



Title	Factors influencing cerebral aneurysm obliteration and reliability of indocyanine green video-angiography
Author(s)	Gekka, Masayuki; Nakayama, Naoki; Uchino, Haruto et al.
Citation	Acta neurochirurgica, 160(2), 269-276 https://doi.org/10.1007/s00701-017-3379-6
Issue Date	2018-02
Doc URL	https://hdl.handle.net/2115/72466
Rights	The final publication is available at link.springer.com
Type	journal article
File Information	ActaNeurochir160_269.pdf



Factors influencing cerebral aneurysm obliteration and reliability of indocyanine green video-angiography

Masayuki Gekka, MD, Naoki Nakayama, MD, PhD^{*}, Haruto Uchino, MD, Kiyohiro Houkin, MD, PhD

Department of Neurosurgery, Hokkaido University Graduate School of Medicine, Sapporo, Japan

^{*}Corresponding author: Department of Neurosurgery, Hokkaido University Graduate School of Medicine

N-15, W-7, Kita-Ku, Sapporo, 060-8638, Japan

Tel: +81-11-706-5987

Fax: +81-11-708-7737

E-mail: naoki-na@med.hokudai.ac.jp

This manuscript was not previously presented at any conference.

Abstract

Background: Indocyanine green video-angiography (ICG-V) is commonly used for intraoperative confirmation of aneurysm obliteration following clipping. However, direct puncture of the aneurysm wall occasionally results in blood leakage in patients for whom ICG-V has indicated complete closure. Therefore, the present study aimed to determine the reliability of ICG-V for confirming complete aneurysm closure, and to elucidate the factors underlying aneurysm obliteration and the occurrence of false-negative ICG-V findings.

Methods: Between June 2012 and June 2016, 89 patients (107 aneurysms total) undergoing aneurysm clipping were examined using ICG-V to confirm aneurysm closure. In ICG-V-negative cases, further confirmation of complete aneurysm closure was obtained via direct puncture of the aneurysm wall, except in cases where this procedure was deemed unsafe. To elucidate the possible causes of ICG-V inaccuracies, positive, negative, and false-negative ICG-V findings were compared in terms of aneurysm location (maximum height and length), neck width (parallel and orthogonal directions to the branching vessels), wall thickness around the neck, bifurcation angle, and direction of the clipping closure line. Statistical analyses were performed using the Welch's t-test and Chi-square test.

Results: Intraoperative ICG-V detected seven cases of incomplete aneurysm closure (6.5%), defined as positive ICG-V findings. Following direct aneurysm wall puncture, nine patients (8.4%) exhibited false-negative ICG-V findings. A Chi-square test revealed that false-negative ICG-V findings were significantly influenced by the presence of heterogeneous arteriosclerosis, and wall thickening at the clipping site, which were subjectively defined by the surgeon and confirmed by an independent observer, depending on the wall color and hardness, respectively.

Conclusions: Although ICG-V is useful for intraoperative confirmation of aneurysm obliteration, our findings further highlight the risk of false-negative ICG-V findings. Acknowledgement of risk factors is crucial for efficient detection of false-negative ICG-V findings.

Keywords: cerebral aneurysm clipping, aneurysm closure, ICG-V, indocyanine green, video-angiography

Introduction

Surgical clipping of cerebral aneurysms is done in order to achieve aneurysm obliteration (i.e., complete closure), thus avoiding subsequent increases in size and the risk of rupture. Therefore, reliable methods for the confirmation of aneurysm obliteration are critical during surgical treatment. One such method is indocyanine green video-angiography (ICG-V), which involves intravenous injection of a near-infrared fluorescent dye [5]. ICG-V is considered as a fast, reliable, and effective method for providing real-time information during neurovascular surgery [1, 4-7, 11, 13, 18, 21-22, 24].

Residual aneurysms are indicated by the presence of contrast agent in the body and/or dome of the aneurysm (dome filling [DF]), or by residual filling of the aneurysmal neck region (neck remnants [NRs]). Upon intraoperative detection of incomplete aneurysm closure following ICG injection, adjustment of existing clips or clip addition can aid in achieving complete closure. Previous studies have reported that clip adjustment rates during ICG-V range from 2 to 61% [5, 9, 11, 16, 19-21]. However, on rare occasions, ICG-V may indicate complete aneurysm closure when direct puncture of the aneurysm wall results in continuous blood leakage, indicating that the closure was incomplete [17]. The mechanisms underlying these false-negative findings are currently unknown. Understanding the factors that influence ICG-V reliability is crucial in determining the most adequate method for intraoperative confirmation of aneurysm obliteration during aneurysm clipping. Therefore, the present study aimed to determine the reliability of ICG-V for confirming complete aneurysm closure, and to elucidate the factors underlying aneurysm obliteration and the occurrence of false-negative ICG-V findings.

