Current Advances in the Management and Rehabilitation of Middle Cerebral Artery Aneurysms: A Comprehensive Review

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Abstract:

Background: Middle cerebral artery (MCA) aneurysms represent a significant subset of intracranial aneurysms, with unique anatomical and pathological characteristics. Their prevalence, pathogenesis, risk factors, and management strategies remain crucial areas of neurosurgical research. Advances in both surgical and endovascular interventions have led to improved outcomes. However, rehabilitation following treatment is an often-overlooked aspect of patient recovery.

Methods: This review synthesizes existing literature on MCA aneurysms, including epidemiology, pathogenesis, clinical presentations, and treatment options. The review further explores the comparative effectiveness of surgical clipping and endovascular coiling and discusses rehabilitation strategies post-treatment.

Results: MCA aneurysms account for approximately 14-43% of all intracranial aneurysms. The primary pathophysiological mechanisms involve extracellular matrix degradation, hemodynamic stress, and genetic predispositions. Surgical clipping remains the preferred treatment due to the anatomical location and morphology of MCA aneurysms, while endovascular techniques continue to evolve as a viable alternative. Rehabilitation post-treatment, including neurorehabilitation and physical therapy, significantly impacts patient outcomes.

Conclusion: Optimal management of MCA aneurysms necessitates a multidisciplinary approach, integrating surgical expertise, endovascular innovation, and structured rehabilitation programs. Future research should emphasize individualized rehabilitation protocols to enhance functional recovery and quality of life post-intervention.

Keywords: Middle Cerebral Artery, Endovascular Interventions, Unruptured Aneurysm, Rehabilitation.

Introduction

Intracranial aneurysms are a frequent concern in neurosurgery, affecting approximately 2-10% of the general population. The growing utilization of radiological imaging has led to an increased detection rate, including cases of unruptured aneurysms (Greving et al., 2014; H. Kang et al., 2015; H. G. Kang et al., 2015; Nader-Sepahi et al., 2004; Zhang et al., 2019). Among these, middle cerebral artery (MCA) aneurysms are particularly common, representing 18-40%

of all intracranial aneurysms, with the majority remaining unruptured (Elsharkawy et al., 2013). The rupture risk of MCA aneurysms is well-established, increasing over time and potentially resulting in intracranial hemorrhage (Juvela et al., 2008; Mehan et al., 2014; Villablanca et al., 2013; You et al., 2010).

The management of unruptured MCA aneurysms includes both surgical and endovascular approaches (Bracard et al., 2010; Eboli et al., 2014; Quadros et al., 2007). Surgical clipping has traditionally been the preferred method due to its accessibility and favorable surgical outcomes (Aghakhani et al., 2008; Choi et al., 2012; Dammann et al., 2014; Diaz et al., 2014). However, advancements in medical technology have gradually increased the preference for endovascular treatment of unruptured MCA aneurysms (Bracard et al., 2010; Eboli et al., 2014). Endovascular procedures have demonstrated promising results, with permanent morbidity and mortality rates of 5.1% in unruptured MCA aneurysms treated using this method (Brinjikji et al., 2011; Hagen et al., 2019; Molyneux, 2002; Schwartz et al., 2018; Spetzler et al., 2015; Toccaceli et al., 2020).

Definition of Intracranial Aneurysm

Intracranial aneurysm is a pathological condition of the cerebral blood vessels characterized by local deterioration of the arterial wall accompanied by loss of the internal elastic lamina and disruption of the tunica media. Aneurysms can occur in all cerebral blood vessels, but the occurrence of aneurysms in the MCA is one of the main cases of intracranial aneurysms. (Chalouhi et al., 2013). The MCA is a cerebral blood vessel that is an extension of the ICA artery and is divided into 4 segments (Yang & Huang, 2015). MCA aneurysms mostly occur at the bifurcation (63%) with the location of the *early cortical branch* M1 as the most specific location (60%) (Elsharkawy et al., 2013)

MCA Aneurysm Occurrence

The prevalence of intracranial aneurysm is estimated to reach 2-10% in the entire population (Nader-Sepahi et al., 2004). Different results were shown in other studies where intracranial aneurysm occurred in the entire population with a narrower incidence range of 3-5% (Chalouhi et al., 2013).

Middle cerebral artery (MCA) *aneurysm* itself is a common occurrence in intracranial aneurysms. The incidence of MCA aneurysms reaches 14 – 43%

of all intracranial aneurysm events according to (Elsharkawy et al., 2013; Molyneux, 2002; Spetzler et al., 2015). MCA aneurysms mostly occur at the bifurcation (63%) with the location at the *early cortical branch* M1 as the most specific location (60%) (Elsharkawy et al., 2013). Rinne *et al* . studied the anatomical and clinical features of MCA aneurysms in a Finnish population of 1,314 consecutive patients and reported that 42.6% of all aneurysm patients had at least one MCA aneurysm, of which 20% had multiple MCA aneurysms, 17.8% had bilateral MCA aneurysms, and 11.2% had *mirror* MCA aneurysms (Rinne et al., 1996).

Pathogenesis of MCA Aneurysms

Vascular Structure and Pathophysiology

The aortic arch gives rise to the brachiocephalic artery, which then branches into the right common carotid artery. Meanwhile, the left common carotid artery originates directly from the aortic arch. Both common carotid arteries run parallel and divide at the mandible into the external and internal carotid arteries. The external carotid supplies blood to the face and neck, whereas the internal carotid remains unbranched until it gives rise to the ophthalmic artery. It then bifurcates into the anterior and middle cerebral arteries (MCA), the latter being the largest terminal branch. The MCA is divided into four segments (M1–M4), with M1 originating from the internal carotid artery and extending into the brain, M2 branching laterally into the Sylvian fissure, M3 extending through the insula, and M4 reaching the cortex.(Navarro-Orozco & Sánchez-Manso, 2025)

The MCA plays a crucial role in supplying oxygenated blood to key brain areas. Its cortical branches irrigate the primary motor and somatosensory cortex, covering the face, trunk, and upper limbs, along with the insular and auditory cortex. The lenticulostriate vessels from the MCA supply the basal ganglia and internal capsule. The superior division of the MCA nourishes the lateral inferior frontal lobe, which includes Broca’s area, essential for speech production and language comprehension. The inferior division supplies the superior temporal gyrus, encompassing Wernicke’s area, which is responsible for language development and speech comprehension.(Navarro-Orozco & Sánchez-Manso, 2025)

Extracellular Matrix Degradation

The extracellular matrix is a dynamic structure that is constantly undergoing *remodeling* through its relationship with vascular cells. Given the secretory function of smooth muscle cells in cerebral arteries rather than contractile function, the mechanical strength of large arteries mainly depends on the cross-linking of elastin and collagen. The longevity of elastin produced in early embryogenesis is similar to the human lifespan, and it rarely undergoes a wear and tear process. Once damage or destruction of the extracellular matrix occurs, the course of the disease may be irreversible. Matrix metalloproteinases (MMPs) and tissue inhibitors of metalloproteinases produced by smooth muscle cells and inflammatory cells mediate the degradation and remodeling processes of the extracellular matrix. An imbalance between MMPs and their inhibitors contributes to the initiation and progression of cerebral aneurysms (Jung, 2018).

