment rate. Morbidity and mortality were seen in 4%, with an intra-operative rupture rate in 6% of cases (Yamaki et al., 2016).

Currently, there are no studies comparing clipping and ET for small aneurysms, and we are left to compare cohort studies, which are likely to include a high selection-bias. Further comparative, preferably randomized studies are necessary to make any conclusions on this topic.

The **giant intracranial aneurysm** study group performed a systematic review on the treatment of 455 giant unruptured aneurysms, where no difference in functional outcome was found between clipping (80.7% mRS 0–2) and ET (84.4%) (Dengler et al., 2016). A meta-analysis of 39 endovascular studies with 894 aneurysms evaluated different endovascular options for unruptured large/giant IA. For coiling, balloon-assisted coiling (BAC), stent-assisted coiling (SAC) and FD, adequate occlusion rates were 59%, 73%, 72% and complication rates 20%, 39% and 29%, respectively. Recanalization was seen in 40% of aneurysms and a retreatment was necessary in 32% (Dengler et al., 2016). When looking at a large surgical series, clipping was performed in 45% and the other 55% was treated with a parent artery occlusion (with or without bypass). An adequate occlusion was achieved in 87%, with a retreatment rate of only 3.5%. A good functional outcome was seen in 81%, although there was a mortality of 13% (Sughrue et al., 2011).

Giant unruptured aneurysms present a population which remains difficult to treat with both clipping and endovascular measures. Surgical occlusion is feasible but comes at the cost of a high mortality in one retrospective case series. Endovascular treatment gives lower occlusion rates and remains associated with a high number of complications and retreatment-rate.

5.2. Wide-neck aneurysms

Aneurysms with a neck-width of ≥4 mm or a dome-neck ratio <2 are classified as wide-neck aneurysms (WNA). Wide-neck aneurysms often require more complex clip reconstructions and endovascular adjuncts such as stents or flow-diverters to prevent coil protrusion in the parent vessel (Hendricks et al., 2020).

WNA were the subject of the EVERRUN-study, a prospective study comparing clipping, coiling, BAC, SAC, and FD, with 224 aneurysms. In this patient cohort, 93.4% had a good functional outcome at 1 year in the ET-group, compared to 84.1% in the clipping-cohort. Final angiographic outcomes were better in the surgical cohort (97.6% vs 86.5%), although periprocedural and general complications were also higher after clipping (Mascitelli et al., 2021). A meta-analysis from 2017 displayed an adequate occlusion in 43.8% and 69.7% for ET and clipping, respectively. Complication rates were 21.1% and 24.3% in those respective groups, but no comparative statistics were performed, and clinical outcomes were not reported (Fiorella et al., 2017). When looking solely at coiling and SAC, the complete occlusion-rates were around 80% and 73%. Recanalization rates were 10% and 9%, with similar retreatment rates of around 5% (Zhao et al., 2016). Goertz et al. compared the Woven EndoBridge (WEB – an intrasaccular flow disruptor) and clipping for unruptured aneurysms, where good functional outcomes at 6 months were similar. Clipped patients did have more complete angiographic occlusions (94 vs 75%) and less technical failures (Goertz et al., 2021).

In conclusion, patients with unruptured wide-neck aneurysms have better functional outcomes and fewer complications after ET. Surgical clipping

provides better angiographic outcomes and subsequently less retreatments. When comparing clipping with WEB-treatment, functional outcomes are similar, but with a higher occlusion rate after surgery.

5.3. Location

Since the inception of coiling, posterior circulation aneurysms were predominantly treated with ET. A large systematic review with 1283 unruptured **basilar apex aneurysms** showed more adequate occlusions in the surgical group (91.7% vs 82.6%), but at the cost of less favorable clinical outcomes in 81.3% for the surgical cohort, compared to 89.8% of ET-patients (Medani et al., 2022).

Unruptured **posterior inferior cerebellar artery (PICA)** aneurysms are more likely to be treated surgically compared to other posterior circulation aneurysms, due to their relative superficial location. A systematic review with 136 unruptured PICA aneurysms (including saccular, dissecting, and fusiform aneurysms) was performed in 2016, evaluating clipping and ET. This study showed a complete occlusion in 93% vs 76%, recurrences in 15% vs 12%, rebleeding in 8% vs 4%, long-term morbidity and mortality in 16% vs 9% and good functional outcome in 91% vs 93%, although there were no comparative studies in this systematic review (Petr et al., 2016). Another systematic review evaluated saccular PICA aneurysms, showing similar functional outcomes (85% vs 86% good outcome) and a superior complete occlusion rate (89% vs 62%). These results are to be interpreted with caution, as only 65 unruptured aneurysms were included in this study (Ali et al., 2022), an overview is provided in Table 2.

