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Intraoperative Assessment Using Indocyanine Green Versus Sodium Fluorescein in Aneurysm Clipping: Review of Cases and Literature

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ABSTRACT
Introduction: The fundamental challenge of aneurysm clipping is to secure a complete neck occlusion while preserving both parent and their subsequent branch arteries along with the surrounding perforators. Indocyanine Green Video angiography (ICG-VA) and Fluorescein Sodium Angiography (FNa-VA) are microscope-integrated fluorescence that offer a more affordable intraoperative evaluation of the cerebral vasculature. We present our experience in using intraoperative ICG-VA and FNa-VA in aneurysm clipping cases along with the literature review to compare both fluorescence techniques. ***Case Series:*** Two patients with subarachnoid arachnoid hemorrhage caused by a ruptured aneurysm were involved, and surgical clipping of the aneurysm was done. Intraoperative assessment of cerebral vasculature was performed using both ICG-VA and FL-VA. ***Conclusion:*** Both ICG-VA and FL-VA each have their own advantages and disadvantages and are safe and effective in routine use for intraoperative evaluation in aneurysm clipping surgery.

Keywords: aneurysm; indocyanine green; sodium fluorescein; stroke; subarachnoid hemorrhage

INTRODUCTION
Stroke is the second cause of death and a major contributor to disability worldwide.(1) Stroke is estimated to occur in 13.7 million people and kills around 5.5 million every year.(2) Aneurysmal SAH is a neurological emergency that has a high death and disability rate. Aneurysm can be managed either with open surgery or an endovascular approach.(3) Open surgery primarily involves clipping the aneurysm through a craniotomy and navigation through the cisterns and natural subarachnoid corridors of the brain.(4,5)

The fundamental challenge of aneurysm clipping is to secure a complete neck occlusion while preserving both parent and their subsequent branch arteries along with the surrounding perforators. Thus, Intraoperative evaluation become a particularly important adjunct in aneurysm surgery. While intraoperative cerebral angiography is considered the gold standard for the assessment of cerebral angioarchitecture, the hybrid setup is considerably expensive and may not be available in every neurosurgical center.[10]

Indocyanine Green Video angiography (ICG-VA) and Fluorescein Sodium Angiography (FNa-VA) are microscope-integrated fluorescence that offer a more affordable intraoperative evaluation of the cerebral vasculature. While both have the same utilization, only a few literature actually compared the distinction between the two techniques.

We present our experience in using intraoperative ICG-VA and FNa-VA in aneurysm clipping cases along with the literature review to compare both fluorescence techniques.

CASE ILLUSTRATIONS

Case I
A 53-year-old female with a history of uncontrolled hypertension presented to our hospital with altered consciousness six hours before being admitted. She previously experienced an abrupt onset of severe migraines and vertigo. Her GCS was 13 with neck rigidity with round equal pupils and intact light reflexes. No sign of motoric lateralization was noted. From the cerebral computed tomography angiography (CTA), an aneurysm on the right anterior communicating artery AcommA was noted (Figure 1), and craniotomy for aneurysm clipping was done with intraoperative evaluation using FNa-VA (Figure 2).

The right personal approach was used. Opticocarotid and Interoptic cisternal drainage was done to soften the brain. The right internal carotid artery (ICA) was followed to A1 and subsequently right comm, where the aneurysm can be appreciated. after temporary clip placement on A1, the permanent clip was applied to the neck of the aneurysm. Fluorescein was injected intravenously and the microscope was turned into Yellow 560 mode to ensure the clip adequacy.

A fluorescein patch on the aneurysm dome was noted, indicating the inadequacy of the first clip to completely occlude the aneurysm neck. An additional tandem clip at the neck was placed, and further fluorescein evaluation confirmed complete occlusion of the aneurysm. The patient tolerated the surgery well with no neurological deficit.

Case II

A 66-year-old female, referred from another hospital, had been comatose for eight hours before her admission. She was on her daily activity when she suddenly experienced severe migraine and acute deterioration of consciousness. The patient also has a history of uncontrolled hypertension for over a decade. The patient presents with GCS 4T, equal and round pupils with intact light reflexes and no lateralization. her head CT Scan showed acute non-communicating hydrocephalus, with intraventricular hemorrhage (IVH) and SAH (Hunt and Hess Gr. V, mFisher grade III). After emergency extraventricular drain placement, her GCS improved to 12, and CTA was performed (Figure 3), which shows a left MCA bifurcation aneurysm with anterior projection, 4 mm neck diameter, and daughter sac at the posteroinferior side. Craniotomy and aneurysm clipping were done through a left pterional approach utilizing intraoperative ICG-VA evaluation (Figure 4).