Lysyl oxidase (LOX) catalyzes a critical step in the cross-linking of elastin and collagen (Rodriguez et al., 2008). LOX requires a tightly bound copper ion for its active role. Since the amount of copper in the diet directly affects LOX activity (Gacheru et al., 1990), copper deficiency during development may impair LOX activity and weaken vessel wall integrity leading to aneurysm development in adulthood. Recently, it was shown that copper deficiency in mice during development resulted in a complex vascular wall abnormality involving thoracic aortic aneurysms and cerebral aneurysms (Jung et al., 2016). The thoracic aorta was dilated with irregular elastic fibers, and fusiform and saccular aneurysms were found in surviving mice. Since copper deficiency often occurs during infancy in cases of cow's milk or low-copper formula feeding **(Lönnerdal, 1998; Lönnerdal et al., 1985)**, the infant's environment and feeding habits may influence the prevalence and outcome of aneurysms. Clinically, various extracellular matrix abnormalities have been detected in patients with connective tissue diseases such as osteogenesis imperfecta, Ehlers-Danlos vascular syndrome, and Marfan syndrome, which are commonly associated with cerebral aneurysms (Jung, 2018).

Hemodynamic Stress and Its Role in Aneurysm Formation

Cerebral aneurysms usually occur in the ACOM, PCOM, MCA bifurcation, and basilar artery bifurcation where the local *(X.-J. Zhang et al., 2018)*. Blood flow at arterial junctions, bifurcations with wider bifurcation angles, or abrupt vascular angles is the most turbulent, and the shear stress in these areas is the greatest. High wall shear stress causes endothelial cell damage, smooth muscle cell degeneration, and media thinning. Hemodynamic forces also cause endothelial and smooth muscle cells to release MMP-2 and MMP-9 and further degrade the extracellular matrix, resulting in aneurysm formation. The magnitude of local shear stress correlates well with the degree of internal elastic lamina loss, medial degeneration, and arterial bulging (Metaxa et al., 2010). Shear stress is clearly a powerful trigger for developing aneurysms in predisposed individuals. In this regard, flow diverters to attenuate shear stress have been recently applied to reduce the risk of aneurysm growth and rupture (Seshadhri et al., 2011). On the other hand, recent investigations with computational fluid dynamics (CFD) models *support* the role of differential hemodynamics in cerebral aneurysm development and rupture. While high wall shear stress promotes aneurysm formation, low stress is associated with aneurysm rupture (Can & Du, 2016). Furthermore, wall shear tension *is* significantly lower at the rupture point of the formed sac, and a meta-analysis suggests that decreased wall shear stress can predict aneurysm rupture (Zhou et al., 2017).

Smoking is associated with a higher prevalence of cerebral aneurysms and a higher risk of rupture. The mechanisms by which smoking results in cerebral aneurysm formation and rupture are suggested to be increased wall *shear stress* due to increased blood volume and viscosity and nicotine-induced vasoconstriction (Can et al., 2017). Extracranial carotid disease may hemodynamically increase shear stress on the contralateral distal vascular bed by increasing blood volume. According to this hypothesis, contralateral carotid artery ligation has been used to create experimental cerebral aneurysms; however, the resulting modeling has been inconsistent and inefficient. When we investigated the relationship between extracranial carotid disease and cerebral aneurysm characteristics, aneurysms were evenly distributed regardless of stenosis laterality. The rate of aneurysm growth and rupture in patients with significant extracranial carotid artery stenosis was also low (Cho et al., 2013).

Genetic and Environmental Factors

Genetic factors play a significant role in intracranial aneurysm (IA) formation, particularly in cases involving multiple or hereditary aneurysms, with the specific genes affected varying based on ethnicity. External factors such as hypertension and smoking contribute to aneurysm development by triggering arterial wall inflammation. The endothelin pathway is a potential target for IA prevention and treatment.(Mohan et al., 2015)

Research has suggested that lipid metabolism disorders influence the formation and rupture of intracranial aneurysms through specific biomarkers. However, the molecular changes caused by these disorders in IA remain insufficiently explored. Although omics technologies have advanced the identification of novel biomarkers and biological pathways, no comprehensive studies have applied proteomics, lipidomics, or multi-omics approaches to systematically investigate the systemic molecular alterations linked to lipid metabolism disorders in IA. Future research should prioritize these areas to better understand the role of lipid metabolism in aneurysm development and rupture.(Pan et al., 2023)

Clinical Presentation and Risk Factors

MCA aneurysm is the most common type of lesion in the intracranial arterial wall, and often causes headache, dizziness, ischemic infarction, neck pain and mass effect, while certain cases may also be asymptomatic (Aoki et al., 2012). A study conducted by Chen and Fang in 2019 showed slightly different symptoms where neck pain was the most common symptom (16.3 - 19.6%) followed by headache and dizziness (10.9 - 13%). It was also reported that 7.6 - 13% of patients were asymptomatic. Symptoms of MCA aneurysm can also cause mass effects shown in the same study as many as 10.9 - 25% of patients experienced signs of mass effect (Chen & Fang, 2019).

Risks of MCA Aneurysm

In the report according to the anatomical relationship of ruptured and unruptured MCA aneurysms, the rupture factors by multivariate analysis were first perpendicular to the neck height/diameter, second flow angle, and third M1-M2 angle. MCA aneurysms are located relatively superficially in the sylvian fissure. MCA aneurysms are relatively easy to find than other aneurysms. However, the neck dome ratio is larger than other aneurysms. MCA branches may emerge from the sac or neck of the MCA aneurysm, making its treatment quite complicated. Therefore, surgical clipping is preferred over coil embolization in treating MCA aneurysms even now. This shows the importance of a neurosurgeon's understanding of the features, specificity, simulation methods, intraoperative monitoring, and surgical techniques of MCA aneurysms (Ikawa, 2019).

Overall patient outcome is largely determined by preoperative circumstances, and surgical morbidity is actually low. A poor Hunt-Hess grade preoperatively is a strong indication for endovascular coiling, unless they have a large temporal hematoma that needs to be evacuated. In addition, some patients may benefit from hemicraniectomy. Open surgery can provide the opportunity to perform reconstructive cutting of most MCA aneurysms; at the same time, the surgeon may be able to perform thrombectomy, bypass, or even aneurysm trapping (Ikawa, 2019)

Classification of MCA Aneurysm

Yoko Kato issued a classification of *unruptured* MCA aneurysms for *the World Federation of Neurosurgeons* (WFNS) based on morphological features (Kato, n.d.).