Methods

Patient selection and demographic information

Between June 2012 and June 2016, we analyzed the medical history and surgical records of 89 patients who had undergone aneurysm clipping. The cohort consisted of consecutive patients treated with aneurysm clipping during the indicated period. Patients with partially thrombosed giant aneurysms were excluded. After the absence of blood flow into the aneurysm had been observed via micro-Doppler ultrasonography or surgical microscopy, intraoperative ICG-V was performed to confirm aneurysm closure in all patients. ICG-V was performed at least twice in each patient (i.e., before and after the clipping procedure).

Incidental aneurysms were surgically treated in 89 patients (69 women, 20 men; mean age: 62 ± 10.3 years [range: 37-81 years]), including 90 unruptured aneurysms (84.1%) and 17 ruptured aneurysms causing subarachnoid hemorrhage (15.9%). Patient characteristics are presented in Table 1.

ICG-V

For all patients in the present study, ICG-V was performed as previously described [18-19]. Briefly, a solution of 0.1 mg/kg ICG was injected through the peripheral vein by an anesthesiologist. An operating microscope with integrated near-infrared ICG angiography capabilities (Zeiss, OPMI Pentero 900, Carl Zeiss Meditec, AG) was used for visualization. To observe the aneurysm, the patency of the parent vessel, and branching of the surrounding perforating vessels, intraoperative ICG-V was performed in all patients who had undergone surgical clipping.

Incomplete closure was determined based on the detection of ICG influx into the aneurysm dome (i.e., DF) or presence of NRs following clipping. Incomplete closure of the

aneurysm was considered a positive ICG-V finding and was resolved via clip adjustment or addition. Complete closure—defined as a negative ICG-V finding—was determined based on the absence of ICG influx into the aneurysm dome (DF) or NRs.

Direct puncture of the aneurysm wall after ICG-V

Direct puncture of the aneurysm wall was used to confirm aneurysm closure in patients with negative ICG-V findings, except in cases where such procedures were considered high-risk (e.g., when the aneurysm wall was located behind the parent vessels after clipping or when additional clip insertion was particularly difficult). Furthermore, direct puncture was not performed in patients with small-domed aneurysms, as the space was insufficient for performing the procedure appropriately. Whenever direct puncture of the wall generated blood leakage, indicating incomplete closure of the aneurysm, the ICG finding was regarded as a false-negative and resolved via clip adjustment or addition.

Investigating the causes of incomplete closure

The causes of incomplete closure were investigated via retrospective analysis of pre-operative and postoperative three-dimensional (3D) computed tomography angiography (CTA), digital or cerebral angiography (CA)/digital subtraction angiography (DSA) images, surgical videos, and intraoperative ICG-V findings.

Collected data included the following aneurysm-related information: aneurysm status (ruptured *versus* non-ruptured), location, dome size (maximum height and length), neck width (parallel and orthogonal directions to the branching vessels) (as presented in Figure 1), wall thickness at the clipping site, and bifurcation angle of the parent artery.

Wall thickness was evaluated intraoperatively, depending on the appearance and color of the aneurysm wall. Specifically, when the aneurysm wall was red colored and re-

mained thin and flexible, it was considered normal. If the aneurysm wall presented a slightly white discoloration with a slight loss of flexibility, it was considered to present with wall thickening. If the aneurysm presented an obvious white or yellow discoloration along with calcifications (i.e., hardening of the aneurysm wall), then it was considered to present atherosclerosis-like changes. This classification, although subjective, was performed twice: first intraoperatively by the surgeon and later confirmed by an independent observer through examination of the video recordings.

The following clipping-related information was also collected: type of clips used (curved *versus* straight), number of clips applied, direction of the closure line [10] generated by the clips to the parent branching vessels, and detailed clipping methods. The relevance of findings from intraoperative ICG-V (negative, positive, or false-negative) was analyzed in terms of the aforementioned factors.