ICA was followed laterally along the MCA to find the bifurcation along with the aneurysm dome. A temporary clip was placed on M1, and a tandem permanent clip was applied to both the neck of the main dome and the daughter sac. Then, we evaluated the clip patency with ICG-VA using near-infrared (NIR) 800 mode to ensure the clip adequacy and preservation of the parent artery.

DISCUSSION

The preservation of tissue perfusion integrity is a crucial premise in the field of neurovascular surgery. Ischemic complication due to occlusion of a branch or perforating arteries is one of the most prevalent complications of aneurysmal clipping surgery. [3] Another pitfall of such intricate surgery is the possibility of residual aneurysmal flow from inadequate clip placement, which is difficult, if not possible, to be evaluated with direct vision alone.[5,6]

Clipping is an established therapeutic approach utilized to manage aneurysms, in which a small metal clip is positioned across the neck, or base, of the protrusion. By effectively obstructing blood flow, the aneurysm is prevented from rupture or the loss of blood into the brain. Following the procedure of clip ligation for cerebral aneurysms, it is necessary to do an intraoperative assessment of aneurysm obliteration and verify the adequacy of both the parent and perforating arteries.[7,8]

Intraoperative digital subtraction angiography (DSA), which can be performed in a hybrid OR setting, is still considered the gold standard in evaluating surgical results, typically in complex aneurysms. Intraoperative DSA offers a complete evaluation of the cerebral angioarchitecture, unhindered by the parenchymal tissue as opposed to the fluorescence technique. The main drawback of intraoperative DSA is that it is not possible to do immediate or simultaneous manipulation while the DSA is carried, and it takes a considerable time to perform, which, in instances of perforator or branch occlusion, may cause delay of clip reposition. The hybrid OR setting itself may not be available in most neurosurgical centers, and routine use may be considered not cost-effective.[9]

Indocyanine green (ICG) and sodium fluorescein (FNa) are two discrete fluorescent agents that have been effectively implemented in aneurysm surgery. Their respective properties endow them with merits and demerits.[10] In order to visualize cerebral blood flow in addition to evaluating anatomical vascular structures, indocyanine green video angiography (ICG-VA) and sodium fluorescein video angiography (FL-VA) were devised under a microscope. The maximal wave lengths of fluorescein and ICG are 465 to 490/520 to 530 nm and 805/835 nm, respectively. Angiography employing these dyes intravenously does not result in any interference with one another's detection.[11,12]

ICG is a fluorescent tri-carbocyanine dye that can be evaluated using a NIR spectrum integrated with the microscope in the FLOW 800 module and is widely used to evaluate vascular blood flow. It has a 3 to 4-minute half-life and may reach the cerebral vascular in a period of 30 seconds, offering real-time information on vascular vessels within the operative field.[13,14] The maximum recommended ICG-VA dosage is 5 mg/kg, with a range of 0.2 to 0.5 mg/kg. Intravenously, a bolus dose of standard ICG (25mg) diluted in 5 mL of water is administered. ICG provides a reliable visual appreciation and has comparable rates of parent artery stenosis and clip readjustment to intraoperative DSA. ICG-VA is regarded as the simpler alternative to DSA with excellent image quality and allows a prompt clip readjustment in case of branch occlusion before an irreversible ischemic event happens. [9,18]

Raabe et al., in their series, found the major limitation of ICG-VA to be the restricted view of the surgical field as the vessels concealed by blood clots, brain tissue, and aneurysm wall are not amenable to be evaluated by the fluorescent. Furthermore, atherosclerotic plaque, calcification, or thick aneurysm wall may hinder the fluorescent signals and may complicate the intraoperative evaluation. This limitation is also observed in the FL-VA technique.[14,15] In accordance with its 3 to 4-minute plasma half-life, ICG injection may be repeated after 10 minutes to prevent false positive aneurysmal dome enhancement from the previous injection. [18]

Another fluorescent agent that can be used for vascular angiography is FNa. Fluorescein angiography was first introduced in 1967 by Feindel et al. who used it to inject the carotid artery.[16] It is considerably less expensive than ICG-VA, which may favor its usage, especially in a high-volume vascular center in a lower-middle-income country.

