Chapter

Clipping Strategies and Intraoperative Tools to Detect Aneurysm Obliteration and Cerebral Vessel Patency

Pasquale Anania and Pietro Fiaschi

Abstract

Cerebral aneurysms are common cerebrovascular diseases most frequently manifest with vascular rupture and subsequent subarachnoid hemorrhage. Microsurgical clipping is considered the best long-term treatment, despite of the increase of endovascular interventional treatments in the latest years. Vascular control is a pivotal concept for aneurysms surgery, which provides the application of temporary clip in case of rupture, whereas the application of permanent clip requires the perfect knowledge of aneurysm anatomy. Several techniques to obtain the obliteration of the aneurysm while preserving the parent vessels and its branches have been described. Micro-Doppler ultrasonography (MUSG), indocyanine green video angiography (ICG-VA), and electrophysiological neuromonitoring (IONM) are all useful intraoperative tools, which can improve the safety of surgical procedures and achieve the goal of aneurysm obliteration with parent vessel and perforating preservation.

Keywords: cerebral aneurysm, clipping techniques, indocyanine, micro-doppler, neuromonitoring

1. Introduction

Cerebral aneurysms are common cerebrovascular diseases with an incidence rate ranging between 2% and 6% [1, 2]. Aneurysm rupture is the most frequent presentation of intracranial aneurysm, causing intracranial hemorrhage, usually subarachnoid hemorrhage (SAH) [3, 4]. The incidence rate of SAH is about 6 to 8 cases per 100,000 in the western population, with about 10,000–20,000 cases per year [3]. SAH-associated mortality is 50% at 30 days, and only up to 30% of patients can return to normal life after SAH [3]. In the latest years, endovascular interventional treatments of intracranial aneurysms have increased rapidly, but microsurgical clipping is still considered the best long-term treatment for this disease [5–10].

Temporary blockage of the feeding artery of the aneurysm, associated with simple or multiple applications of clips along the neck, are techniques that can allow the dissection and remodeling of the neck with obliteration of the aneurysm [11, 12].

However, all these techniques are associated with the risk of parent vessel stenosis and perforating artery damage, leading to brain ischemic damage and neurological defect [1]. The morbidity related to ischemic complications of the surgery of cerebral aneurysms is up to 7.6% [13, 14]. Therefore, the goal of surgical treatment is an optimal obliteration of the aneurysms without residual, while preserving the parent vessels and their branches [5].

Micro-Doppler ultrasonography (MUSG), indocyanine green video angiography (ICG-VA), and electrophysiological neuromonitoring (IONM) are useful intraoperative tools that are used to improve the safety of surgical procedures and achieve the goal of aneurysm obliteration with parent vessel and perforating preservation [1, 5, 11].

The aim of this chapter is to describe the strategies for surgical treatment of cerebral aneurysms and the tools to detect the correct aneurysm obliteration and the patency of the parent vessel and its branches. These techniques allow for improving the safety of surgical procedures, while reducing the risk of aneurysm remnants and avoiding irreversible damage to the brain tissue with consequent neurological derangement.

2. Techniques of clipping

Despite the technical skills and expertise of the surgeon revest a pivotal role, aneurysms surgery is often associated with a high risk of intraoperative rupture because of the fragility of the aneurysm and surgical manipulation. For this reason, vascular control is a pivotal concept that the neurosurgeon must respect during aneurysms surgery. Vascular control means the exposition of the afferent and efferent arteries, which move blood to the aneurysm in anterograde and retrograde direction, respectively. Vascular control is mandatory to allow the application of temporary clip on the afferent artery and eventually on efferent arteries in case of difficult aneurysm dissection or intraoperative rupture. Permanent clipping means the application of a definitive clip on the neck of the aneurysm to arrest the blood flow into the dome [12].

