学位論文　博士（医学）　乙

Efficacy of endoscopic fluorescein video angiography in aneurysm surgery

— Novel and innovative assessment of vascular blood flow

in the dead angles of the microscope

（脳動脈瘤手術における内視鏡下フルオレセイン蛍光血管造影の有用性

：顕微鏡死角での新規血流観察法）

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Efficacy of Endoscopic Fluorescein Video Angiography in Aneurysm Surgery—Novel and Innovative Assessment of Vascular Blood Flow in the Dead Angles of the Microscope

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BACKGROUND: In aneurysm surgery, assessment of the blood flow around the aneurysm is crucial. Recently, intraoperative fluorescence video angiography has been widely adopted for this purpose. However, the observation field of this procedure is limited to the microscopic view, and it is difficult to visualize blood flow obscured by the skull base anatomy, parent arteries, and aneurysm.

OBJECTIVE: To demonstrate the efficacy of a new small-caliber endoscopic fluorescence video angiography system employing sodium fluorescein in aneurysm surgery for the first time.

METHODS: Eighteen patients with 18 cerebral aneurysms were enrolled in this study. Both microscopic fluorescence angiography and endoscopic fluorescein video angiography were performed before and after clip placement.

RESULTS: Endoscopic fluorescein video angiography provided bright fluorescence imaging even with a 2.7-mm-diameter endoscope and clearly revealed blood flow within the vessels in the dead angle areas of the microscope in all 18 aneurysms. Consequently, it revealed information about aneurysmal occlusion and perforator patency in 15 aneurysms (83.3%) that was not obtainable with microscopic fluorescence video angiography. Furthermore, only endoscopic video angiography detected the incomplete clipping in 2 aneurysms and the occlusion of the perforating branches in 3 aneurysms, which led to the reapplication of clips in 2 aneurysms.

CONCLUSION: The innovative endoscopic fluorescein video angiography system we developed features a small-caliber endoscope and bright fluorescence images. Because it reveals blood flow in the dead angle areas of the microscope, this novel system could contribute to the safety and long-term effectiveness of aneurysm surgery even in a narrow operative field.

KEY WORDS: Clipping, Endoscope, Fluorescein video angiography, Intracranial aneurysm, Intraoperative monitoring

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ABBREVIATIONS: AChA, anterior choroidal artery; **BA,** basilar artery; **CTA,** computed tomography angiography; **DSA,** digital subtraction angiography; **ICA,** internal carotid artery; **ICG,** indocyanine green; **LED,** light-emitting diode; **MEP,** motor evoked potential; **MCA,** middle cerebral artery; **mRS,** modified Rankin scale; **PCA,** posterior cerebral artery; **PICA,** posterior inferior cerebellar artery; **PCoA,** posterior communicating artery; **SCA,** superior cerebellar artery; **VA,** vertebral artery

In surgery for intracranial aneurysm, it is essential to confirm aneurysmal obliteration and the patency of parent and perforating arteries. Recently, intraoperative fluorescence video angiography has been widely used for this purpose.[1-7] However, the observation field for this procedure has been limited to a microscopic view, and it has been difficult to confirm blood flow in areas obscured by skull base anatomy such as the clinoid process, cerebellar tentorium, parent arteries, and nerves. Consequently, the endoscope has been adopted for microsurgery

to enable visualization of cerebral blood vessels in the dead angle areas of the microscope,[8-12] but the endoscope cannot itself reveal real-time blood flow through the vessel walls. To overcome this problem, we adapted endoscopic indocyanine green (ICG) video angiography for cerebrovascular surgery and reported its efficacy for aneurysm surgery.[13] However, this system and another commercial ICG endoscope system currently available require a diameter exceeding 4.0 mm to gain sufficient fluorescence, which makes it difficult to bring the endoscope into an appropriate position within the limited space available between eloquent areas.[13-15] Therefore, the need arose to develop a small-caliber endoscope with a fluorescence video angiography system.

In contrast, sodium fluorescein—another fluorescence dye used in intraoperative video angiography—was introduced into the field of neurosurgery in 1967 by Feindel et al,[16] and Suzuki et al[5] reported the usefulness of this dye in microscopic fluorescence video angiography during aneurysm surgery in 2007. Several studies have recently demonstrated the sharp contrast of microscopic fluorescein video angiography and its ability to depict fine arteries,[5,6,17] as sodium fluorescein yields approximately 20 times the fluorescence of ICG.[18] Therefore, the use of sodium fluorescein in endoscopic video angiography had the potential to provide much brighter fluorescence even with a small-caliber endoscope.

In this study, we developed a small-caliber endoscopic video angiography system employing sodium fluorescein, applied this innovative method to aneurysm surgery, and demonstrated its efficacy in this area for the first time.

METHODS

Patient Population

This study was approved by the ethics committee of the University of Yamanashi. Between February 2013 and June 2015, patients of consecutive cases of cerebral aneurysm treated with clipping performed with an endoscopic video angiography system employing sodium fluorescein were enrolled in this prospective study. All patients were interviewed to determine any history of anaphylactic reaction to dye injection and all provided written informed consent, including agreement to undergo endoscopic fluorescein video angiography with our new endoscope system.

Microscopic Fluorescence Video Angiography

Intraoperative microscopic fluorescence video angiography was performed with fluorescein sodium (FLUORESCITE; Alcon Laboratories Inc., Fort Worth, Texas) or ICG dye (Diagnogreen; Daiichi Sankyo Co., Ltd, Tokyo, Japan). Intraoperative microscopic fluorescein video angiography was carried out with a surgical microscope (OPMI Neuro/NC-4; Carl Zeiss, Oberkochen, Germany). As previously reported, a barrier long-pass (blue-cut) filter was introduced into the light pathway of the operating microscope. The microscope light source was turned off, and the target arteries were illuminated with an excitation beam from a blue light-emitting diode (LED) atop a pencil-type probe.[2,5,18-20] On the other hand, for microscopic ICG video angiography, an ICG-integrated microscope (OPMI PENTERO 900; Carl Zeiss, Oberkochen, Germany) was used.[4] The operative field was illuminated through the microscope with a light source having a wavelength that covered part of the ICG absorption band (700-850 nm range, 805 nm peak).

Endoscopic Fluorescein Video Angiography

Two types of rigid endoscopes with outer diameters of 4.0 mm (A70941A; Olympus Optical Co., Tokyo, Japan) and 2.7 mm (A81011A; Olympus Optical Co.) were used with 30° angled lenses. The endoscope system consisted of a xenon light source (Visera CLV-S40Pro; Olympus Optical Co.), a video processor system (Visera OTV-S7Pro; Olympus Optical Co.), and a camera head with a built-in charge coupled device. A barrier long-pass (blue-cut) filter was introduced into the light pathway between the camera head and rigid endoscope. The excitation beam was projected through the tip of the rigid endoscope from a blue LED(PFB2-20BL-F-JT-SAD4; CCS Inc., Kyoto, Japan) that we adapted especially for this study.