Statistical analysis

The data were tested for normality using the Kolmogorov-Smirnov test. As this test revealed a non-normal distribution, non-parametric tests were utilized for subsequent analyses. Welch's t-test was performed to compare dome size (height and length), neck width in the parallel and orthogonal directions, and number of clips applied between cases in which complete and incomplete closure had occurred, and between cases with negative and false-negative findings. Chi-square tests were used to verify the association between complete or incomplete closure and wall thickness/direction of the closure line. Chi-square tests were also used to verify this association for negative and false-negative findings. For all tests, the level of statistical significance was set at $p < 0.05$.

Results

Aneurysm characteristics

A total of 107 aneurysms were included in this study. The aneurysms were presented by 90 patients, among which 76 had a single aneurysm and 14 had multiple aneurysms (11 patients had 2 aneurysms, whereas 3 patients had 3 aneurysms). Among the 14 patients with multiple aneurysms, two presented separate aneurysms on the left and right sides. For those two patients, two surgeries were performed on different days. For the remainder 12 patients, the multiple aneurysms were treated in the same surgery.

Thirty-nine aneurysms (36.4%) were located in the carotid artery, 38 (35.5%) in the middle cerebral artery, and eight (7.5%) in the arterial branches of the posterior circulation. The maximum height and length of the domes were 5.6 ± 2.8 mm and 5.3 ± 2.7 mm, respectively. Neck widths in the parallel and orthogonal directions were 4.5 ± 1.6 mm and 3.9 ± 1.36 mm, respectively. A total of 40 aneurysms (37.4%) exhibited thickening around the neck, with a mean bifurcation angle of $178.2 \pm 27.9^\circ$.

Of the 107 aneurysms, 82 (ruptured 13, unruptured 69) were less than 7 mm, whereas 22 (ruptured 3, unruptured 19) were between 7-15 mm, and 3 were (ruptured 1, unruptured 2) larger than 15 mm.

Clipping procedure

A total of 88 aneurysms (82.2%) required multiple clips, with a mean of 1.78 ± 0.76 clips per aneurysm. A total of 86 aneurysms (80.4%) were clipped orthogonally to the efferent arteries, whereas seven (6.5%) were clipped parallel to the efferent arteries. In the remaining 14 cases, an ideal closure line could not be achieved due to the type of the aneurysm and the required clipping line. Therefore, an oblique closure line was used in four cases (combined-type aneurysms), while the clips were applied along the circumference of the parent blood vessel in 10 cases (trunk-type aneurysms).

ICG-V findings

The results of ICG-V analysis are presented in Table 2, while a representative case is presented in Figure 2. Intraoperative ICG-V findings were positive in seven cases (6.5%). Among these seven cases, DF and NRs were observed in four and three cases, respectively. In these cases, complete closure was achieved by changes to clipping design or via clip addition. Complete closure was subsequently confirmed using ICG-V.

Direct wall puncture

Results concerning false-negative ICG-V findings are presented in Table 4, while a representative case is presented in Figure 3.

In 65 cases with negative ICG-V findings, direct puncture of the aneurysm wall was performed for further confirmation of complete aneurysm closure. In the remaining cases, direct wall puncture was either considered unsafe or inadequate given the small size of the aneurysm. Nine aneurysms (8.4%) exhibited continuous blood leakage following direct wall puncture, despite negative ICG-V findings (Table 4). Major leakage (indicated by a thin stream of blood spurting vigorously from the site of puncture) was observed in two such cases (3.1%), whereas minor leakage (i.e., slow blood leakage from the site of puncture) was observed in seven cases.

Causes of incomplete closure

A comparison of the aneurysm characteristics between positive and negative ICG findings is presented in Table 3. For positive ICG-V findings, aneurysm sizes were significantly larger, particularly with reference to neck width in the parallel direction (6.63 ± 0.36 mm vs 4.17 ± 0.18 mm; $p=0.0014$).

There was no association between the number of clips used and ICG-V findings (i.e., positive, negative, and false-negative findings) (Table 3). We further investigated the association between the completeness of aneurysm closure and the direction of clipping. ICG-V findings were positive in one of seven patients with parallel closure lines (14.3%) and six of 86 (7%) patients with orthogonal closure lines. Although parallel closure lines tended to be associated with positive ICG-V findings, there was no significant association between the completeness of aneurysm closure based on ICG-V findings and the direction of the closure line.