2.1 Temporary clipping

Temporary clipping is the application of the clip to the vessels that move the blood flow into the aneurysm. Thus, temporary clipping is usually referred to the apposition of the temporary clip on the afferent vessels in order to stop the anterograde blood flow. However, since the blood could flow into the aneurysm retrogradely through the efferent vessels, it could be needed the application of temporary clip on these vessels in case of persisting bleeding [12, 15]. Therefore, proximal control is referred to the exposition of the afferent vessels, distal control of the efferent vessels [12]. The application of temporary clip is useful in case of complex aneurysm, to facilitate the dissection without risk of bleeding. Moreover, arresting the flow, temporary clipping led the aneurysm to soften, allowing an easier dissection for the visualization of the parent vessels [16].

Temporary clipping is also a savage maneuver in case of aneurysm rupture because it stops the blood flow into the aneurysm, facilitating the dissection of the parent vessels and the neck, allowing the application of the permanent clip [15, 17].

Aneurysms with a single afferent vessel, or with multiple afferent and efferent vessels, could be classified. For this reason, different vessels should be exposed during the surgery considering aneurysm location:

- Middle cerebral artery (MCA) aneurysm:
    - Proximal control: sphenoidal segment of MCA (tract M1)
    - Distal control: post-bifurcation segments (tract M2–M3)
- Anterior communicating artery (ACoA) aneurysm:
    - Proximal control: precommunicating segment of anterior cerebral artery (tract A1) of both sides
    - Distal control: postcommunicating segments of anterior cerebral artery (tract A2) of both sides
- Pericallosal artery (PCaA) aneurysm:
    - Proximal control: precallosal (tract A3) or supracallosal (tract A4) segments of anterior cerebral artery, in relation to aneurysm location
    - Distal control: supracallosal (tract A4) or postcallosal (tract A5) segments of anterior cerebral artery, in relation to aneurysm location
- Posterior communicating artery (PCoA) aneurysm:
    - Proximal control: ophthalmic segments (tract C6) of internal carotid artery (ICA). Ophthalmic segments begins from the distal dural ring and end at the origin of PCoA.
    - Distal control: communicating segments (tract C7) of ICA, PCoA. Communicating segments begins from the origin of PCoA and ends at ICA bifurcation.
- Ophthalmic artery (OphA) aneurysm:
    - Proximal control: clinoidal segments (tract C5, which is the tract between the proximal and the distal dural ring) and ophthalmic segments (tract C6) of ICA, exposed through anterior clinoidectomy.
    - Distal control: supraclinoidal segments (tract C6-ophtalmic and C7-communicating) of ICA, OphA and PCoA.
- Basilar artery (BA) aneurysm:
    - Proximal control: basilar artery (BA)
    - Distal control: precommunicating segment (tract P1) of posterior cerebral artery (PCA), superior cerebellar artery (SCA)
- Posterior Inferior Cerebellar Artery (PICA) aneurysm:
    - Proximal control: vertebral artery (VA), anterior medullary segment (trac p1), lateral medullary segments (tract p2), tonsillomedullary segment (tract p3), or telovelotonsillar segments (tract p4) of PICA, in relation to aneurysm location

  - Distal control: anterior medullary segment (trac p1), lateral medullary segments (tract p2), tonsillomedullary segment (tract p3), or telovelotonsillar segments (tract p4) of PICA, in relation to aneurysm location

2.2 Permanent clipping

The application of a permanent clip requires the perfect knowledge of aneurysm anatomy, which should follow the Rothon rules [18]:

- Rule 1: aneurysms develop at sites where the parent artery branches off, which may be the origin of a side branch or a bifurcation

- Rule 2: aneurysm develops at hemodynamically stressful turns or curves in the artery's outer wall

- Rule 3: aneurysm points in the direction that blood would have flowed if the aneurysm site's curve had not been presented

- Rule 4: aneurysm is connected to a set of perforating arteries that (must be preserved)

Different clipping techniques have been described: simple clipping and multiple clipping.