Surgical Procedure

The craniotomy and subarachnoid dissection were performed in the usual manner. After the aneurysm neck and sac were exposed, the endoscope was manually introduced with the aid of the microscope to reveal the area behind the parent arteries and aneurysms and was fixed in place with a holding system (EndoArm, Olympus Optical Co.; UniArm, Mitaka Kohki Co., Tokyo, Japan).

For internal carotid artery (ICA) and middle cerebral artery (MCA) aneurysms, surgery was performed via the pterional approach. For inspection of the medial side of the ICA, the endoscope was introduced medially parallel to the anterior skull base to the prechiasmatic cistern or the opticocarotid triangle and was fixed there. For observing the lateral side of the ICA, the endoscope was inserted laterally into the space between the ICA and the temporal lobe. The subtemporal approach was used for clipping of basilar artery (BA) bifurcation and BA-superior cerebellar artery (SCA) bifurcation aneurysms, and the endoscope was introduced through the space either above or below the oculomotor nerve and fixed in front of the BA. This setting of the endoscope provides the view obtained with the pterional approach, and the wide viewing angle of the endoscope clearly reveals the perforators. Surgery on vertebral artery (VA) aneurysms was performed via the lateral suboccipital approach. The endoscope was inserted through the narrow and limited spaces between the skull base and the cerebellar hemisphere, rostrally or caudally to the aneurysm.

For complex, large, or deep-seated aneurysms, an angiography catheter was placed in the ICA or the VA to enable intraoperative digital subtraction angiography (DSA) to confirm the aneurysmal occlusion and the preservation of the surrounding arteries. In the intraoperative DSA cases, intra-arterial injection fluorescein video angiography was also performed as reported previously.[2] Ten milliliter of 0.01% or 0.02% sodium fluorescein solution diluted with saline was injected intra-arterially through the angiography catheter before and after clip placement. In the other cases, 5 mL of 10% sodium fluorescein was injected intravenously in the usual manner, as reported previously.[2,5,18] ICG dye, on the other hand, was injected into a peripheral vein as a bolus (25 mg of ICG dissolved in 5 mL of water).[3,4,13] Corticosteroid was intravenously administered before the injection of sodium fluorescein to counter potential allergic reaction.[5,18] Fluorescence imaging was observed under the surgical microscope and the endoscope, which was placed near the aneurysms, to confirm complete clipping and

preservation of blood flow in normal vessels. The images were recorded with a digital video camera and reviewed by surgeons and 2 independent observers. The findings obtained with endoscopic fluorescein video angiography regarding aneurysms and perforators were compared with those of microscopic fluorescence video angiography and endoscopic imaging without fluorescein video angiography.

Postoperative computed tomography angiography (CTA) was routinely carried out on postoperative days 5 to 7. Postoperative DSA was conducted only in selected cases because of its invasive potential.[21,22]

RESULTS

Background of the Cases

Between February 2013 and June 2015, 124 cases of cerebral aneurysm in our clinical practice were treated with either clipping or coiling. Among these, 18 cerebral aneurysms were enrolled in this study. The subjects were 1 male and 17 female patients ranging from 37 to 78 (mean 63) years of age. Aneurysms were located at the ICA-posterior communicating artery (PCoA) bifurcation in 8, ICA-anterior choroidal artery (AChA) bifurcation in 3, MCA bifurcation in 2, BA bifurcation in 2, BA-SCA bifurcation in 1, ICA bifurcation in 1, and VA-posterior inferior cerebellar artery (PICA) bifurcation in 1. Seven of these aneurysms had ruptured (Table).

The 4.0-mm-diameter endoscope was used in the initial 9 aneurysms, and the 2.7-mm-diameter model was used in the other 9 aneurysms. In these 18 aneurysms, endoscopic fluorescein video angiography enabled visual observation of blood flow in the dead angle areas of the microscope. Although the 4.0-mm-diameter endoscope provided a higher quality fluorescence image, the image provided by the 2.7-mm-diameter endoscope was sufficiently bright and clear to reveal blood flow during surgery.

In the 12 ICA aneurysms, the endoscope was introduced medial to the ICA in 10 aneurysms and lateral in 2. The endoscope was inserted anterior to the BA in BA bifurcation and BA-SCA bifurcation aneurysms, posterior to the MCA, and rostral to the VA aneurysms. In 4 of 9 aneurysms viewed with the 2.7-mm-diameter endoscope, simultaneous monitoring of the microscope and endoscope during the clip procedures was achieved, which facilitated clip application in the best position as reported previously.[10] On the other hand, due to the limited space, such monitoring was possible with the 4.0-mm endoscope in only 1 aneurysm. The 2.7-mm-diameter endoscope was employed with the other 5 aneurysms and the 4.0-mm-diameter endoscope with 8 aneurysms; observation with the endoscope was conducted before and after clipping.

Fluorescein video angiography of intra-arterial and intravenous injection was performed in 13 and 5 aneurysms, respectively.

Confirmation of Aneurysmal Occlusion

Although the microscope allowed the surgeons to observe the upper surface of the aneurysmal neck, in most aneurysms it is difficult to observe the entire aneurysmal neck. The entire aneurysmal neck was observed with the microscope alone in only 3 aneurysms (16.7%). On the other hand, the 30° angled endoscopes used in tandem with the microscope enabled us to observe the entire neck in all aneurysms and the unveiled neck remnant in 3 aneurysms (patients 6, 15, and 16). An additional fenestrated clip was applied to the residual neck, and complete aneurysm occlusion was obtained in patient 15. The clip was not repositioned because the minimal neck remnant was necessary to spare the branching vessels in patients 6 and 16.

In addition, endoscopic fluorescein video angiography revealed incomplete clipping in the dead angle areas of the microscopic view. In all cases, microscopic fluorescence video angiography confirmed no inflow of fluorescein into the aneurysm and the endoscopic observation without fluorescein video angiography showed the clips were applied in the appropriate position. However, endoscopic fluorescein video angiography clearly showed incomplete occlusion of the aneurysm by revealing fluorescein influx into the aneurysmal dome in 2 aneurysms (patients 17 and 18). After reapplication of the clips, repeated endoscopic fluorescein video angiography confirmed complete obliteration in both aneurysms.