1. Type 1 (simple aneurysm) is an aneurysm that originates as a bulge from a well-defined weakness in the arterial wall and is confined to the area of greatest hemodynamic stress at the bifurcation and does not extend proximally to the M1 vessel.

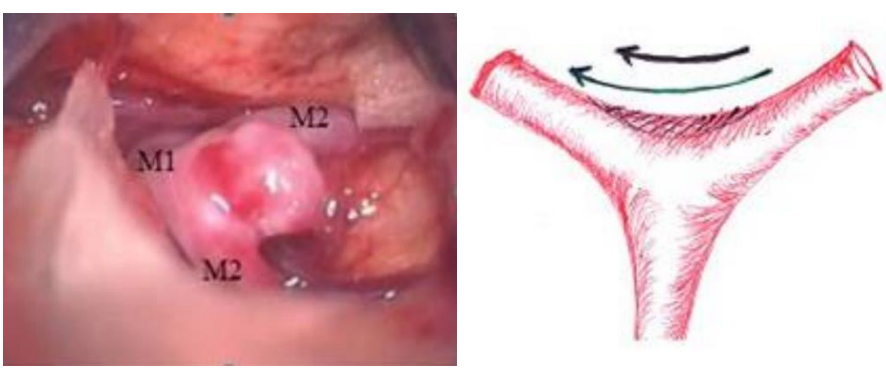

Figure 2.3 Imaging of an unruptured MCA aneurysm type 1. Intraoperative view (left) and schematic drawing of the MCA branching with the axis of the M2 branch at the branching (green arrow) parallel to the axis of the aneurysm neck (black arrow) in a type I aneurysm with the shaded area indicating the origin of the aneurysm.

2. Type 2 (central type) is an aneurysm with an initial area of weakness in the vessel wall reaching M1 proximally and generally occludes or hangs over the bifurcation.

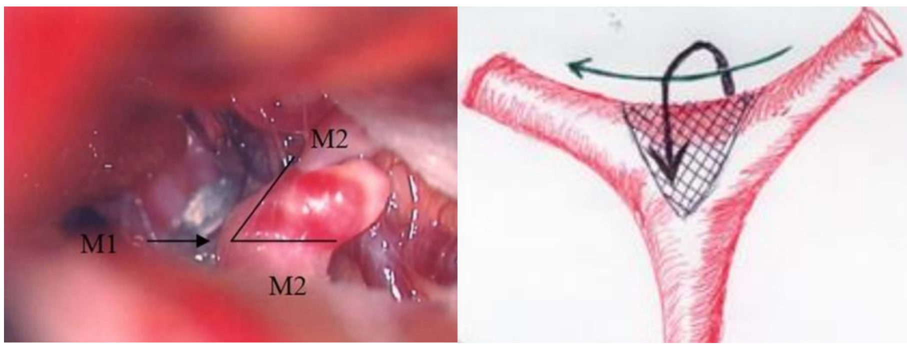

Figure 2.4 Image of an unruptured MCA aneurysm type 2. Intraoperative view (left) and schematic representation of the MCA branching with the axis of the M2 branch at the branching (green arrow) perpendicular to the axis of the aneurysm neck (black arrow) in a type II aneurysm with the shaded area indicating the origin of the aneurysm extending proximally to M1.

3. Type 3 is an aneurysm with an aneurysm neck that has complications in the form of perforators or branches coming out of the neck.

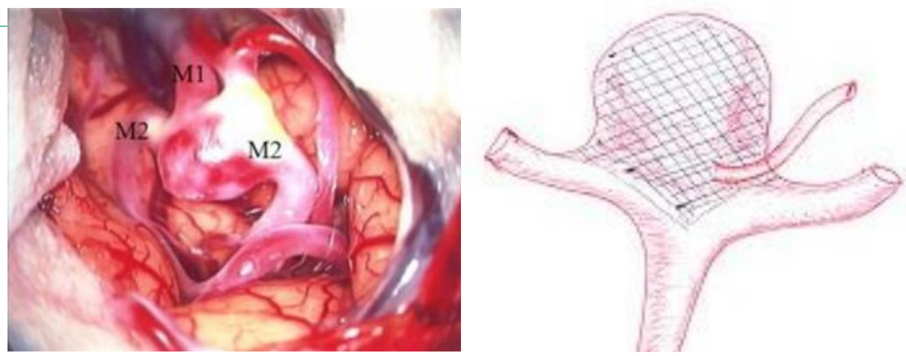

Figure 2.5 Image of an unruptured MCA aneurysm type 3.

4. Type 4 (complex aneurysm) is an aneurysm with M2 branches appearing to originate from the aneurysm and not from M1 due to complete involvement of the walls of M1 and/or M2. These aneurysms are generally large in size as *giant* MCA *bifurcation aneurysms* involving the proximal portions of the existing branches and requiring reconstruction of the bifurcation.

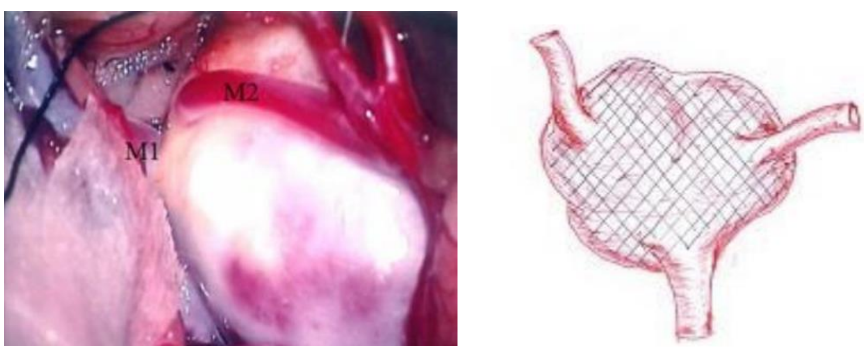

Figure 2.6 Image of an unruptured MCA aneurysm type 4. Intraoperative image (left) and schematic image (right) showing that M2 arises from the aneurysm and not from M1.

5. Type 5 (*blister aneurysm*) is an aneurysm seen during surgery for aneurysms in a different location.

Figure 2.7 Image of an unruptured MCA aneurysm type 5. Intraoperative view (left) and schematic (right).

MCA Aneurysm Surgery

Many surgeons report good results with surgical treatment of unruptured aneurysms, although some studies suggest that unruptured aneurysms should not be operated on (Chang & Kirino, 1995). Outcomes worse than good or excellent are unacceptable for asymptomatic incidental aneurysms. However, it must be recognized that morbidity is never zero, even with extensive surgical experience. Unruptured MCA aneurysms pose technical problems because many aneurysms are large (15%), and there is often a need for reconstruction and preservation of the MCA branches. This often makes the direct surgical approach the procedure of choice for the management of unruptured MCA aneurysms (Flamm et al., 2000).