To date, unruptured posterior circulation aneurysms are mostly treated through endovascular means, as ET is associated with better functional outcomes and less long-term morbidity. Data from PICA-aneurysms should be interpreted with more caution (combination of several types of aneurysms or underpowered data). The angiographic outcomes, however, were better in surgically treated patients in PICA aneurysms, and perhaps shouldn't be considered as a definitive endovascular aneurysm.

Aneurysms of the **ICA bifurcation** are rare and infrequently the subject of studies. There are two studies including both endovascularly and surgically treated patients, but either include both unruptured and ruptured aneurysms, or are underpowered to draw any conclusions (Konczalla et al., 2015; La et al., 2016).

Concerning **anterior communicating artery** (AComm) aneurysms, a review with 862 patients compared clipping, coiling and SAC. A good functional outcome (mRS 0–1) was found in 95.6%, 99.2% and 92.1% respectively, favoring coiling. Angiographic recurrences were not seen in clipped patients but were noted in 7% of coiled patients and in 12.3% treated with SAC (O'Neill et al., 2017). More advanced endovascular options (FD, SAC and intrasaccular flow diverters) were also compared to clipping and showed fewer major complications (3 vs 7%), and better clinical outcomes, but did display lower occlusion-rates (48–66 vs 81%) (Diana et al., 2022).

In general, evidence from unruptured AComm aneurysms shows that ET has less complications and a better functional outcome compared to clipping. Again, surgery was associated with higher occlusion rates and fewer recurrences, but at the cost of a higher morbidity.

Unruptured **distal anterior cerebral artery (DACA) aneurysms** originate distal from the communicating artery segment, and or often called pericallosal artery aneurysms. They were evaluated in a systematic review with 30 studies and 223 unruptured aneurysms. Surgically treated patients had

Higher complete occlusion rates (89% vs 54%) and lower recurrences (6% vs 22%). The long-term morbidity and mortality were similar between surgical and endovascular groups (11% vs 18%) (Petr et al., 2017). Anatomy can also guide treatment-decisions, and for DACA aneurysms they are based on the relative position of the aneurysm compared to the genu of the corpus callosum. So-called supra-genu aneurysms are preferably treated surgically, and infra-genu IA treated with ET for their ease of accessibility (Take et al., 2021; Carvi y and Nievas, 2013).

In conclusion, DACA aneurysms can be treated safely by both treatment modalities, with surgery offering better angiographical outcomes. Anatomical factors, such as the location compared to the genu of the corpus callosum are important in determining the best treatment strategy.

Middle cerebral artery (MCA) aneurysms are often treated surgically due to their complex anatomy, especially for unruptured aneurysms. When comparing coiling versus surgery, a complete occlusion was seen in 53% after coiling, in contrast to 94.2% for surgery. Unfavorable functional outcomes were found in 2.1% for clipping and 6.5% for ET (Smith et al., 2015; Alreshidi et al., 2018). A systematic review compared clipping with novel endovascular techniques (FD, SAC and intrasaccular FD) with 29 studies and 1552 patients. Clipping had better adequate occlusion-rates (95.7% vs 78.1%), with lower retreatment rates (1% vs 6%) and fewer complications (2.9% vs 5.6%), but ET was associated with higher rates of good neurologic outcomes (97%) compared to the surgical group (84%), which contradicts the previous studies (Toccaceli et al., 2020). The only randomized comparison between both treatment techniques comes from a subgroup analysis of CURES. This showed significantly less treatment failure in the surgical-group (2.3% vs 31.2%)[27]. An earlier subgroup analysis on the CURES-data found a similar amount of new neurological deficits (14–17%), but angiographic outcomes again favored surgically treated patients, with 75% vs 35% of complete occlusions (Darsaut et al., 2019). The use of WEB-devices in MCA aneurysms showed an adequate occlusion in 86%, with a 6.3% retreatment ratio, with 13% thrombotic or hemorrhagic complications and a good functional outcome in 94% of patients in a retrospective study with 165 patients (Adeeb et al., 2023).

Table 2
Overview of aneurysmal locations influencing treatment outcomes for different modalities in unruptured CA. *Treatment failure was defined as a composite endpoint of either initial failure of aneurysm treatment, occurrence of an intracranial hemorrhage during follow-up or evidence of a residual or recurrent aneurysm. Abbreviations; MnM: Morbidity and Mortality, SR: systematic review, RCT: randomized controlled trial.