Confirmation of Perforator Patency

The findings of preoperative CTA and DSA strongly suggested that perforating arteries were present around the aneurysmal neck of 15 aneurysms, but microscopic observation was unsuccessful at revealing the origin of the perforators in all 15 aneurysms (ICA-PCoA bifurcation in 8, ICA-AChA bifurcation in 3, BA bifurcation in 2, BA-SCA bifurcation in 1, and ICA bifurcation in 1). The 30° angled endoscope, however, readily revealed the perforating arteries of the dead angle areas, including their origins, in all 15 aneurysms. Furthermore, endoscopic fluorescein video angiography provided a direct view of the blood flow (stream) in these arteries. Although the endoscope revealed no kinking and no clip involvement with these arteries in all 15 aneurysms, endoscopic fluorescein video angiography demonstrated the unexpected occlusion of the perforating branch in 3 aneurysms (patients 7, 17, and 18). In these cases, blood flow was restored after reapplication of the clips, a finding confirmed by repeated endoscopic fluorescein video angiography in patients 17 and 18; in patient 7, however, reapplication of the clip was not attempted because the origin of the occluded perforating branch was close to the bleeding point at the aneurysmal neck.

Comparison of Endoscopic Fluorescein Video Angiography With Microscopic Video Angiography and Endoscopic Imaging Without Fluorescein Video Angiography

Endoscopic fluorescein video angiography provided new information in addition to microscopic video angiography in all but 3 cases (83.3%; 2 MCA aneurysms and a VA-PICA aneurysm), including aneurysmal occlusion in 15 (83.3%) aneurysms and perforator patency in 15. Furthermore, compared to the endoscopic images alone, endoscopic fluorescein video

TABLE. Summary of Patients' Characteristics

						Intraoperative findings								Postoperative findings				
						Microscope				Endoscope								
						AN neck		Origin of perforators		AN neck		Origin of perforators		CT	CTA or DSA			
Patient no	Age/ sex	Type of onset	AN location	Endoscope diameter (mm)	Endoscope monitoring	Optical observation	FLUO	Visibility	FLUO	Optical observation	FLUO	Visibility	FLUO		Perforators	AN	Postoperative symptom	Outcome (mRS)
1	43/F	Un	MCA	4.0	Intermittent	Entire, NR(−)	CO	(−)	(−)	Entire, NR(−)	CO	(−)	(−)	None	(−)	CO	None	0
2	73/F	Un	BA-top	4.0	Continuous	FS, NA	CO	Invisible	Invisible	Entire, NR(−)	CO	Visible	P	None	Invisible	CO	IIIrd N palsy	0
3	52/M	Un	MCA	4.0	Intermittent	Entire, NR(−)	CO	(−)	(−)	Entire, NR(−)	CO	(−)	(−)	None	(−)	CO	None	0
4	62/F	Un	ICA-AChA	4.0	Intermittent	FS, NA	CO	Invisible	Invisible	Entire, NR(−)	CO	Visible	P	None	Invisible	CO	None	0
5	66/F	Un	BA-top	4.0	Intermittent	FS, NA	CO	Invisible	Invisible	Entire, NR(−)	CO	Visible	P	None	Invisible	CO	IIIrd N palsy	0
6	69/F	Un	ICA-PCoA	4.0	Intermittent	FS, NA	CO	Invisible	Invisible	Entire, NR(+)	NR	Visible	P	None	Invisible	NR	None	0
7	37/F	R (Gr 1)	ICA-AChA	4.0	Intermittent	FS, NA	CO	Invisible	Invisible	Entire, NR(−)	CO	Visible	O	None	Invisible	CO	None	0
8	69/F	Un	ICA-PCoA	4.0	Intermittent	FS, NA	CO	Invisible	Invisible	Entire, NR(−)	CO	Visible	P	None	Invisible	CO	None	0
9	57/F	Un	ICA-PCoA	4.0	Intermittent	FS, NA	CO	Invisible	Invisible	Entire, NR(−)	CO	Visible	P	None	Invisible	CO	None	0
10	72/F	R (Gr 3)	VA-PICA	2.7	Intermittent	Entire, NR(−)	CO	(−)	(−)	Entire, NR(−)	CO	(−)	(−)	None	(−)	CO	None	0
11	78/F	R (Gr 4)	ICA-PCoA	2.7	Intermittent	FS, NA	CO	Invisible	Invisible	Entire, NR(−)	CO	Visible	P	None	Invisible	CO	None	4
12	64/F	Un	ICA-PCoA	2.7	Continuous	FS, NA	CO	Invisible	Invisible	Entire, NR(−)	CO	Visible	P	None	Invisible	CO	None	0
13	63/F	R (Gr 2)	ICA-PCoA	2.7	Intermittent	FS, NA	CO	Invisible	Invisible	Entire, NR(−)	CO	Visible	P	None	Invisible	CO	None	1
14	73/F	Un	BA-SCA	2.7	Intermittent	FS, NA	CO	Invisible	Invisible	Entire, NR(−)	CO	Visible	P	None	Invisible	CO	None	0
15	41/F	R (Gr 1)	ICA-terminal	2.7	Continuous	FS, NA	CO	Invisible	Invisible	Entire, NR(+)→(−)	NR→CO	Visible	P	None	Invisible	CO	None	0
16	66/F	R (Gr 4)	ICA-AChA	2.7	Continuous	FS, NA	CO	Invisible	Invisible	Entire, NR(+)	NR	Visible	P	None	Invisible	NR	None	4
17	72/F	Un	ICA-PCoA	2.7	Continuous	FS, NA	CO	Invisible	Invisible	Entire, NR(−)	ICO→CO	Visible	O→P	LDA	Invisible	CO	None	0
18	73/F	R (Gr 4)	ICA-PCoA	2.7	Intermittent	FS, NA	CO	Invisible	Invisible	Entire, NR(−)	ICO→CO	Visible	O→P	None	Invisible	CO	None	4

AN, aneurysm; CO, complete occlusion; FS, front surface; FLUO, fluorescence video angiography; ICO, incomplete occlusion; Gr, World Federation of Neurosurgeons grade; LDA, low-density area; NA, not assessable; NR, neck remnant; O, occlusion; P, preservation; R, ruptured; Un, unruptured; IIIrd N, oculomotor nerve; (+), exist; (−), not exist