One notable characteristic of FNa-VA is its ability to offer real-time, three-dimensional visualization of the surgical site through the utilization of microscope binoculars. The reason for this discrepancy lies in the fact that FNa emits light within the visible light spectrum.(9,17,18) Fluorescein can be given in a 60mg bolus dosage intravenously, which is visualized using the microscope-integrated YELLOW 560 module. The fluorescent agent will reach the cerebral vasculature in approximately 20 seconds after injection, which induces a yellow-green enhancement on the vascular structure. The fluorescent signal will remain impinged on the vascular vessels for 20-30 minutes before being cleared. This may cause difficult interpretation, for instance, in the case of clip repositioning. Fluorescein also readily leaks into extravascular space, which may cause enhancement in the dural structure. (10,11)

Assessment of ICG utilizes NIR with a wavelength longer than the visible spectrum. This does not allow simultaneous clip manipulation along with ICG evaluation, as the surrounding structure other than the vascular vessel itself is not visible. This is different from the FL-VA in comparison, which uses white light in its evaluation, making it possible for a simultaneous clip readjustment during the fluorescein evaluation.(11) Despite that, the distinguished contrast between the vascular and darkened surrounding structure with ICG-VA may allow a focused evaluation of the cerebral vasculature better than the FL-VA. The image resolution of ICG-VA may decline at a higher magnification due to chromatic aberration, which may hinder evaluation in a deep surgical field. In comparison, high magnification does not affect FL-VA images, which gives superior detail even in the deep surgical field across the magnification range. This provides a better evaluation of a small perforating branch, which is usually only available for observation in a higher magnification. This is aligned with a series by Singh et al., who found that in contrast to intravenous FNa, which detected all perforators visible under white light (68/68), ICG detected only 56 (82.35%) perforators.5 Another study by Saito et al. also stated that FL-VA can identify every perforator, whereas ICG-VA detected only 30 perforators (88.2%).(11,15)

The main drawback of FL-VA is that it stains the dura, making it more difficult to selectively assess the important arteries, especially those located near the tentorium.(11) FL-VA impregnates the vessel and aneurysm wall for a longer period, compared to the short plasma half-life of ICG, making it difficult to serially evaluate the vascular vessels after a repeat injection. For instance, if used early, the aneurysm dome may still enhance even after adequate clip placement. Thus, FL-VA evaluation is best reserved for final evaluation after the permanent aneurysmal clip has already been applied. It is also considerably more difficult to assess flow using FL-VA compared to ICG-VA. However, both fluorescents only provide a qualitative blood flow evaluation, which does not give valuable information on whether the blood flow is adequate to prevent infarction.(11,19)

CONCLUSION

ICG and Fluorescein video-angiography are both safe and effective to be utilized in aneurysm surgery. When multiple study parameters were taken into account, including the capability to evaluate branching vessels, small-sized perforators, the effectiveness of aneurysmal clipping, and valuable data regarding repeat imaging, both of these two techniques (ICG-VA and FL-VA) each has advantages and disadvantages.