A comparison between negative and false-negative ICG-V findings (Table 5) revealed that the dome size tended to be larger in patients with false-negative ICG-V findings, although no significant difference was observed.

Wall thickness around the neck was significantly greater in patients with false-negative ICG-V findings than in those with negative ICG-V findings ($p=0.0009$). In all cases with false-negative ICG-V findings, wall thickening (identified as yellow or white discoloration) was observed at the clipping site. Additionally, arteriosclerosis-like changes were observed at the clipping site in seven of nine patients with false-negative ICG-V findings, although the thickness of the wall at the clipping site was heterogeneous.

Discussion

ICG-V is increasingly used for the intraoperative confirmation of aneurysm obliteration during clipping surgery. Although ICG-V is considered accurate and reliable, previous reports have demonstrated the possibility for false-negative findings, particularly with respect to the persistence of blood flow and NRs [6, 17]. As direct puncture of the aneurysm wall is a routine procedure used to confirm obliteration after clipping [14, 17], false-negative findings may place patients at a risk for severe complications. In order to

elucidate the factors influencing complete aneurysm obliteration and ICG-V, the present study investigated the use of ICG-V in 89 patients undergoing aneurysm clipping surgery. To our knowledge, the present study is the first to address factors underlying the occurrence of false-negative ICG-findings.

The rate of clip adjustment in the present study was 6.5%, which falls within the range of 2%-38% reported in previous studies [5, 9, 11, 16, 18-21]. However, while previous studies relied on ICG-V to confirm kinks/occlusions of the perforating vessel or stenosis/occlusion of the parent vessel, ICG-V was used only after confirmation of vessel preservation via micro-Doppler ultrasonography in the present study.

In the present study, we observed an association between the width of the aneurysmal neck in the parallel direction of the branching vessels and incomplete intraoperative closure, which occurred more frequently as the neck of the aneurysm increased in width. Moreover, we observed no association between the direction of the clipping closure line/number of clips applied and incomplete intraoperative closure. False-negative ICG-V findings were detected in nine (13.8%) cases, two and seven of which involved major and minor leakage, respectively.

To understand the factors underlying ICG-V inaccuracy, we investigated both aneurysm-related factors and clipping-related factors. Our analysis revealed an association between heterogeneous thickness of the aneurysm wall at the clipping site (specifically, along the site of contact with the clip blade) and failure of ICG-V to detect incomplete closure. In contrast, no association was observed between clipping-related factors and ICG-V inaccuracy. Furthermore, there was no association between the number of clips used and ICG-V findings, which may have been due to the small and homogenous size of the aneurysms included in this study (i.e., varying between 5- 6 mm). In larger aneurysms, the number of clips applied is likely to be higher, with a larger variability among

the cases; hence, it would be then possible to establish such an association. In a large aneurysm with an atheromatous neck, forcibly closing the aneurysm with a single clip can lead to incomplete, heterogeneous closure. Therefore, the use of multiple clips should be considered in line with the size of the aneurysm, as well as with the presence of atherosclerotic tissue, in order to obtain a complete and natural closure line. On the other hand, in small aneurysms, booster clips are usually adequate to achieve a uniform and secure closure.

These results suggest that the presence of a thick, heterogenous wall at the clipping site may allow for residual influx of blood into the neck of the aneurysm, in turn resulting in low intravascular flow inside the aneurysmal dome. This area cannot be penetrated by the ICG dye due to the opposing pressure of the blood within the dome and the lowering of blood pressure due to general anesthesia.

For aneurysms exhibiting a thick, heterogeneous wall at the clipping site, intraoperative angiography (IA) may represent an alternative method for the confirmation of aneurysm obliteration. A comparative study by Washington and colleagues [23] demonstrated that IA was more effective in detecting incomplete closure in seven patients (total n=49, 14.3%) in whom ICG-V provided false-negative findings. However, the use of IA is limited, as this procedure can only be performed in hospitals specialized in cerebrovascular surgery, whereas ICG-V—which requires only an adequate surgical microscope—can be performed at any institution.