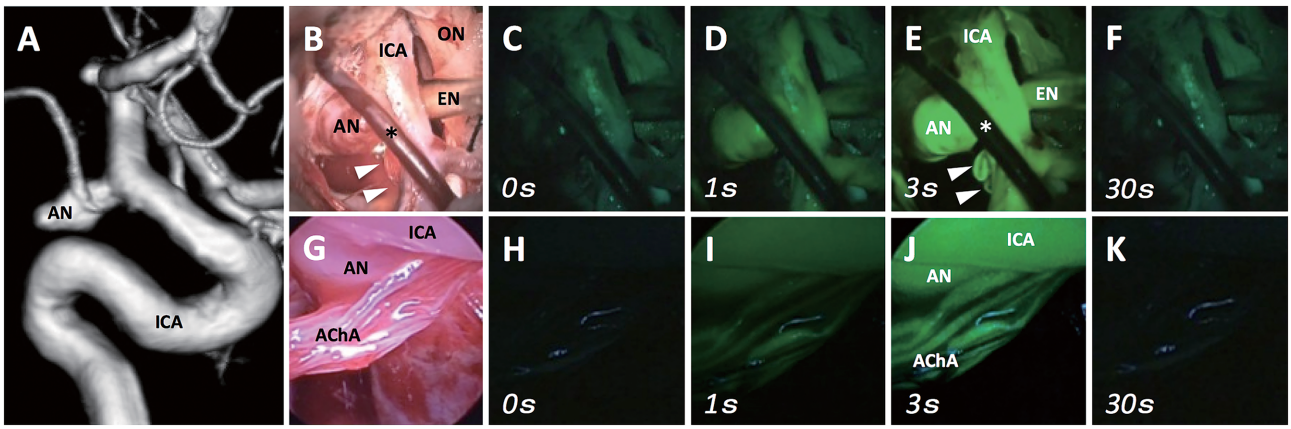

FIGURE 1 **A**, *Preoperative 3-dimensional DSA (lateral view) showing a left ICA-AChA aneurysm.* **B**, *Microscopic view before clip placement showing the aneurysm.* **C-F**, *Microscopic fluorescein video angiography.* **C**, *Fluorescence is not observed before injection of sodium fluorescein.* **D**, *One second after injection, fluorescence appears.* **E**, *Three seconds after injection, strong fluorescence appears in the parent artery, aneurysm, and distal part of the AChA.* **F**, *Thirty seconds after injection, fluorescence has disappeared.* **G**, *Endoscopic view before clip placement showing aneurysm and origin of the AChA.* **H-K**, *Endoscopic fluorescein video angiography.* **H**, *Fluorescence is not observed before injection of sodium fluorescein.* **I**, *One second after injection, fluorescence rapidly appears.* **J**, *Three seconds after infection, fluorescence clearly shows the parent artery, aneurysm, and origin of the AChA.* **K**, *Thirty seconds after injection, fluorescence has disappeared. AN, aneurysm; EN, endoscope with the diameter of 2.7 mm; ON, optic nerve. The asterisk indicates bridging vein; arrowheads, the distal part of the AChA.*

angiography directly revealed the blood flow (stream) in all cases. Notably, only the novel endoscopic video angiography system revealed incomplete clipping and the occlusion of the perforating branch in 2 and 3 aneurysms, respectively.

Comparison of Endoscopic Fluorescein Video Angiography With Postoperative Findings

DSA was performed after clipping either intraoperatively in 13 aneurysms (72.2%) or postoperatively in 6 (33.3%). All patients underwent postoperative CTA. Although accurate evaluation of fine perforating arteries was difficult even with DSA, the findings of postoperative angiography regarding aneurysmal occlusion and neck remnant were compatible with those of intraoperative endoscopic fluorescein video angiography in all aneurysms.

Postoperative Symptoms and Outcomes

Transient oculomotor nerve palsy without permanent neurological deficit was observed in 2 patients after surgery. Postoperative CT demonstrated a newly developed spotty ischemic lesion in the territory of the perforators in 1 aneurysm (patient 17). The outcomes were excellent (modified Rankin scale [mRS] 0 or 1) in all cases except for 3 cases of ruptures whose preoperative clinical grades were poor (patients 11, 16, and 18). No side effects such as allergic reactions to fluorescein administration or morbidity related to the endoscope were detected.

Illustrative Cases

Case 1 (Patient 16)

A 66-year-old female was transferred to our hospital 8 h after onset of subarachnoid hemorrhage (World Federation of Neurosurgical Societies grade 4). Preoperative DSA showed a left ICA-AChA aneurysm (Figure 1A). Surgery was performed via a left pterional approach under motor evoked potential (MEP) monitoring. The aneurysm, with a maximum diameter of 6.1 mm, was located on the posterior surface of the ICA, and the distal part of the AChA was confirmed (Figure 1B). Before clip placement, intra-arterial microscopic fluorescein video angiography was performed through a catheter for intraoperative DSA, revealing the blood flow in the aneurysm and the surrounding arteries including the distal part of the AChA (Figures 1C-1F). The 2.7-mm-diameter endoscope, which was introduced medial to the ICA, revealed the origin of the AChA behind the parent artery and the aneurysm as well as the aneurysmal neck on the opposite side of the microscopic view (Figures 1G). Endoscopic fluorescein video angiography clearly revealed the blood flow in the origin of the AChA behind the parent artery and the aneurysm (Figures 1H-1K). The aneurysm was occluded with a straight clip under simultaneous monitoring with the microscope and endoscope (Figure 2A). Microscopic fluorescein video angiography showed no fluorescence in the aneurysmal dome, while blood flow in the distal part of the AChA was preserved (Figures 2B and 2C). The endoscope revealed the minimal neck remnant (Figure 2D), and endoscopic fluorescein video angiography clearly demonstrated the patency of the origin of the AChA behind the parent artery and the aneurysm (Figures 2E and 2F). Postoperative CTA confirmed the minimal neck remnant of the aneurysm and the preservation of the parent artery (Figure 2G). Postoperative CT showed no new ischemic lesions, and the patient was transferred to another hospital for rehabilitation of the