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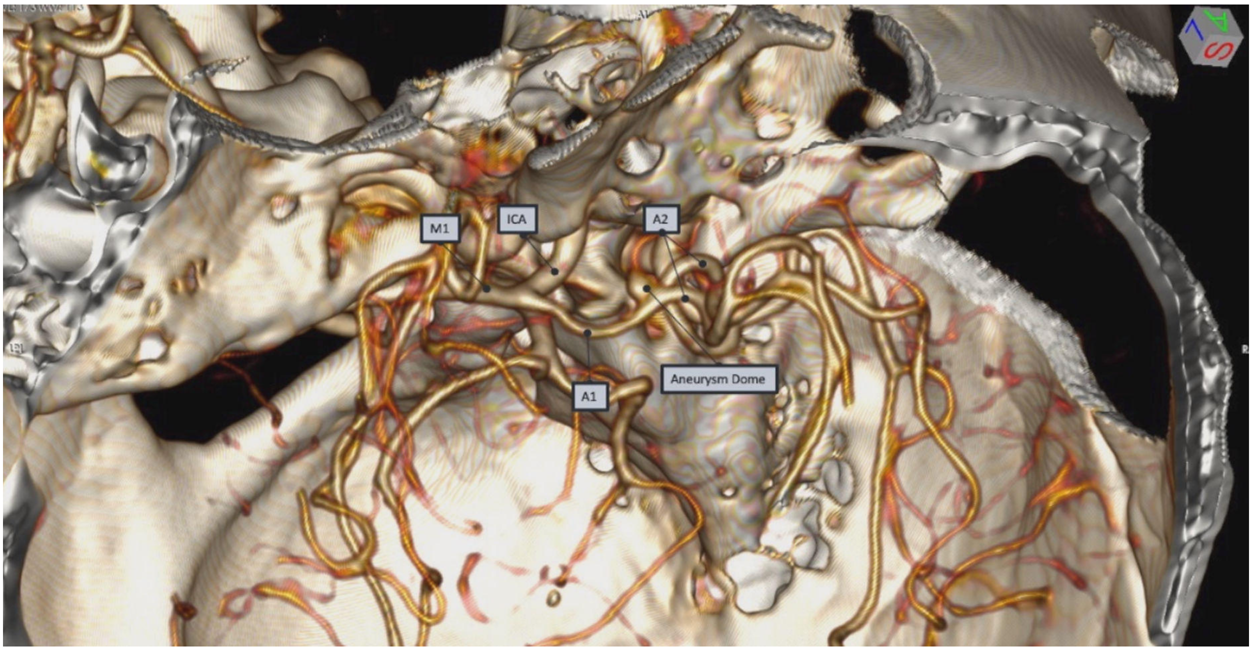

FIGURE 1: Pre-operative imaging of Computed tomography angiography (CTA) shows saccular aneurysm on right AComm artery.

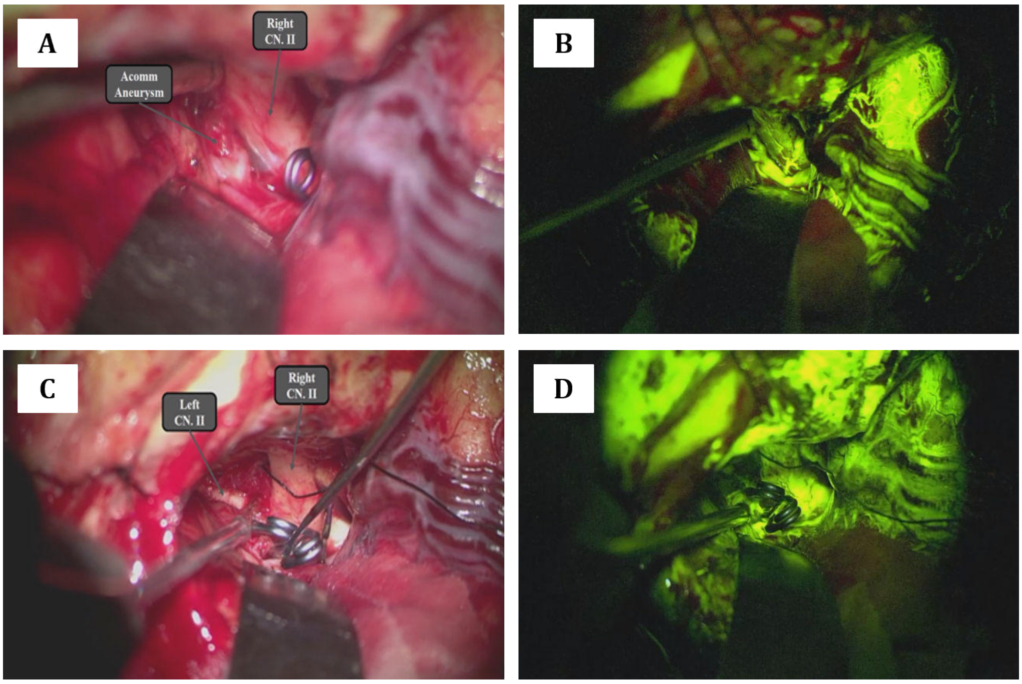

FIGURE 2: Intraoperative image shows: a) identified right AComm aneurysm dome and neck, with temporary clip on right A1 artery; b) evaluate with FNa, blood flow fills the aneurysm; c) placement of permanent clip and additional tandem clip at the neck of the main dome; d) evaluate with FNa after clip placement, there is no blood flow into the aneurysm.