MCA aneurysms themselves can be easily accessed through surgery due to their location and relatively superficial configuration. This makes surgery still widely used as first-line management (Wiebers, 2003). Unruptured MCA aneurysms cause problems in surgical techniques because many aneurysms are large (15%), and there is often a need for reconstruction and preservation of MCA branches. This often makes a direct surgical approach the procedure of choice in the management of unruptured MCA aneurysms (Flamm et al., 2000). Unruptured MCA aneurysms with small sizes still have a risk of rupture so that intervention can still be considered (Suzuki et al., 2009). A study conducted by Choi, *et al* ., showed that unruptured MCA aneurysms treated with surgery and *clipping* had good results. These results are mainly associated with the location of the MCA which is easily accessible through various surgical approaches so that surgical treatment is recommended in patients with favorable MCA aneurysm angiography and small size (S. W. Choi et al., 2012).

Outcomes surgical procedures

MCA aneurysms are located peripherally and usually have a wide neck that incorporates one or both M2 segments. The consequence of this configuration is that most MCA aneurysms are within the scope of surgical intervention. A report by Nussbaum showed that microsurgical aneurysm clipping yielded better outcomes than endovascular intervention for unruptured MCA aneurysms, which should be reserved for older patients, those considered at high risk for complications from open surgery based on medical comorbidities or aneurysm-related factors, such as arterial wall atheroma, or certain aneurysm morphologies. A study of 750 cases of unruptured MCA aneurysms showed good outcomes for surgical intervention even though they were performed in hospitals that adopted and recommended endovascular intervention for such cases (Nussbaum et al., 2007).

Several authors have described series of surgically treated MCA aneurysms, often as part of larger reported studies (Aghakhani et al., 2008; S. W. Choi et al., 2012; Dammann et al., 2014; Diaz et al., 2014). Surgical treatment is generally associated with good outcomes and excellent long-term survival in these aneurysmal anomalies. In the hands of experienced microvascular surgeons treating intracranial aneurysms in high-volume centers/hospitals, surgical occlusion rates for aneurysms have exceeded 95%, while major complication rates have been less than 3% (Smith et al., 2015).

Endovascular Intervention for MCA Aneurysm

Despite the technical disadvantages, an increasing trend towards endovascular procedures has emerged over the last decade with the emergence of reports regarding Coiling as an option in the management of MCA aneurysms. Continuous innovations in endovascular techniques and devices have been introduced to address these technical challenges, including stent-assisted coiling, improved catheters with increased inner *diameter* and flexibility, balloon remodeling, and three-dimensional rotational angiography. (Yang & Huang, 2015). In an early report by Iijima et al. in 2005 with a case series of 149 MCA aneurysm patients, the overall mortality and morbidity rates were 6 and 1% for ruptured aneurysms and 1 and 3% for unruptured aneurysms, respectively (Iijima et al., 2005). The reported outcomes were comparable and even appeared superior when compared to microsurgical treatment. However, only 77.2% of all patients achieved complete occlusion of the aneurysm. Another report also identified a recurrence rate of 20.0% at 15 months of follow-up , of which 11.4% required re-treatment (Mortimer et al., 2014; Vendrell et al., 2009)Following these studies, several studies on the feasibility and efficacy of endovascular treatment in the management of MCA aneurysms have been reported . The most recent series reported by Kadkhodayan et al. in 2014 including 292 patients and 346 MCA aneurysms showed an intraoperative thromboembolic event rate of 13.6%, an overall morbidity rate of 2.9% at 30-day follow-up and a complete or near-complete occlusion rate of 91.8%, with a mean follow-up of 2 years [38]. These endovascular studies on the management of MCA aneurysms achieved comparable outcomes to surgical management and established the rationale for extending the " *coil first* " policy to the management of MCA aneurysms. (Yang & Huang, 2015).

Despite the dramatic trend of increasing endovascular management of MCA aneurysms, evidence to justify *coiling* as a management strategy for MCA aneurysms is inadequate. When examining short-term (1-year) follow-up outcomes in ISAT, patients with MCA aneurysms were the only subgroup in which superiority of clipping over coiling regarding treatment outcomes was demonstrated. Furthermore, as suggested by Rodriguez, the distribution of aneurysm locations in the ISAT study was significantly different from what was previously reported, with MCA aneurysms comprising only 14.0% of all aneurysms in ISAT compared to approximately 25.0% in the reported literature, suggesting a potential sampling bias favoring maximal outcomes in the coiling group **(Rodríguez-Hernández et al., 2013)**. Furthermore, currently available comparative studies and meta-analyses on the treatment of MCA aneurysms suggest little to moderate advantage of coiling clipping. Therefore, further investigation is needed to justify endovascular therapy as a viable alternative to surgical therapy in the definitive treatment of MCA aneurysms (Yang & Huang, 2015).

Various endovascular procedures can be performed in cases of MCA aneurysm, both in ruptured and unruptured conditions. Endovascular treatment options include coiling procedures with either *single-* or *double - catheter* , *stent-assisted techniques coiling* (*self expendable, standard* or *round* or *double-balloon*), and *flow diverter* (either *flow re-direction endoluminal device* (FRED) from MicroVention, *Woven EndoBridge* (WEB) from Sequent Medical, or Pipiline from Medtronic) with a variety of device options from different manufacturers with their respective purposes of use and indications (Gory et al., 2014; Hagen et al., 2019).

Outcomes endovascular procedure

Endovascular treatment of ruptured intracranial aneurysms has been considered the treatment of choice since the publication of the ISAT study in 2002. Recently, ISUIA confirmed that unruptured aneurysms can also be treated with endovascular treatment. Because MCA aneurysms were underrepresented in the ISAT study, there is still debate about the best way to treat aneurysms. Hagen, *et al* ., reported a mortality rate of 0.6% at hospital discharge and 2.7% at long-term *(Hagen et al., 2019)*. This is also in line with other studies that showed similar mortality rates for mortality during hospitalization but in the study by McDonald, *et al* ., showed worse outcomes for the operated group in long-term *(McDonald et al., 2013)*. Comparison between *clipping* and endovascular surgical procedures showed comparable results (1.9 – 2.0%) **(J. H. Choi et al., 2016; Rodríguez-Hernández et al., 2013)**.

Degree of occlusion after endovascular procedures

The increasing use of endovascular procedures, especially *coiling procedures* for intracranial aneurysms, has led to the need for a classification to standardize intervention outcomes. The most commonly used classification is the *Raymond-Roy Occlusion Classification* or also known as *the Montrel Scale* or *Raymond Montreal Scale* (Roy et al., 2001). This scale has been widely used and agreed upon as the standard classification of aneurysm occlusion grade. Class 1 is complete obliteration. Class 2 is residual aneurysm neck. Class 3 is referred to as residual aneurysm. In class 3, previous studies have shown a high risk of failure to achieve total occlusion and a high potential for bleeding or *rebleeding* (Johnston et al., 2008; Ries et al., 2007a).