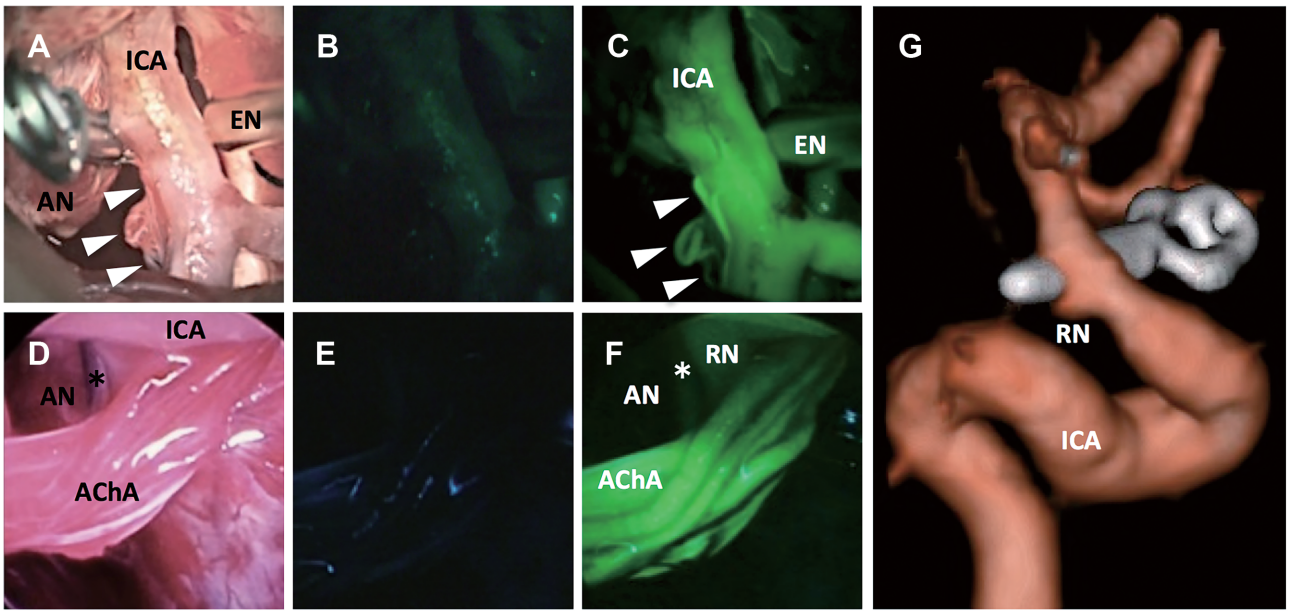

FIGURE 2. **A**, *Microscopic view after placement of clip.* **B** *and* **C**, *Microscopic fluorescein video angiography.* **B**, *Fluorescence is not observed before injection of sodium fluorescein.* **C**, *Microscopic fluorescein video angiography obtained after placement of clip showing no fluorescence in the aneurysm and preservation of blood flow in the ICA and distal part of the AChA.* **D**, *Endoscopic view showing occlusion of the aneurysm and origin of the AChA.* **E**, *Endoscopic fluorescein video angiography before injection of sodium fluorescein showing no fluorescence.* **F**, *Endoscopic fluorescein video angiography after clipping clearly reveals the minimal residual neck of the aneurysm and preservation of blood flow in the origin of the AChA.* **G**, *Postoperative CTA showing minimal residual neck of the aneurysm. AN, aneurysm; EN, endoscope with the diameter of 2.7 mm; RN, residual neck. The asterisk indicates the clip blade; arrowheads, the distal part of the AChA.*

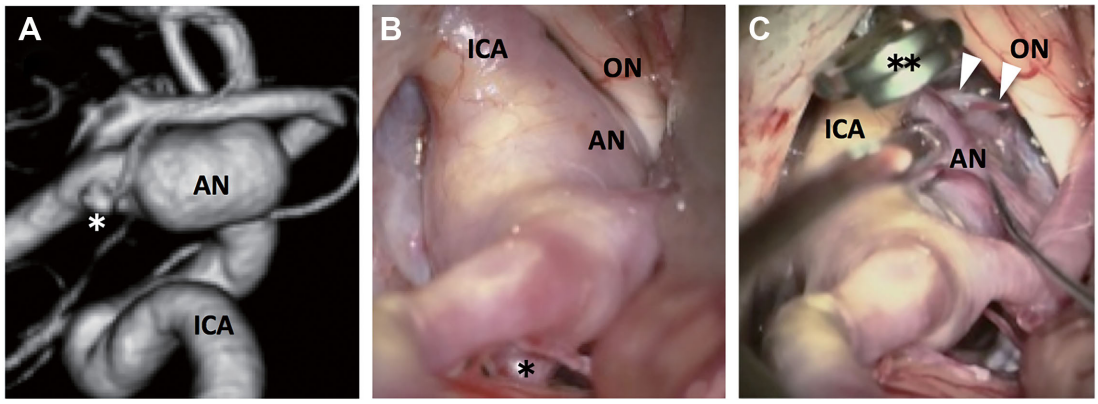

FIGURE 3. **A**, *Preoperative 3-dimensional DSA (posterolateral view) showing a posteriorly projecting left ICA-PCoA.* **B**, *Microscopic view before clipping showing the ICA-PCoA aneurysm.* **C**, *Microscopic view before clipping reveals the PCoA behind the aneurysm. AN, aneurysm; ON, optic nerve. The asterisk indicates ICA-AChA aneurysm; the double asterisk indicates temporary clip; Solid arrowheads, PCoA.*

symptoms due to primary brain damage from subarachnoid hemorrhage.

Case 2 (Patient 17)

A 72-year-old female was admitted to our institution for treatment of an unruptured left ICA-PCoA aneurysm. Preoperative DSA demonstrated a left ICA-PCoA aneurysm with a maximum diameter of 10 mm and a small left ICA-AChA aneurysm (Figure 3A). Surgery was performed via a left pterional approach under MEP monitoring. The ICA-PCoA aneurysm projected posteromedially (Figure 3B), and the PCoA was confirmed through gentle retraction of the aneurysm (Figure 3C).