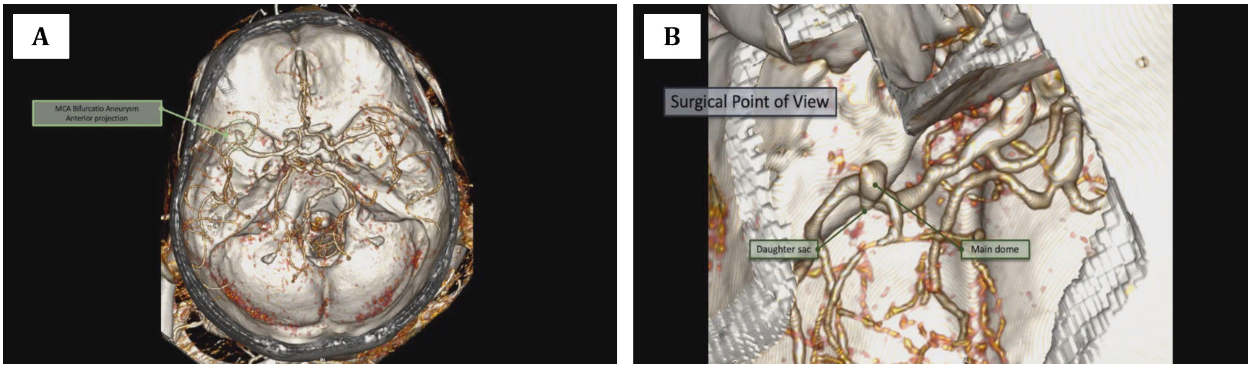

FIGURE 3: Pre-operative imaging of Computed tomography angiography (CTA) shows a saccular aneurysm on the left M1-M2 bifurcation artery.

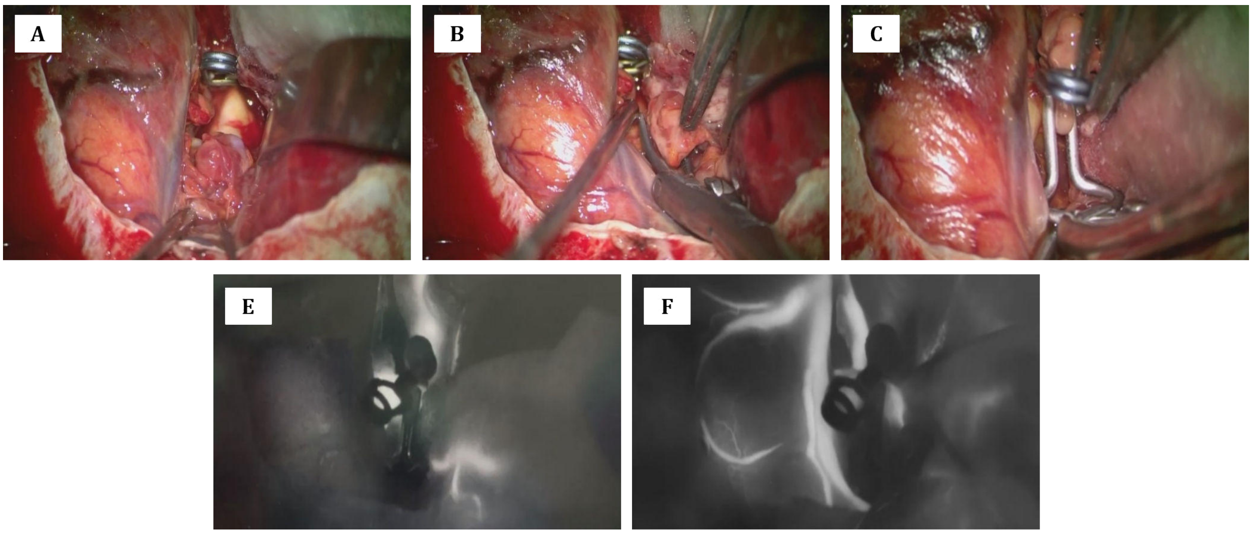

FIGURE 4: Intraoperative image shows: a,b) identified left M1-M2 bifurcation aneurysm dome and neck, with temporary clip on left M1; c) placed two permanent clips, at the neck of the main dome (slightly curved clip) and the daughter sac (right angle clip); d,e) evaluate with ICG after clip placement, there is no blood flow into the aneurysm.