Another endovascular procedure is *a flow diverter* that utilizes blood flow diversion. Two variables are assessed: the volume of contrast filling and the degree of contrast material stasis. Aneurysm filling is graded as: A - complete (>95%); B - incomplete (5-95%); C - residual neck (<5%); or D - no filling (0%). The degree of stasis is determined by the time of contrast clearance from the aneurysmal sac as determined by the angiogram phase: 1 - No stasis (clearance in the arterial phase, before the capillary phase); 2 - Moderate stasis (clearance before the venous phase); 3 - Significant stasis (contrast remains in the aneurysm until the venous phase and beyond). This creates a total of ten possible grades, with the stasis grade being assigned to each filling grade except Grade D, no filling. (A1, A2, A3, B1, B2, etc.) **(O'Kelly et al., 2010)**.

Recanalization after endovascular procedures

management after endovascular embolization has a higher recanalization frequency compared to surgical clipping, ranging from 6.1% to 33.6% (Ries et al., 2007b). Assessment of aneurysm recurrence is essential after endovascular treatment given the risk of recanalization. Several risk factors have been proposed to explain aneurysm recurrence, including aneurysm morphological features, coil compaction and/or migration, and different types of endovascular embolization techniques (Jeon et al., 2016; Ries et al., 2007b). Studies using CFD have also demonstrated a key role of cerebral hemodynamics in aneurysm recurrence (Luo et al., 2011; Sugiyama et al., 2016). However, previous reports based on CFD were mainly conducted on relatively small patient-specific cases (e.g.: less than 10 cases) or on a subset of patients, which challenges the representativeness of hemodynamic findings (Q. Zhang et al., 2018).

Outcomes post-endovascular procedure

Results reported by several studies reported comparable endovascular outcomes compared to published surgical data of unruptured MCA aneurysms (mRS 0-2 in 92%). Intraprocedural aneurysm rupture is considered an important complication in unruptured aneurysm interventions especially in surgical *clipping* . Rodriguez-Hernandez, *et al* ., found a 2-fold higher risk for such complications during surgery compared to endovascular treatment (3.4% versus 1.7%). The main complication in endovascular treatment is still thromboembolic events (3.2%) **(Rodríguez-**

Hernández et al., 2013). Another report by Chyatte, *et al* ., showed the superiority of surgery in a 6-month follow-up where 94% of patients showed no significant decrease in functional outcome (Chyatte & Porterfield, 2001).

clipping surgery , there are still many studies that support endovascular procedures. A study conducted in 2017 on coiling procedures in cases of unruptured MCA aneurysms showed good results for clinical outcomes after endovascular procedures. The study reported that endovascular procedures had a good level of safety and neurological outcomes in endovascular procedures. The good functional outcomes were not significantly different from *clipping procedures* (Alreshidi et al., 2018)(Alreshidi et al., 2018). It should be noted that the differences in the results of these various studies have decreased in size from previously published meta-analyses, which may indicate that the safety of endovascular procedures increases with proper patient selection and increasing technology or experience plays a major role (Smith et al., 2015). Studies, especially meta-analyses, that examine the outcomes of endovascular procedures with *clipping* increasingly tend to support endovascular procedures, although many still show that the outcomes of patients who receive *clipping procedures* are better (Blackburn et al., 2014).

The Importance of Rehabilitation in Patient Recovery

Rehabilitation plays a crucial role in the recovery of patients following aneurysmal subarachnoid hemorrhage (aSAH), significantly influencing functional outcomes and overall quality of life. In this study, patient demographics aligned with existing literature, with the majority being middle-aged women of varying educational and employment backgrounds. Despite the absence of randomization, the control and early rehabilitation groups were comparable, as data collection spanned consecutive years. Early rehabilitation was successfully implemented within neurointensive care, with interventions tailored to clinical status, particularly for those with motor deficits. One year post-aSAH, most survivors regained independence, with early rehabilitation demonstrating notable benefits in poor-grade patients by enhancing motor recovery and promoting neuronal plasticity. However, no significant improvements were observed in good-grade patients, likely due to a ceiling effect in global outcome measures. Potential confounding factors, such as age and initial clinical severity, were accounted for, confirming their negative impact on recovery. While the inability to randomize patients and the exclusion of those requiring prolonged intensive care were study limitations, findings suggest that early rehabilitation is a safe and effective intervention for poor-grade aSAH patients, warranting further investigation into optimal rehabilitation timing and strategies for severe cases (Karic et al., 2016)

Cognitive impairments following aSAH remain a major challenge, affecting executive function, language, and memory, often hindering survivors from returning to work and diminishing their quality of life. While advances in acute-phase management have reduced mortality, long-term cognitive rehabilitation remains understudied. This review highlights the cognitive deficits associated with aSAH, their contributing factors, and potential interventions, drawing insights from traumatic brain injury (TBI) research due to shared pathophysiological mechanisms. Neurorehabilitation strategies, such as attention process training, metacognitive therapy, and cognitive-behavioral interventions, show promise, while pharmacological options like amantadine and donepezil may provide additional benefits. A structured, comprehensive approach incorporating standardized neuropsychological assessments, early intervention, and long-term follow-up is essential to optimize cognitive recovery. Further research is needed to validate these interventions, ensuring targeted rehabilitative strategies that enhance functional independence and overall quality of life for aSAH survivors (Abdelgadir et al., 2024)

Exercise-based rehabilitation is another essential component of post-stroke recovery, with strong evidence supporting the inclusion of cardiorespiratory and mixed training to improve mobility, balance, and overall fitness. Although the low number of deaths suggests that exercise is a safe intervention, it remains inconclusive whether it directly reduces mortality or the risk of dependency. Cardiorespiratory training, particularly walking-based exercises, has been linked to improved disability outcomes and a ~7% reduction in stroke-related hospitalizations due to an increase in VO2 peak. However, cognitive function remains an underexplored yet critical area for patients recovering from aSAH and stroke. Further well-designed randomized trials are needed to establish the optimal exercise regimen, its comprehensive benefits, and long-term effects on both physical and cognitive recovery. Integrating tailored exercise programs within post-stroke and post-aSAH rehabilitation protocols may enhance overall patient outcomes and improve long-term functional independence.(Saunders et al., 2020)

Conclusions

The management of MCA aneurysms requires a multidisciplinary approach combining surgical and endovascular advancements with structured rehabilitation. While surgical clipping remains the standard, endovascular techniques continue to evolve. Early neurorehabilitation significantly improves functional outcomes, particularly in poor-grade patients, while cognitive impairments remain a major challenge. Exercise-based rehabilitation enhances mobility and cardiovascular health, yet cognitive recovery needs further exploration. Future research should optimize rehabilitation timing and strategies to enhance long-term outcomes and quality of life for MCA aneurysm patients.