Simple clipping refers to using a single clip for aneurysms with narrow neck and uncomplicated anatomy. It requires the use of the optimal clip in relation to neck conformation and size, considering that the application of the clip pressing the neck will increase its length and that the final part of the blade should cross the neck [12].

Multiple clipping is a technique that allows the application of more than one clip to close the neck of the aneurysm in sequential steps, and it is usually adopted to treat aneurysms with complex anatomy, including intersecting clips, stacked clips, and overlapping clips [12]. *Intersecting clipping* technique describes the application of the second clip angled into the first clip and intersecting it, thus allowing the remodeling of the aneurysm with a *bleb* that otherwise would be impossible to exclude with a simple clipping (**Figure 1A**) [19, 20].

Stacked clipping consists of the application of clips in the same direction and parallel to each other, in which usually the first one closes the aneurism, and the other ones closes the remnant *of the neck* beneath to the first clip (understacked). In case of application of the first clip on the neck, if another clip is necessary over the first one to complete the closure, this is defined overstacked (**Figure 1B**) [12, 20, 21].

Overlapping clipping describes the application of a second fenestrated clip over a first straight clip encircling it, in order to close a distal remnant beneath the initial clip (**Figure 1C**) [12, 20].

Tandem clipping is the technique described by Drake, which consists of the application of a first straight fenestrated clip to close the distal aneurysm (encircling in the fenestration a parent vessel), and a second clip to close the fenestration (**Figure 1D**) [12, 20, 21].

A. Intersecting clipping

B. Stacked clipping

C. Overlapping clipping

D. Tandem clipping

Figure 1.
The figure depicts the most common techniques for permanent clipping of cerebral aneurysms.

3. Intraoperative strategies to detect aneurysm obliteration and parent vessels patency

3.1 Micro-Doppler ultrasonography (MUSG)

Doppler ultrasonography was first employed to assess cerebral hemodynamics in extracranial arteries. This method was further refined for the transcranial examination of brain vessels [22]. Technological advancements allowed the reduction of the ultrasound probe's size by raising the ultrasonic frequency. Microprobes for the direct examination of small brain vessels were created as a result of further research [23–25].

Before and after the aneurysm clipping, blood flow velocities in the aneurysm sac and the nearby arteries could be measured using intraoperative microvascular Doppler ultrasonography (MUSG). The probe with a 1 mm-diameter pulsed wave mode is used to make the Doppler measurements. In addition, a suction cannula could be used to insert the Doppler probe, thus allowing precise positioning and stability. With an insonation angle of 30 to 60 degrees, the probe is used to examine all exposed arteries close to the aneurysm as well as the aneurysmal sac [26].

MUSG was first described by Lanborde et al. for intraoperative monitoring of large cerebral aneurysms [27]. MUSG has the ability to identify the orientation and hemodynamics of the parent arteries, as well as the vortex flow or thrombus within the aneurysm sac, prior to the positioning of clip. Particularly in large and challenging aneurysm surgery, MUSG monitoring could determine if the aneurysm sac is entirely clipped and whether parent or perforating arteries are stenosed or accidentally clipped. MUSG can detect all vessels in the Wills circle and its branches, including those with a diameter of less than 1 mm, because of the availability of a high-frequency micro-probe [28].

Bailes et al. [28] investigated the use of MUSG in aneurysm surgery, observing a capability to detect occlusion or stenosis of parent vessels in 31% of cases after clip positioning, and therefore allowing immediate adjusting.

Stendel et al. [26] MUSG discovered a meaningful stenosis of an adjacent artery caused by clip location in 17 out of 90 (18.9%) aneurysms. In addition, 11 out of 90 (12.2%) patients evaluated with Doppler ultrasound showed a predominantly unoccluded aneurysm. In 26 out of 90 (28.8%) patients, the aneurysm clip was repositioned based on the MDUG findings.