Unruptured aneurysms	Favors endovascular	No significant difference	Favors microsurgical	Most relevant evidence	Type of study
Basilar apex	mRS		Occlusion	Medani et al. (2022)	SR
PICA	Morbidity	mRS	Occlusion	Petr et al. (2016)	SR
			Retreatment	Ali et al. (2022)	SR
AComm	mRS		Occlusion	O'Neill et al. (2017)	SR
	Complication		Recurrence	Diana et al. (2022)	
DACA		Long-term MnM	Occlusion	Petr et al. (2017)	SR
			Recurrence		
MCATreatment failure*	mRS		Occlusion	Smith et al. (2015)	SR
			mRS	Alreshidi et al. (2018)	Meta-analysis
			Retreatment		
			Complication	Toccaceli et al. (2020)	SR
			Treatment failure*	Darsaut et al. (2023)	RCT

Table 3
Overview of anatomical factors influencing treatment decisions.

Unfavorable for ET	Unfavorable for clipping
Vessel branching from aneurysm neck	Atherosclerotic plaque at neck
Partially thrombosed IA	Presence of perforating arteries
Aberrations of extracranial vasculature	Difficult surgical access

A dedicated RCT was started to evaluate the differences in clinical and angiographic outcome for middle cerebral artery aneurysms, the MCAAT (Darsaut et al., 2022).

Large systematic reviews on this subject give conflicting evidence. The only RCT on unruptured aneurysm treatment performed a subgroup analysis on MCA aneurysms which showed significantly less treatment failure for surgically treated patients, with a similar amount of new neurological deficits. This indicates that unruptured MCA aneurysms might be better suited for surgical strategies.

5.4. Anatomical considerations

Decision-making often comes down to interpreting the different anatomical factors of an aneurysm which are hard to grasp in randomized trials, but information can be obtained from case series, as they mention what factors influenced the decision-making prior to inclusion. These factors are represented in Table 3.

When looking at a single-surgeon series of unruptured aneurysms, a complication rate (mRS >1) of 10.1% was noted, with a 2.6% mortality rate. The variables found to affect both the complication rate and effectiveness of clipping (absence of rupture or retreatment) were aneurysm size, age, and posterior circulation location. With these variables, a scoring-system was devised to predict the risk of poor outcome for an effective aneurysm treatment (Morgan et al., 2016). A German study identified 5 anatomical factors (location, ruptured status, aspect-ratio, irregular shape, and aneurysm angle >110°) as risk-factors for an aneurysm remnant following clipping (Goertz et al., 2020). A risk-stratification score was also made by a Chinese group, where IA size ≥10 mm, core areas (containing small diencephalic and brainstem perforators), and cerebral ischemic comorbidity were found to significantly increase

Neurological morbidity in ET (Ji et al., 2016). All these studies show individual contributing factors, but when a scoring-system is devised, it was never externally validated.

6. Conclusion

This review offers an overview of the most relevant literature in decision-making for unruptured saccular intracranial aneurysms. Current literature on the comparative treatment of unruptured aneurysms is severely lacking, as there is only one completed RCT (CURES), which can give us unbiased results. New trials such as the MCAAT were initiated and should be commended.

In general, microsurgical treatment for aneurysms often results in superior angiographical outcomes, but at the cost of an increased morbidity. This results in ET often being chosen as the primary treatment option, but when looking at certain subsets of unruptured aneurysms, especially MCA and DACA aneurysms do seem to benefit more from a surgical treatment. There were some attempts at devising scoring-systems to predict good outcomes after aneurysmal treatment, but they often rely on individual case series, except for the SAFETEA-score, but even this scoring-system remains to be externally validated. Perhaps future endeavors might be aimed at including artificial intelligence in the complication predication of unruptured cases. This might allow for added clinical information which will influence decision-making, preventing the neurosurgeon and/or interventionalist from initiating in high-risk interventions (Staartjes et al., 2020).

Decision-making for unruptured aneurysms remains a precarious matter, as this is one of the few procedures that neurosurgeons and interventional radiologists can perform which is purely preventive in nature. Most patients presenting to our practice will be asymptomatic, and the treatment should not only aim at reducing the rupture-risk of a given aneurysm but should also not debilitate a patient. Given that there is still a lot of disparity among individual practitioners, teams and specialists with a similar background, decision-making should occur in a multi-disciplinary fashion. In these meetings, not only interventional radiologists and neurosurgeons should be present, but also the neurologist, to provide a middle ground for constructive discussions.

Declaration

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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