While ICG-V is useful for confirming aneurysm obliteration, it is crucial to acknowledge the risk factors for false-negative ICG-V findings and perform a second confirmatory procedure. One such procedure consists of holding and squeezing the dome of the aneurysm with forceps following clipping [8]. In cases of incomplete closure, the dome will bulge again once released from the forceps. This method is useful

for detecting the presence of small residual orifices in the neck of the closed aneurysm. Alternatively, direct puncture of the aneurysm wall can be used in patients presenting with neurologic symptoms due to the presence of mass signs, such as those with internal carotid artery-posterior communicating artery aneurysms, which result in oculomotor nerve palsy. Direct puncture has also been utilized in patients with giant aneurysms in the medial wall of the C2 region of the internal carotid artery, which have been associated with the development of optic nerve disorders. However, direct wall puncture is not considered safe in all patients. In patients with risk factors and in whom direct puncture is deemed unsafe, IA should be considered, a plan should be made for a second clipping procedure, and clinicians should be prepared to take an appropriate course of action in the event of new bleeding.

The occurrence of false-negative findings suggests that a proportion of clipped aneurysms are likely to thrombose, as observed in cases of coiled aneurysms [2]. The fact that, in the two representative cases, aneurysm puncture resulted in a prominent blood flow, leads us to hypothesize that these aneurysms could have not thrombosed if left untreated. Therefore, caution should be exercised in evaluating aneurysm cases and performing selective treatment.

The present study has some limitations. In our study, direct wall puncture was not performed in all patients with negative ICG-V findings. Puncture was not performed in patients for whom it was considered unsafe, including cases in which the aneurysm dome was located at a deep site or behind the parent vessel. Furthermore, puncture was not performed in patients with particularly small aneurysmal domes, which render the addition of clips difficult. Further studies involving the use of a second method for confir-

mation of negative ICG-V findings are required in order to verify the present results, and to identify factors that may improve the accuracy of ICG-V.

Conclusions

The findings of the present study indicate that during clipping surgery for aneurysm obliteration, complete closure of the aneurysm is influenced by wall thickness and neck width in the direction parallel to the branching vessels. Although ICG-V is useful for the intraoperative confirmation of aneurysm obliteration, our findings further highlight the risk of false-negative ICG-V findings, which are significantly influenced by the presence of heterogeneous arteriosclerosis at the clipping site. Acknowledgement of these risk factors is crucial for efficient detection of false-negative ICG-V findings.

Compliance with Ethical Standards

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Ethical approval

All procedures involving human participants were performed in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.

Funding

No funding was received for this research.

Acknowledgements

We would like to thank Editage (www.editage.jp) for medical writing and English language editing.

References

1. Awano T, Sakatani K, Yokose N, Hoshino T, Fujiwara N, Nakamura S, Murata Y, Kano T, Katayama Y, Shikayama T, Miwa M (2010) EC–IC bypass function in Moyamoya disease and non-Moyamoya ischemic stroke evaluated by intraoperative indocyanine green fluorescence angiography. *Adv Exp Med Biol* 662:519-524
2. Bandeira A, Raphaeli G, Balériaux D, Bruneau M, De Witte O, Lubicz B (2010) Selective embolization of unruptured intracranial aneurysms is associated with low retreatment rate. *Neuroradiol* 52:141-146
3. Batjer HH, Purdy PD (1990) Enlarging thrombosed aneurysm of the distal basilar artery. *Neurosurgery* 26:695-699
4. Bruneau M, Sauvageau E, Nakaji P, Vandesteene A, Lubicz B, Chang SW, Balériaux D, Brotchi J, De Witte O, Spetzler RF (2010) Preliminary personal experiences with the application of near-infrared indocyanine green videoangiography in extracranial vertebral artery surgery. *Neurosurgery* 66:305-311
5. Dashti R, Laakso A, Niemela M, Porras M, Celik O, Navratil O, Romani R, Hernesniemi J (2010) Application of microscope integrated indocyanine green video-angiography during microneurosurgical treatment of intracranial aneurysms: a review. *Acta Neurochir Suppl* 107: 107-109