In conclusion, the complete closure of cerebral aneurysms and the patency of parent arteries, arterial branches, and main perforators could be documented by intraoperative MUSG, which is safe, rapid, efficient, dependable, and economical tool. In many situations, this method can be utilized safely in addition to other tools to monitor surgical aneurysms, reducing the risk of postoperative cerebral stroke. The limitations of MUSG include its vulnerability to changes in detecting angle and depth, fluid surrounding vessels, and tractor, as well as its inability to detect the aneurysm's back or minute remnant of its neck.

3.2 Indocyanine green video angiography (ICG-VA)

In 1956, the United States Food and Drug Administration (FDA) approved the use of indocyanine green (ICG) dye, a near-infrared (NIR) fluorescent tricarbocya-9 dye, to assess liver and cardiocirculatory functions. Ophthalmic angiography received additional FDA approval in 1975. ICG dye has an absorption and emission peak (805 and 835 nm, respectively) within the "optical window" of tissue, where endogenous chromophores have minimal absorption. After intravenous administration, ICG primarily binds to globulins (1 lipo-proteins) within 1 to 2 seconds. There is typical vascular permeability, and the dye is still intravascular. The liver is the only organ in the body that can excrete the indocyanine green dye, which has a plasma half-life of 3 to 4 minutes. ICG dye should be administered for video angiography (VA) at a dose of 0.2 to 0.5 mg/kg, with a daily maximum dose of 5 mg/kg.

The use of intraoperative NIR VA was first described by Raabe et al. in 2003, where ICG dye was used for intraoperative observation of vascular flow [29]. A light source that has a wavelength covering a portion of the ICG absorption band illuminates the operating field from the microscope (range 700–850 nm, maximum 805 nm). A bolus of the ICG dye is administered via peripheral vein (the standard 25-mg dose dissolved in 5 ml of water), and a nonintensified video camera captures the fluorescence (spectral range 780–950 nm, maximum 835 nm). To exclusively collect ICG-induced fluorescence, ambient and excitation light are blocked using an optical filter. As a result, real-time viewing of venous, capillary, and artery angiographic pictures is possible [30].

Some authors compared intraoperative and postoperative findings on the patency of the parent, branching, and perforating arteries and the clip occlusion of the aneurysm as indicated by ICG-VA, with the standard digital subtractive (DS) angiography. They observed that in 90% of cases, the results of ICG-VA matched those of intra and postoperative DS angiography. In 7.3% of patients, the ICG method failed to detect a modest but hemodynamically insignificant stenosis that was visible on

DS angiography. In three cases, the ICG approach failed to pick up angiographically significant findings. In two of the cases, the missed findings had no clinical or surgical repercussions; in the third, a 4-mm residual neck may necessitate additional surgery. In 9% of cases, indocyanine green VA gave the surgeon useful information about clip repair [30].

In 90% of instances, the results of ICG-VA matched those of intra- and post-operative DS angiography. In 7.3% of patients, the ICG method failed to detect a modest but hemodynamically insignificant stenosis that was visible on DS angiography. In three cases (one hemodynamically important stenosis and two residual aneurysm necks [2.7% of cases]), the ICG approach failed to pick up angiographically significant findings. In two of the cases, the missed findings had no clinical or surgical repercussions; in the third, a 4-mm residual neck may necessitate additional surgery. A substantial amount of information was provided to the surgeon using indocyanine green VA. The authors concluded that ICG-VA using a microscope is easy to perform and gives real-time data on the aneurysm sac and the patency of all diameters of arteries.

Many others studied compared the safety and efficacy of ICG-VA with DS angiography [1, 5, 13, 14, 17, 19, 20, 31, 32].

Ozgiray et al. [5] described that in 93.5% of aneurysms ICG-VA accurately determined vascular patency and aneurysm obliteration; only in 3.6% of cases ICG-VA showed no flow after clipping whereas puncturing the aneurysm's dome indicated residual flow, in 0.9% it demonstrated sustained flow within the aneurysm in one whereas MUSG and puncture of the dome did not, and in 0.9% it failed to show residual neck.