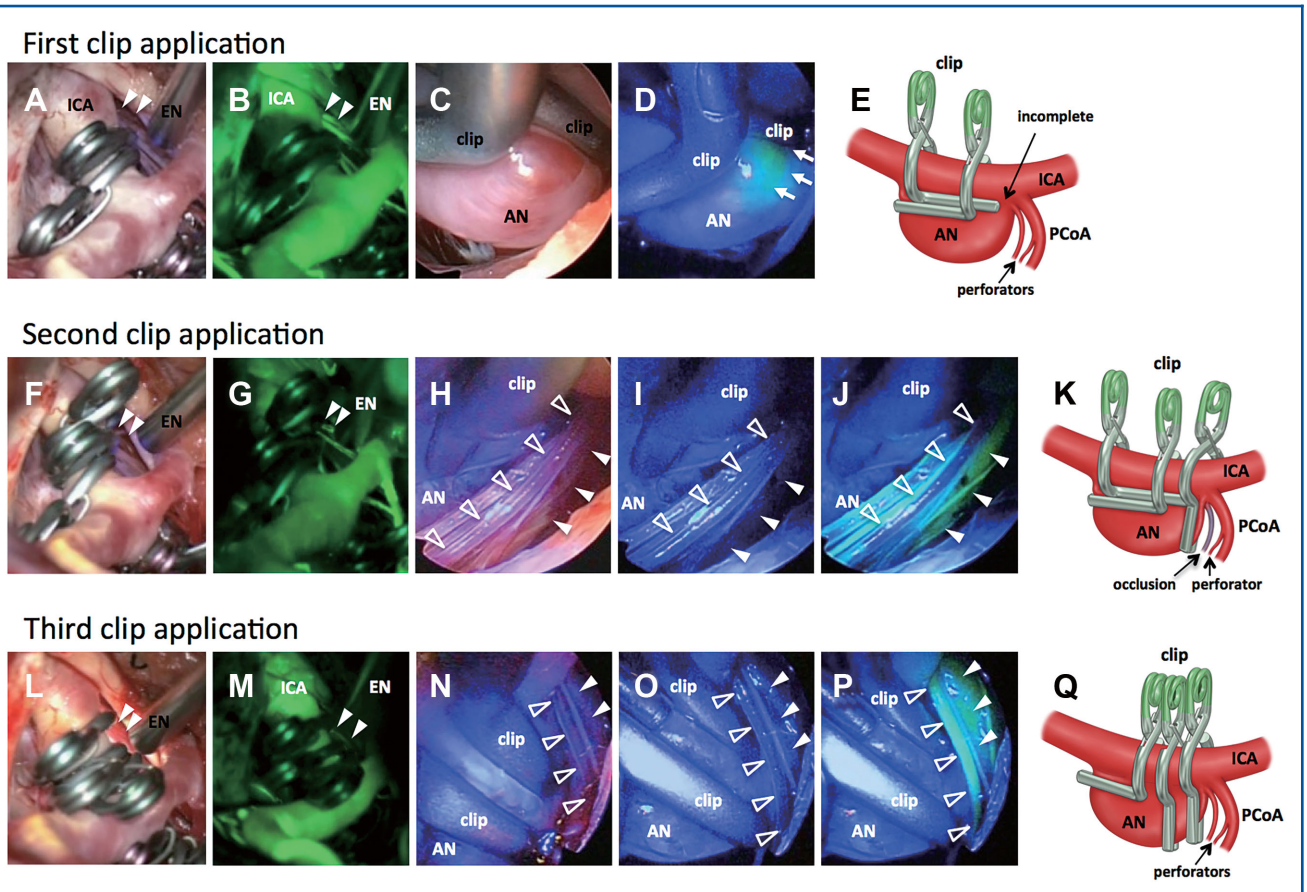

FIGURE 4. **A**, *Microscopic view after placement of multiple clips.* **B**, *Microscopic fluorescein video angiography after clipping showing no fluorescence in the aneurysm and preservation of blood flow in the ICA and PCoA.* **C**, *Endoscopic view showing no neck remnant of the aneurysm.* **D**, *Endoscopic fluorescein video angiography after clipping, revealing inflow of fluorescence (arrows) into the aneurysmal dome.* **E**, *Schematic illustration at first clip application.* **F**, *Microscopic view after additional clip.* **G**, *Microscopic fluorescein video angiography after additional clip showing no fluorescence in the aneurysm and preservation of blood flow in the ICA and PCoA.* **H**, *Endoscopic view showing no kinking of the PCoA and perforating arteries.* **I**, *Endoscopic view before injection of sodium fluorescein.* **J**, *Endoscopic fluorescein video angiography after additional clip placement revealing disappearance of blood flow in the perforating artery of the PCoA.* **K**, *Schematic illustration at the second clip application.* **L**, *Microscopic view after the reapplication of clips.* **M**, *Microscopic fluorescein video angiography after reapplication of clips showing no fluorescence in the aneurysm and preservation of blood flow in the ICA and PCoA.* **N**, *Endoscopic view showing no neck remnant of the aneurysm and no kinking of the PCoA or perforating arteries.* **O**, *Endoscopic view before injection of sodium fluorescein.* **P**, *Endoscopic fluorescein video angiography after reapplication of clips revealing preservation of blood flow in the PCoA and perforating arteries.* **Q**, *Schematic illustration at application of third clip. AN, aneurysm; EN, endoscope with the diameter of 2.7 mm. Solid arrowheads, PCoA; open arrowheads, the perforating artery of the PCoA.*

The 2.7-mm-diameter endoscope was introduced into the narrow space medial to the ICA, and held in the operative field during the clip procedure. Initially, the ICA-PCoA aneurysm was occluded with 2 angled ring clips, and the ICA-AChA aneurysm was occluded with 2 curved mini clips (Figure 4A). Although microscopic fluorescein video angiography by intra-arterial injection showed no fluorescence of aneurysmal domes (Figure 4B) and the endoscope revealed complete clipping (Figure 4C), endoscopic fluorescein video angiography showed slow inflow of a small amount of fluorescence into the dome of the ICA-PCoA aneurysm, indicating incomplete clipping (Figures 4D and 4E). An additional straight ring clip was applied to the proximal aneurysm neck (Figure 4F), eliminating the flow of fluorescence into the aneurysmal dome. However, occlusion of the PCoA perforator was revealed by endoscopic video angiography but not by microscopic video angiography or endoscopic imaging (Figures 4G-4K). Therefore, the angled ring clips were replaced with 2 straight ring clips (Figures 4L and 4M). Repeated follow-up endoscopic video angiography showed complete occlusion of the aneurysms and preservation of blood flow in all PCoA perforators (Figures 4N-4Q). No MEP change was detected during surgery. Although postoperative CT showed a minimal spotty ischemic lesion (arrow) at the left thalamus (Figure 5A), no symptomatic complication was evident. Postoperative CTA revealed the

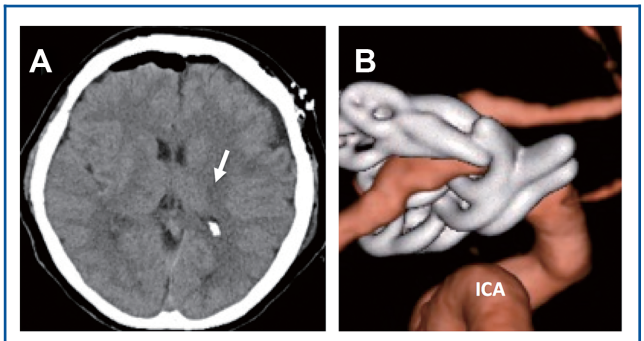

FIGURE 5. **A**, *Postoperative CT showing a small low-density area (arrow).* **B**, *Postoperative CTA showing occlusion of the aneurysm.*

disappearance of the aneurysm and preservation of the parent arteries (Figure 5B).