References:

Abdelgadir, J., Gelman, J., Dutko, L., Mehta, V., Friedman, A., & Zomorodi, A. (2024). Cognitive outcomes following aneurysmal subarachnoid hemorrhage: Rehabilitation strategies. *World Neurosurgery: X*, *22*, 100341. https://doi.org/10.1016/j.wnsx.2024.100341

Aghakhani, N., Vaz, G., David, P., Parker, F., Goffette, P., Ozan, A., & Raftopoulos, C. (2008). Surgical management of unruptured intracranial aneurysms that are inappropriate for endovascular treatment: Experience based on two academic centers. *Neurosurgery*, *62*(6), 1225–1227. https://doi.org/10.1227/01.neu.0000333294.52115.28

Alreshidi, M., Cote, D. J., Dasenbrock, H. H., Acosta, M., Can, A., Doucette, J., Simjian, T., Hulou, M. M., Wheeler, L. A., Huang, K., Zaidi, H. A., Du, R., Aziz-Sultan, M. A., Mekary, R. A., & Smith, T. R. (2018). Coiling Versus Microsurgical Clipping in the Treatment of Unruptured Middle Cerebral Artery Aneurysms: A Meta-Analysis. *Neurosurgery*, *83*(5), 879–889. https://doi.org/10.1093/neuros/nyx623

Aoki, T., Yoshitomi, M., Yamamoto, M., Hirohata, M., & Morioka, M. (2012). Ruptured De Novo Aneurysm Arising at a Site Remote From the Anastomosis 14 Years After Superficial Temporal Artery-Middle Cerebral Artery Bypass. *Neurosurgery*, *71*(4), E905–E909. https://doi.org/10.1227/NEU.0b013e318260ffcf

Blackburn, S. L., Abdelazim, A. M., Cutler, A. B., Brookins, K. T., Fargen, K. M., Hoh, B. L., & Kadkhodayan, Y. (2014). Endovascular and Surgical Treatment of Unruptured MCA Aneurysms: Meta-Analysis and Review of the Literature. *Stroke Research and Treatment*, *2014*, 348147. https://doi.org/10.1155/2014/348147

Can, A., Castro, V. M., Ozdemir, Y. H., Dagen, S., Yu, S., Dligach, D., Finan, S., Gainer, V., Shadick, N. A., Murphy, S., Cai, T., Savova, G., Dammers, R., Weiss, S. T., & Du, R. (2017). Association of intracranial aneurysm rupture with smoking duration, intensity, and cessation. *Neurology*, *89*(13), 1408–1415. https://doi.org/10.1212/WNL.0000000000004419

Can, A., & Du, R. (2016). Association of Hemodynamic Factors With Intracranial Aneurysm Formation and Rupture: Systematic Review and Meta-analysis. *Neurosurgery*, *78*(4), 510–520. https://doi.org/10.1227/NEU.0000000000001083

Chalouhi, N., Hoh, B. L., & Hasan, D. (2013). Review of cerebral aneurysm formation, growth, and rupture. *Stroke*, *44*(12), 3613–3622. https://doi.org/10.1161/STROKEAHA.113.002390

Chang, H. S., & Kirino, T. (1995). Quantification of operative benefit for unruptured cerebral aneurysms: A theoretical approach. *Journal of Neurosurgery*, *83*(3), 413–420. https://doi.org/10.3171/jns.1995.83.3.0413

Chen, F., & Fang, X. (2019). Endovascular treatment of middle cerebral artery aneurysm with a (LVIS) device: Comparison of LVIS stent and non-LVIS stent. *Experimental and Therapeutic Medicine*, *17*(3), 1656–1662. https://doi.org/10.3892/etm.2018.7139

Cho, Y. D., Jung, K.-H., Roh, J.-K., Kang, H.-S., Han, M. H., & Lim, J. W. (2013). Characteristics of intracranial aneurysms associated with extracranial carotid artery disease in South Korea. *Clinical Neurology and Neurosurgery*, *115*(9), 1677–1681. https://doi.org/10.1016/j.clineuro.2013.03.001

Choi, J. H., Park, J. E., Kim, M. J., Kim, B. S., & Shin, Y. S. (2016). Aneurysmal Neck Clipping as the Primary Treatment Option for Both Ruptured and Unruptured Middle Cerebral

Artery Aneurysms. *Journal of Korean Neurosurgical Society*, *59*(3), 269–275. https://doi.org/10.3340/jkns.2016.59.3.269

Choi, S. W., Ahn, J. S., Park, J. C., Kwon, D. H., Kwun, B. D., & Kim, C. J. (2012). Surgical Treatment of Unruptured Intracranial Middle Cerebral Artery Aneurysms: Angiographic and Clinical Outcomes in 143 Aneurysms. *Journal of Cerebrovascular and Endovascular Neurosurgery*, *14*(4), 289. https://doi.org/10.7461/jcen.2012.14.4.289

Chyatte, D., & Porterfield, R. (2001). Functional outcome after repair of unruptured intracranial aneurysms. *Journal of Neurosurgery*, *94*(3), 417–421. https://doi.org/10.3171/jns.2001.94.3.0417

Dammann, P., Schoemberg, T., Müller, O., Özkan, N., Schlamann, M., Wanke, I., Sandalcioglu, I. E., Forsting, M., & Sure, U. (2014). Outcome for unruptured middle cerebral artery aneurysm treatment: Surgical and endovascular approach in a single center. *Neurosurgical Review*, *37*(4), 643–651. https://doi.org/10.1007/s10143-014-0563-5

Diaz, O. M., Rangel-Castilla, L., Barber, S., Mayo, R. C., Klucznik, R., & Zhang, Y. J. (2014). Middle cerebral artery aneurysms: A single-center series comparing endovascular and surgical treatment. *World Neurosurgery*, *81*(2), 322–329. https://doi.org/10.1016/j.wneu.2012.12.011

Elsharkawy, A., Lehečka, M., Niemelä, M., Billon-Grand, R., Lehto, H., Kivisaari, R., & Hernesniemi, J. (2013). A new, more accurate classification of middle cerebral artery aneurysms: Computed tomography angiographic study of 1009 consecutive cases with 1309 middle cerebral artery aneurysms. *Neurosurgery*, *73*(1), 94–102. https://doi.org/10.1227/01.neu.0000429842.61213.d5

Flamm, E. S., Grigorian, A. A., & Marcovici, A. (2000). Multifactorial Analysis of Surgical Outcome in Patients with Unruptured Middle Cerebral Artery Aneurysms. *Annals of Surgery*, *232*(4), 570–575. https://doi.org/10.1097/00000658-200010000-00012

Gacheru, S. N., Trackman, P. C., Shah, M. A., O'Gara, C. Y., Spacciapoli, P., Greenaway, F. T., & Kagan, H. M. (1990). Structural and catalytic properties of copper in lysyl oxidase. *The Journal of Biological Chemistry*, *265*(31), 19022–19027.