Della Puppa et al. [13] analyzed the role of ICG-VA added to the other techniques, observing that ICG-VA was useful for detecting parent vessels occlusion or residual aneurysm in 8.3% of cases. Moreover, only one false negative remnant neck was noted, with a negative predictive value of 98.8%, and ICG-VA was more sensitive to reveal remnant primarily in atherosclerotic aneurysms ($P < 0.05$).

In conclusion, ICG-VA represents the best tool to directly observe parent vessels patency and aneurysm obliteration. The surgical microscope's integration and its ability to show perforating arteries with submillimeter widths are two of its distinctive advantages. Its utility during aneurysm surgery is supported by its ease use, rapidity, and high level of accuracy for identifying partially clipped aneurysms and accidentally occluded vessels. Moreover, the ICG-VA has the potential to be more broadly accessible than intraoperative DS angiography.

3.3 Electrophysiological monitoring

Electroencephalography (EEG), motor evoked potentials (MEPs), somatosensory evoked potentials (SSEPs), visual evoked potentials (VEPs), and auditory evoked potentials are few of the intraoperative neuromonitoring (IONM) techniques available for cerebrovascular surgery. The overall objective of each modality is to improve the patient's functional outcome by detecting changes in brain activity that can indicate possible neurological compromise. Each modality has its own unique applications [33, 34]. Electrophysiological monitoring is useful to observe potential early ischemia during temporary clipping or after permanent clipping, allowing to remove of the temporary clip to restore the flow, or to explore the parent and perforating vessels after permanent clip detecting a possible erroneous clipping [15, 35].

Usually, the motor pathway is monitored by stimulating the motor area using electrodes inserted in C1–C2 (C3–C4) through a train of 4 to 5 stimuli with the intensity of 250 to 500 Hz. The somatosensory pathway is monitored by stimulating contralateral medianus nerve at the wrist for the upper limb SSEPs, and the contralateral tibial nerve at the medial malleolus for the lower limb SSEPs. General anesthesia could affect the results of IONM; thus, total intravenous anesthesia is recommended, possibly avoiding the use of neuromuscular blockers unless absolutely necessary [13, 36].

Knowing the N20 peak's amplitude in relation to the evoked parietal response is crucial. N20 peak amplitude was decreased by more than 50% when compared to its absolute values, indicating a decrease in rCBF values of around 12–16 mL/100 g/min. This is comparable to cerebral ischemia that may be reversible, however, chronic maintenance of a low rCBF may result in cerebral infarct [37, 38].

Penchet et al. observed a significant reduction of SSEP (more than 50%) in 25.9% of the patients, of which 6.9% with postoperative ischemic stroke and partial or no recovery, 19% with complete recovery, and only two postoperative ischemic strokes. The authors concluded that changes in SSEP had a strong correlation with postoperative stroke incidence [34].

Staarmann et al. [36] described IONM alterations in 15 cases out of 133 clipped aneurysms, including 12 transient changes without new postoperative deficits and 3 permanent changes with new postoperative deficits. Transcranial motor evoked potentials and somatosensory evoked potentials predicted 2 and 1 of the postoperative deficits, respectively. Moreover, they observed only 1.1% incidence of IONM alterations and permanent neurological deficits associated with temporary clipping [36].

Della Puppa et al. [13] observed a reduction of evoked potential in 11 patients during temporary or permanent clipping, 10 in accordance with MEPs, and 1 in accordance with SSEP. All these IONM normalized after temporary clip removal or permanent clip repositioning. MEP was significantly correlated with proximal located aneurysm (ACoA, ICA, M1).

In conclusion, multimodal IONM is very sensitive and specific for identifying new deficits. The early detection of potential reversible ischemia allows maneuvers such as temporary clipping removal or the identification of another component (such as releasing brain retraction or reposition of permanent clip) to lower the likelihood of postoperative complications.