Case 3 (Patient 5)

A 66-year-old female with an unruptured BA bifurcation aneurysm (Figure 6A) underwent aneurysm clipping via a right subtemporal approach. The aneurysm, with a maximum diameter of 5.5 mm, was oriented superiorly (Figure 6B1). Before clip placement, intra-arterial microscopic fluorescein video angiography was performed through a catheter for intraoperative DSA (Figure 6B2). The 4.0-mm-diameter endoscope, introduced anterior to the BA, revealed that the perforator, originating from the left P1 segment, adhered to the aneurysmal dome in the dead angle areas of the microscopic view (Figure 6B3). Endoscopic fluorescein video angiography was also performed before clip placement (Figures 6B4 and 6B5). The aneurysm was occluded with a curved clip (Figure 6B6). Microscopic fluorescein video angiography showed no fluorescence of the aneurysmal dome and preservation of blood flow in the bilateral PCA and part of the perforating artery (Figure 6B7). However, the blood flow in the distal part of the perforator could not be confirmed. Endoscopic fluorescein video angiography showed preservation of blood flow in both the origin and distal part of the perforating artery (Figures 6B8-6B10). Postoperative CTA confirmed complete occlusion of the aneurysm and preservation of the parent arteries (Figure 6C). Although she presented with transient oculomotor nerve palsy, the patient left our hospital with all neurological deficits eventually disappearing.

DISCUSSION

We have developed an endoscopic video angiography system employing sodium fluorescein, a strong fluorescence dye, and have demonstrated for the first time that this innovative system provides clear and bright fluorescence imaging of the blood flow hidden in the dead angle areas of the microscope. Endoscopic fluorescein video angiography provides a new opportunity for detecting occlusion of perforating arteries and incomplete occlusion in aneurysmal clipping that could not be confirmed with a microscope or endoscope or with conventional microscopic fluorescence (ICG and fluorescein) video angiography, resulting in reapplication of clips to achieve optimal neck clipping. Because no complications have been associated with endoscope use, endoscopic fluorescein video angiography can contribute to the safety and long-term effectiveness of aneurysmal clipping.

The efficacy of endoscopic ICG video angiography with commercially available endoscopes for aneurysm surgery has been reported previously. However, to ensure sufficient fluorescence, endoscopes used for ICG video angiography must exceed 4.0 mm in diameter.[13-15] Therefore, it can be difficult to avoid neural and vascular injuries when inserting the endoscope into the appropriate location in the narrow skull base area. In fact, in 9 of the 29 aneurysm cases, the 4.0-mm-diameter endoscope was too large for the tip to be set in the optimal position for proper imaging behind the parent artery or aneurysm (our unpublished data). In contrast, fluorescein video angiography can be performed with a 2.7-mm-diameter endoscope, which was safely and adequately employed in all cases. Although the quality of the fluorescence images from a 2.7-mm endoscope is not as good as that from a 4.0-mm diameter endoscope, it is sufficiently clear to confirm blood flow in aneurysm surgery. Moreover, the 2.7-mm-diameter endoscope can be used for simultaneous monitoring with a microscope and endoscope more often than is possible with the 4.0-mm-diamter one. As reported previously,[10] simultaneous monitoring is quite useful in aneurysm surgery because it facilitates clip application in the optimal position. Thus, use of the smaller caliber endoscope in fluorescein video angiography has another advantage in aneurysm surgery.

In this study, sodium fluorescein was injected intra-arterially in 13 cases (intraoperative DSA cases) and intravenously in 5 cases. The intra-arterial injection method resulted in clear high-contrast images and enabled repeat examination within a short time, as reported previously.[2] However, both the intra-arterial and intravenous injection methods provided images of sufficient brightness and contrast in endoscopic fluorescein video angiography.

The results of intraoperative endoscopic fluorescein video angiography were consistent with those of postoperative angiography in all cases. However, DSA remains the gold standard for both perioperative and intraoperative vessel and perforator evaluation. DSA, when performed with digital flat panel detectors in the recent hybrid operating room, can clearly evaluate aneurysm obliteration as well as parent arteries and perforating arteries of relatively large diameter. But the microscopic and endoscopic fluorescence video angiography can depict even fine perforating arteries. Therefore, combined use of microscopic and endoscopic fluorescence video angiography and intraoperative DSA would provide most reliable observational results of the vascular patency.

The other noteworthy feature of this study is the application of the angled-view (30° angled) endoscope. Mielke et al[15] previously reported the usefulness of endoscopic ICG video angiography in 30 aneurysm cases. However, they used a straight-view