6. Dashti R, Laakso A, Niemela M, Porras M, Hernesniemi J (2009) Microscope-integrated near-infrared indocyanine green videoangiography during surgery of intracranial aneurysms: the Helsinki experience. *Surg Neurol* 71:543-550
7. de Oliveira JG, Beck J, Seifert V, Teixeira MJ, Raabe A (2008) Assessment of flow in perforating arteries during intracranial aneurysm surgery using intraoperative near-infrared indocyanine green videoangiography. *Neurosurgery* 62:1300-1310
8. Della Puppa A, Ristemi O, Scienza R (2017) The “ICG Entrapment Sign” in cerebral aneurysm surgery assisted by Indocyanine Green Videoangiography. *World Neurosurg* 97:287-291
9. Fischer G, Stadie A, Oertel JM (2010) Near-infrared indocyanine green videoangiography versus microvascular Doppler sonography in aneurysm surgery. *Acta Neurochir (Wien)* 152: 1519-1525
10. Ishikawa T, Nakayama N, Moroi J, Kobayashi N, Kawai H, Muto T, Yasui N (2009) Concept of ideal closure line for clipping of middle cerebral artery aneurysms--technical note. *Neurol Med Chir* 49:273-277
11. Jing Z, Ou S, Ban Y, Tong Z, Wang Y (2010) Intraoperative assessment of anterior circulation aneurysms using the indocyanine green video angiography technique. *J Clin Neurosci* 17:26-28
12. Komotar RJ, Mocco J, Lavine SD, Solomon RA (2006) Angiographically occult, progressively expanding, giant vertebral artery aneurysm. Case report. *J Neurosurg* 105:468-471
13. Ma CY, Shi JX, Wang HD, Hang CH, Cheng HL, Wu W (2009) Intraoperative indocyanine green angiography in intracranial aneurysm surgery: microsurgical clipping and revascularization. *Clin Neurol Neurosurg* 111:840-846

14. Mery FJ, Amin-Hanjani S, Charbel FT (2008) Is an angiographically obliterated aneurysm always secure? *Neurosurgery* 62:979-982
15. Nagahiro S, Takada A, Goto S, Kai Y, Ushio Y (1995) Thrombosed growing giant aneurysms of the vertebral artery: growth mechanism and management. *J Neurosurg* 82:796-801
16. Oda J, Kato Y, Chen SF, Sodhiya P, Watabe T, Imizu S, Oguri D, Sano H, Hirose Y (2011) Intraoperative near-infrared indocyanine green-videoangiography (ICG-VA) and graphic analysis of fluorescence intensity in cerebral aneurysm surgery. *J Clin Neurosci* 18:1097-1100
17. Özgiray E, Aktüre E, Patel N, Baggott C, Bozkurt M, Niemann D, Başkaya MK (2013) How reliable and accurate is indocyanine green video angiography in the evaluation of aneurysm obliteration? *Clin Neurol Neurosurg* 115:870-878
18. Raabe A, Nakaji P, Beck J, Kim LJ, Hsu FP, Kamerman JD, Seifert V, Spetzler RF (2005) Prospective evaluation of surgical microscope-integrated intraoperative near-infrared indocyanine green videoangiography during aneurysm surgery. *J Neurosurg* 103:982-989
19. Rabbe A, Beck J, Gerlach R, Zimmermann M, Seifert V (2003) Near infrared indocyanine green video angiography: a new method for intraoperative assessment of vascular flow. *Neurosurgery* 52:132-139
20. Roessler K, Krawagna M, Dörfler A, Buchfelder M, Ganslandt O (2014) Essentials in intraoperative indocyanine green videoangiography assessment for intracranial aneurysm surgery: conclusions from 295 consecutively clipped aneurysms and review of the literature. *Neurosurg Focus* 36:1-7

21. Wang S, Liu L, Zhao Y, Zhang D, Yang M, Zhao J (2010) Evaluation of surgical microscope-integrated intraoperative near-infrared indocyanine green videoangiography during aneurysm surgery. *Neurosurg Rev* 34:209-215
22. Wang S, Liu L, Zhao YL, Zhang D, Yang MQ, Zhao JZ (2009) Effects of surgical microscope-based indocyanine green videoangiography during aneurysm surgery. *Zhonghua Yi Xue Za Zhi* 89:146-150
23. Washington CW, Zipfel GJ, Chicoine MR, Derdeyn CP, Rich KM, Moran CJ, Cross DT, Dacey RG Jr (2013) Comparing indocyanine green videoangiography to the gold standard of intraoperative digital subtraction angiography used in aneurysm surgery. *J Neurosurg* 118:420-427
24. Woitzik J, Horn P, Vajkoczy P, Schmiedek P (2005) Intraoperative control of extracranial–intracranial bypass patency by near-infrared indocyanine green videoangiography. *J Neurosurg* 102:692-69