Gory, B., Rouchaud, A., Saleme, S., Dalmay, F., Riva, R., Caire, F., & Mounayer, C. (2014). Endovascular Treatment of Middle Cerebral Artery Aneurysms for 120 Nonselected Patients: A Prospective Cohort Study. *American Journal of Neuroradiology*, *35*(4), 715–720. https://doi.org/10.3174/ajnr.A3781

Hagen, F., Maurer, C. J., & Berlis, A. (2019). Endovascular Treatment of Unruptured MCA Bifurcation Aneurysms Regardless of Aneurysm Morphology: Short- and Long-Term Follow-Up. *American Journal of Neuroradiology*. https://doi.org/10.3174/ajnr.A5977

Iijima, A., Piotin, M., Mounayer, C., Spelle, L., Weill, A., & Moret, J. (2005). Endovascular Treatment with Coils of 149 Middle Cerebral Artery Berry Aneurysms. *Radiology*, *237*(2), 611–619. https://doi.org/10.1148/radiol.2372041015

Ikawa, F. (2019). Surgery of Middle Cerebral Artery (MCA) Aneurysm. In *Neurovascular Surgery* (pp. 125–134). Springer Singapore. https://doi.org/10.1007/978-981-10-8950-3_15

Jeon, J. P., Cho, Y. D., Rhim, J. K., Yoo, D. H., Kang, H. S., Kim, J. E., Cho, W. sang, & Han, M. H. (2016). Extended monitoring of coiled aneurysms completely occluded at 6-month follow-up: Late recanalization rate and related risk factors. *European Radiology*, *26*(10), 3319–3326. https://doi.org/10.1007/s00330-015-4176-3

Johnston, S. C., Dowd, C. F., Higashida, R. T., Lawton, M. T., Duckwiler, G. R., & Gress, D. R. (2008). Predictors of Rehemorrhage After Treatment of Ruptured Intracranial Aneurysms. *Stroke*, *39*(1), 120–125. https://doi.org/10.1161/STROKEAHA.107.495747

Jung, K.-H. (2018). New Pathophysiological Considerations on Cerebral Aneurysms. *Neurointervention*, *13*(2), 73–83. https://doi.org/10.5469/neuroint.2018.01011

Jung, K.-H., Chu, K., Lee, S.-T., Shin, Y.-W., Lee, K.-J., Park, D.-K., Yoo, J.-S., Kim, S., Kim, M., Lee, S. K., & Roh, J.-K. (2016). Experimental Induction of Cerebral Aneurysms by Developmental Low Copper Diet. *Journal of Neuropathology & Experimental Neurology*, *75*(5), 455–463. https://doi.org/10.1093/jnen/nlw020

Karic, T., RÃ¸e, C., Nordenmark, T., Becker, F., & Sorteberg, A. (2016). Impact of early mobilization and rehabilitation on global functional outcome one year after aneurysmal subarachnoid hemorrhage. *Journal of Rehabilitation Medicine*, *48*(8), 676–682. https://doi.org/10.2340/16501977-2121

Kato, Y. (n.d.). *A New Classification Of Unruptured Middle Cerebral Artery Bifurcation Aneurysms*.

Lönnerdal, B. (1998). Copper nutrition during infancy and childhood. *The American Journal of Clinical Nutrition*, *67*(5), 1046S-1053S. https://doi.org/10.1093/ajcn/67.5.1046S

Lönnerdal, B., Bell, J. G., & Keen, C. L. (1985). Copper absorption from human milk, cow's milk, and infant formulas using a suckling rat model. *The American Journal of Clinical Nutrition*, *42*(5), 836–844. https://doi.org/10.1093/ajcn/42.5.836

Luo, B., Yang, X., Wang, S., Li, H., Chen, J., Yu, H., Zhang, Y., Zhang, Y., Mu, S., Liu, Z., & Ding, G. (2011). High Shear Stress and Flow Velocity in Partially Occluded Aneurysms

Prone to Recanalization. *Stroke*, *42*(3), 745–753. https://doi.org/10.1161/STROKEAHA.110.593517

McDonald, J. S., McDonald, R. J., Fan, J., Kallmes, D. F., Lanzino, G., & Cloft, H. J. (2013). Comparative effectiveness of unruptured cerebral aneurysm therapies: Propensity score analysis of clipping versus coiling. *Stroke*, *44*(4), 988–994. https://doi.org/10.1161/STROKEAHA.111.000196

Metaxa, E., Tremmel, M., Natarajan, S. K., Xiang, J., Paluch, R. A., Mandelbaum, M., Siddiqui, A. H., Kolega, J., Mocco, J., & Meng, H. (2010). Characterization of Critical Hemodynamics Contributing to Aneurysmal Remodeling at the Basilar Terminus in a Rabbit Model. *Stroke*, *41*(8), 1774–1782. https://doi.org/10.1161/STROKEAHA.110.585992

Mohan, D., Munteanu, V., Coman, T., & Ciurea, A. (2015). Genetic factors involves in intracranial aneurysms – actualities. *Journal of Medicine and Life*, *8*(3), 336–341.

Molyneux, A. (2002). International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: A randomised trial. *The Lancet*, *360*(9342), 1267–1274. https://doi.org/10.1016/S0140-6736(02)11314-6

Mortimer, A. M., Bradley, M. D., Mews, P., Molyneux, A. J., & Renowden, S. A. (2014). Endovascular treatment of 300 consecutive middle cerebral artery aneurysms: Clinical and radiologic outcomes. *AJNR. American Journal of Neuroradiology*, *35*(4), 706–714. https://doi.org/10.3174/ajnr.A3776

Nader-Sepahi, A., Casimiro, M., Sen, J., & Kitchen, N. D. (2004). IS ASPECT RATIO A RELIABLE PREDICTOR OF INTRACRANIAL ANEURYSM RUPTURE? *Neurosurgery*, *54*(6), 1343–1348. https://doi.org/10.1227/01.NEU.0000124482.03676.8B

Navarro-Orozco, D., & Sánchez-Manso, J. C. (2025). Neuroanatomy, Middle Cerebral Artery. In *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK526002/

Nussbaum, E. S., Madison, M. T., Myers, M. E., & Goddard, J. (2007). Microsurgical treatment of unruptured intracranial aneurysms. A consecutive surgical experience consisting of 450 aneurysms treated in the endovascular era. *Surgical Neurology*, *67*(5), 456–457. https://doi.org/10.1016/j.surneu.2006.08.069