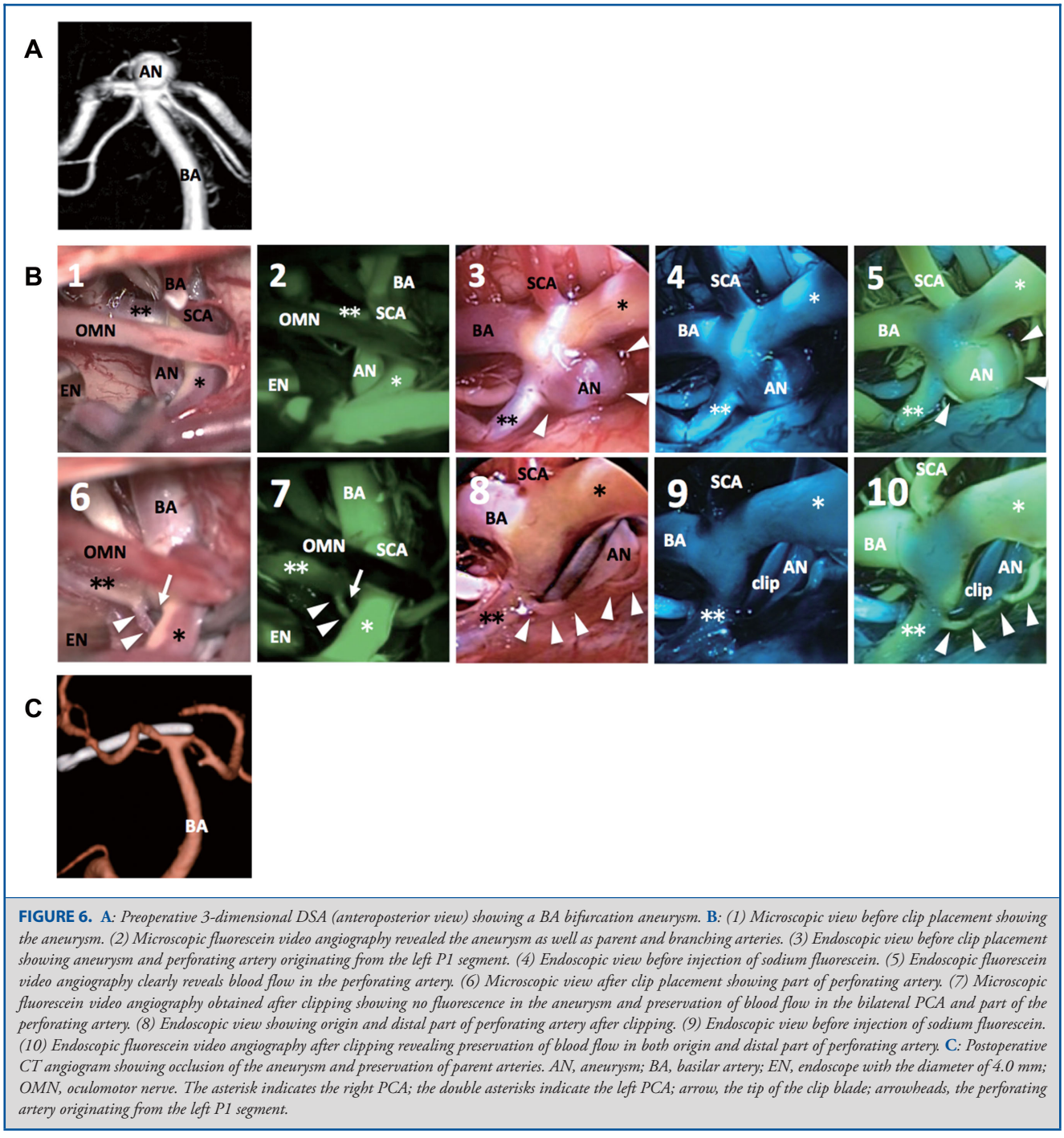

FIGURE 6. **A**: *Preoperative 3-dimensional DSA (anteroposterior view) showing a BA bifurcation aneurysm.* **B**: *(1) Microscopic view before clip placement showing the aneurysm. (2) Microscopic fluorescein video angiography revealed the aneurysm as well as parent and branching arteries. (3) Endoscopic view before clip placement showing aneurysm and perforating artery originating from the left P1 segment. (4) Endoscopic view before injection of sodium fluorescein. (5) Endoscopic fluorescein video angiography clearly reveals blood flow in the perforating artery. (6) Microscopic view after clip placement showing part of perforating artery. (7) Microscopic fluorescein video angiography obtained after clipping showing no fluorescence in the aneurysm and preservation of blood flow in the bilateral PCA and part of the perforating artery. (8) Endoscopic view showing origin and distal part of perforating artery after clipping. (9) Endoscopic view before injection of sodium fluorescein. (10) Endoscopic fluorescein video angiography after clipping revealing preservation of blood flow in both origin and distal part of perforating artery.* **C**: *Postoperative CT angiogram showing occlusion of the aneurysm and preservation of parent arteries. AN, aneurysm; BA, basilar artery; EN, endoscope with the diameter of 4.0 mm; OMN, oculomotor nerve. The asterisk indicates the right PCA; the double asterisks indicate the left PCA; arrow, the tip of the clip blade; arrowheads, the perforating artery originating from the left P1 segment.*

endoscope and were able to obtain, in addition to the microscopic findings, new information such as perforator patency and aneurysmal occlusion in the dead angle of the microscope in 42.3% of their cases. [15] In contrast, the angled-view endoscope revealed the obscured view under the microscope in all but 3 cases (83.3%) in this study. The application of angled-view endoscopes contributed to excellent visualization of the dead angle areas of the microscope. In particular, the origin of the perforating arteries located behind the parent artery could be observed and blood flow along the entire length was confirmed in all cases. Furthermore, in 2 cases this method unexpectedly detected incomplete occlusion of the aneurysm.

Limitations

As shown in this study, endoscopic fluorescein video angiography clearly confirmed blood flow in the perforators; however, unexpected spotty asymptomatic cerebral infarction related to the perforator surrounding aneurysms still occurred in 1 case (5.6%; patient 17). Since neither microscopic ICG/fluorescein video angiography nor endoscopic fluorescein video angiography demonstrated perforator occlusion in the patient, this infarction might be due to the dissection or endothelial damage due to the surgical manipulation leading to delayed occlusion of the perforators. Another limitation of this study is the small number of patients. However, the advantages of this innovative method in monitoring the status of aneurysmal occlusion and real-time blood flow in the arteries hidden under the microscope could be demonstrated even in this small number of patients. Of course, further study with a larger number of patients is necessary to establish the effectiveness of this procedure.

CONCLUSION

Our innovative method of endoscopic fluorescein video angiography for aneurysm surgery provided real-time assessment of blood flow in the dead angles of the microscope and presented no procedural complications. In addition, the smaller caliber and angled-view endoscope was ideal for performing safe aneurysm surgery with long-term effectiveness. This procedure is an excellent way to confirm blood flow in the fine perforators surrounding aneurysms. Consequently, this method will reduce operative morbidity related to vascular occlusion and improve the long-term effectiveness of aneurysm surgery by reducing incomplete clipping, thus improving outcomes.

Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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COMMENT

In this interesting paper, the authors describe their experience using the endoscope to perform fluorescein video angiography on 18 patients who underwent open clipping for identifying perforators and larger vessels, particularly in the "blind" angles of the microscope. The small endoscope they used was tuned to the emission spectrum of fluorescein.

The use of endoscopes during aneurysm surgery dates back a long way (Perneczky 1998).[1] It was promoted as a way to improve visualization around and behind aneurysms where microscopic visualization was often impossible. The difficulties encountered were that the endoscopes were often too large (>4 mm) to fit into the cisterns, working with the rigid

endoscope between major blood vessels was felt to be too perilous, and the endoscope itself could not visualize flow. Although there are some users, for the most part, endoscopy as an adjunct to aneurysm surgery has not come into common use. The authors have attempted to address the last of these concerns with the addition of fluorescein as a fluorophore to aid in visualizing flow. They, along with others, have tuned endoscopes to the infrared spectrum to visualize indocyanine green (ICG) in a similar fashion Bruneau 2013.[2] The advantage of ICG is that it is in wide use for cerebrovascular surgery as a microscopic tool, and that it is rapidly metabolized, making repeat administration easier. However, fluorescein has proved attractive for vascular visualization in that it produces images that are much sharper, owing to the shorter wavelength of the photons it emits and its high quantum yield. This has led some cerebrovascular surgeons to prefer fluorescein to ICG for microscopic use, particularly for small vessels such as perforators. The same qualities of brightness made it possible for the authors to decrease the size of their endoscope which could visualize fluorescein, from 4 mm initially to 2.7 mm for their last 9 patients.

The debate about whether video endoscopy is necessary or superior for aneurysm surgery is not likely to be settled here. That fluorescein is a better choice than ICG as a fluorophore for this application is very logical based upon its properties. In the hands of a skilled endoscopist, the risk of using a rigid endoscope for visualization should be very low. Figuring out how to position the endoscope to obtain good images and accurately interpreting them undoubtedly have learning curves. The results of the authors' study suggest that there is a high rate identifying perforator occlusion and other significant finding using their technique, even over and above the findings of microscopic videoangiography. Given the potential high cost to the patient and society of complications in aneurysm clipping, the extra trouble and expense associated with this technique could well be justified. It behooves cerebrovascular surgeons to explore this and other related technologies to make aneurysm surgery as safe as it can be.

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