4. Future perspectives

ICG-VA represents the most dominant innovation of the latest years for the surgical treatment of brain aneurysms. Future technological advances should potentially allow to facilitate three-dimensional (3D) orientation, optimize clip placement, and manage the proximal and distal control [39].

One of the first considerations that it could be done about future advances in vascular neurosurgery is that brain aneurysm surgery represents a specific technical challenge for young neurosurgeons, due to the huge increase in endovascular technology in the latest years. Since endovascular treatments continue to develop, a similar focus on technological innovation in open surgical repair should be implemented, for patients to continue to benefit from whichever treatment option is most effective for their aneurysm. Thus, training in this subspeciality of neurosurgery represents an increasing challenge in the modern era and a specific field that applies to increased learning opportunities [40]. High-fidelity surgical simulators may provide a partial answer by enabling surgeons to gain expertise. In fact, preoperative simulation tailored to the patient who will be operated, as well as 3D models, could be detrimental to compensate for the lack of opportunities to learn vascular surgery, leading young neurosurgeons to an easier improvement of technical skills, thus facilitating 3D orientation and optimizing the management of surgical procedures [41].

Another issue to be considered regarding future advances is the identification of technologies that would improve clip application (e.g., advances in applicators, advances in clips) and intraoperative visualization (e.g., endoscopes and intraoperative imaging). Endoscopes are not usually included in the aneurysm surgical workflow, but they could improve the visualization of aneurysm "blind spot", facilitating aneurysm management and 3D orientation [39].

Hybrid operating theaters, which include intraoperative CT scans and intraoperative angiography, are not very diffused. Still, they should be identified as potential future advances to optimize clip application and 3D orientation, increasing the safety of aneurysm obliteration and neck reconstruction, reducing surgical morbidity despite of the reduced surgical cases compared to the past.

In conclusion, the majority of future advances in vascular neurosurgery should be targeted to optimize clip application and improve 3D visualization and orientation, for example, increasing the use of endoscopic-assisted surgery, implementing the development of surgical simulators, and investing in the growth of hybrid opened-endovascular technique thanks to hybrid operating theaters [39].

5. Conclusions

Microsurgical obliteration of cerebral aneurysms represents the best long-term treatment for this pathology. Despite high surgical expertise, aneurysm surgery is often associated with an increased risk of intraoperative rupture. For this reason, vascular control is pivotal and should be aimed at by the neurosurgeon during aneurysm surgery. The application of single or multiple definitive clips on the neck of the aneurysm can be achieved with different techniques in order to arrest the blood flow into the dome [12]. Intraoperative use of ICG-VA, MUSG, and IONM can effectively reduce brain tissue ischemia ad morbidity after clipping intracranial aneurysm, thus improving the surgical outcome. Microsurgical clipping with the use of a multimodal monitoring method led to a high incidence of aneurysm exclusion with little morbidity [13].

Conflict of interest

The authors declare no conflict of inte 3rest.

Acronyms and abbreviations

SAH	subarachnoid hemorrhage
MUSG	Micro-Doppler ultrasonography
ICG-VA	indocyanine green video angiography
IONM	electrophysiological neuromonitoring
MCA	Middle cerebral artery aneurysm

ACoA	Anterior communicating artery
PCaA	Pericallosal artery
PCoA	Posterior communicating artery
OphA	Ophthalmic artery
BA	basilar artery
PICA	Posterior Inferior Cerebellar Artery
ICA	internal carotid artery
FDA	Food and Drug Administration
ICG	indocyanine green
NIR	near-infrared
VA	video angiography
DS	digital subtractive
EEG	Electroencephalography
MEPs	motor evoked potentials
SSEPs	somatosensory evoked potentials
VEPs	visual evoked potentials
CBF	cerebral blood flow
3D	three-dimensional

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