O'Kelly, C. J., Krings, T., Fiorella, D., & Marotta, T. R. (2010). A Novel Grading Scale for the Angiographic Assessment of Intracranial Aneurysms Treated Using Flow Diverting Stents. *Interventional Neuroradiology*, *16*(2), 133–137. https://doi.org/10.1177/159101991001600204

Pan, T., Shi, Y., Yu, G., Mamtimin, A., & Zhu, W. (2023). Intracranial Aneurysms and Lipid Metabolism Disorders: From Molecular Mechanisms to Clinical Implications. *Biomolecules*, *13*(11), Article 11. https://doi.org/10.3390/biom13111652

Ries, T., Siemonsen, S., Thomalla, G., Grzyska, U., Zeumer, H., & Fiehler, J. (2007a). Long-Term Follow-Up of Cerebral Aneurysms after Endovascular Therapy Prediction and Outcome of Retreatment. *American Journal of Neuroradiology*, *28*(9), 1755–1761. https://doi.org/10.3174/ajnr.A0649

Ries, T., Siemonsen, S., Thomalla, G., Grzyska, U., Zeumer, H., & Fiehler, J. (2007b). Long-Term Follow-Up of Cerebral Aneurysms after Endovascular Therapy Prediction and

Outcome of Retreatment. *American Journal of Neuroradiology*, *28*(9), 1755–1761. https://doi.org/10.3174/ajnr.A0649

Rinne, J., Hernesniemi, J., Niskanen, M., & Vapalahti, M. (1996). Analysis of 561 Patients with 690 Middle Cerebral Artery Aneurysms: Anatomic and Clinical Features As Correlated to Management Outcome. *Neurosurgery*, *38*(1), 2–9. https://doi.org/10.1097/00006123-199601000-00002

Rodriguez, C., Martinez-Gonzalez, J., Raposo, B., Alcudia, J. F., Guadall, A., & Badimon, L. (2008). Regulation of lysyl oxidase in vascular cells: Lysyl oxidase as a new player in cardiovascular diseases. *Cardiovascular Research*, *79*(1), 7–13. https://doi.org/10.1093/cvr/cvn102

Rodríguez-Hernández, A., Sughrue, M. E., Akhavan, S., Habdank-Kolaczkowski, J., & Lawton, M. T. (2013). Current management of middle cerebral artery aneurysms: Surgical results with a "clip first" policy. *Neurosurgery*, *72*(3), 415–427. https://doi.org/10.1227/NEU.0b013e3182804aa2

Roy, D., Milot, G., & Raymond, J. (2001). Endovascular Treatment of Unruptured Aneurysms. *Stroke*, *32*(9), 1998–2004. https://doi.org/10.1161/hs0901.095600

Saunders, D. H., Sanderson, M., Hayes, S., Johnson, L., Kramer, S., Carter, D. D., Jarvis, H., Brazzelli, M., & Mead, G. E. (2020). Physical fitness training for stroke patients. *The Cochrane Database of Systematic Reviews*, *2020*(3), CD003316. https://doi.org/10.1002/14651858.CD003316.pub7

Seshadhri, S., Janiga, G., Beuing, O., Skalej, M., & Thévenin, D. (2011). Impact of Stents and Flow Diverters on Hemodynamics in Idealized Aneurysm Models. *Journal of Biomechanical Engineering*, *133*(7). https://doi.org/10.1115/1.4004410

Smith, T. R., Cote, D. J., Dasenbrock, H. H., Hamade, Y. J., Zammar, S. G., El Tecle, N. E., Batjer, H. H., & Bendok, B. R. (2015). Comparison of the Efficacy and Safety of Endovascular Coiling Versus Microsurgical Clipping for Unruptured Middle Cerebral Artery Aneurysms: A Systematic Review and Meta-Analysis. *World Neurosurgery*, *84*(4), 942–953. https://doi.org/10.1016/j.wneu.2015.05.073

Spetzler, R. F., McDougall, C. G., Zabramski, J. M., Albuquerque, F. C., Hills, N. K., Russin, J. J., Partovi, S., Nakaji, P., & Wallace, R. C. (2015). The Barrow Ruptured Aneurysm Trial: 6-year results. *Journal of Neurosurgery*, *123*(3), 609–617. https://doi.org/10.3171/2014.9.JNS141749

Sugiyama, S., Niizuma, K., Sato, K., Rashad, S., Kohama, M., Endo, H., Endo, T., Matsumoto, Y., Ohta, M., & Tominaga, T. (2016). Blood Flow Into Basilar Tip Aneurysms. *Stroke*, *47*(10), 2541–2547. https://doi.org/10.1161/STROKEAHA.116.013555

Suzuki, S., Tateshima, S., Jahan, R., Duckwiler, G. R., Murayama, Y., Gonzalez, N. R., & Viñuela, F. (2009). Endovascular treatment of middle cerebral artery aneurysms with detachable coils: Angiographic and clinical outcomes in 115 consecutive patients. *Neurosurgery*, *64*(5), 876–879. https://doi.org/10.1227/01.NEU.0000343534.05655.37

Vendrell, J.-F., Menjot, N., Costalat, V., Hoa, D., Moritz, J., Brunel, H., & Bonafe, A. (2009). Endovascular treatment of 174 middle cerebral artery aneurysms: Clinical outcome and radiologic results at long-term follow-up. *Radiology*, *253*(1), 191–198. https://doi.org/10.1148/radiol.2531082092

Wiebers, D. O. (2003). Unruptured intracranial aneurysms: Natural history, clinical outcome, and risks of surgical and endovascular treatment. *The Lancet*, *362*(9378), 103–110. https://doi.org/10.1016/S0140-6736(03)13860-3

Yang, W., & Huang, J. (2015). Treatment of middle cerebral artery (MCA) aneurysms: A review of the literature. *Chinese Neurosurgical Journal*, *1*(1), 1. https://doi.org/10.1186/s41016-015-0001-8

Zhang, Q., Jing, L., Liu, J., Wang, K., Zhang, Y., Paliwal, N., Meng, H., Wang, Y., Wang, S., & Yang, X. (2018). Predisposing factors for recanalization of cerebral aneurysms after endovascular embolization: A multivariate study. *Journal of NeuroInterventional Surgery*, *10*(3), 252–257. https://doi.org/10.1136/neurintsurg-2017-013041

Zhang, X.-J., Gao, B.-L., Hao, W.-L., Wu, S.-S., & Zhang, D.-H. (2018). Presence of Anterior Communicating Artery Aneurysm Is Associated With Age, Bifurcation Angle, and Vessel Diameter. *Stroke*, *49*(2), 341–347. https://doi.org/10.1161/STROKEAHA.117.019701

Zhou, G., Zhu, Y., Yin, Y., Su, M., & Li, M. (2017). Association of wall shear stress with intracranial aneurysm rupture: Systematic review and meta-analysis. *Scientific Reports*, *7*(1), 5331. https://doi.org/10.1038/s41598-017-05886-w