Figure legends

Fig 1 Characteristics of a representative aneurysm: a) maximum height and width of the aneurysmal dome, b) neck width at the parallel and orthogonal directions to the branching vessels

Fig 2 Intraoperative indocyanine green (ICG) video-angiogram and preoperative three-dimensional (3D) computed tomography (CT) angiogram of patient 1. Patient 1 exhibited intraoperative incomplete closure on an ICG video-angiogram. (A) The preoperative 3D CT angiogram revealed an aneurysm at the origin of the bifurcation of the left middle cerebral artery (MCA). (B) Intraoperative microscopic view depicting the aneurysm of the MCA. (C) The view after applying multiple clips. (D) The ICG video-angiogram depicting a to-and-fro sign inside the aneurysmal dome (*, to-and-fro sign). (E) Intraoperative microscopic view depicting the final clipping arrangement. (F) ICG video-angiogram depicting the absence of flow within the aneurysm

Fig 3 Intraoperative indocyanine green (ICG) video-angiogram and preoperative three-dimensional (3D) computed tomography (CT) angiogram of Patient 2. Patient 2 exhibited false-negative ICG video-angiography findings. (A) The preoperative 3D CT angiogram revealed an aneurysm at the origin of the bifurcation of the left middle cerebral artery (MCA). (B) Intraoperative microscopic view depicting the aneurysm of the MCA. (C) The view after applying multiple clips. (D) ICG video-angiogram depicting the absence of flow within the aneurysm. (E) The view after the dome had been punctured with a 25-gauge needle. (F) After puncturing the dome, strong blood leakage was visible (*, site of bleeding following puncture). (G) Intraoperative microscopic view depicting the final clipping arrangement. (H) Postoperative 3D CT angiogram revealed complete obliteration of the aneurysm

Tables

Table 1 Summary of patient characteristics

Parameter	No. or Size
No. of patients	90 (M 20, F 70)
Mean age, years (range)	62.2 (37-81)
No. of patients with SAH	17 (15.9%)
No. of aneurysms by location	107
ICA	39 (36.5%)
MCA	38 (35.5%)
ACA	23 (21.5%)
PCA, BA-VA	7 (6.5%)
Size of the aneurysm, mm (mean)	5.3±2.7
dome size, max. length	5.6±2.8
neck width, max. height	3.9±1.6
orthogonal direction	4.5±1.6
parallel direction	

Wall thickness around the neck	40
circumference	9 (22.5%)
single-sided	6 (15%)
heterogeneous	25 (62.5%)
Bifurcation angle (°)	178.2±27.9
Number of clips applied (mean)	1.8
Direction of the closure line	
orthogonal	86 (80.4%)
parallel	7 (6.5%)

SAH, subarachnoid hemorrhage; ICA, internal carotid artery; MCA, middle cerebral artery; ACA, anterior cerebral artery; PCA, posterior cerebral artery BA-VA, vertebral and cerebral arteries; F, female; M, male; max., maximum

Table 2 Summary of cases in which intraoperative incomplete aneurysm closure was observed via ICG-V

Patient no.	Age (years) Sex	Aneurysm Location	Size (mm)	Aneurysm Characteristics	ICG-V Result	Action Taken after ICG-V
1	69 M	IC (top)	5.2	Small Wide neck	NR	Another (2 nd) clip was added at the NR
2	61 F	IC (C2)	6.3	Saccular Wide neck	NR	Another (2 nd) clip was added at the NR
3	43 M	M1-ATA	6.5	Multilobulated	NR	The 2 nd clip (curved clip) was changed to a straight clip
4	72 F	Acom	6	Multilobulated Neck calcification	DF	Another (3 rd) clip was added parallel to the 2 nd fenestrated clip through the partial length of the aneurysm

5	61	MCA bif.	7.0	Wide neck	DF	Another (3 rd) clip was added parallel to the 2 nd straight clip through the entire length of the dome
	M			Neck calcification		
6	66	MCA bif.	6.1	Wide neck	DF	Another (3 rd) clip was added parallel to the 1 st curved clip through the entire length of the aneurysm
	F					
7	61	MCA bif.	6.8	Multilobulated	DF	Another (4th) clip was added parallel to 2 nd curved clip through the partial length of the aneurysm
	F			Wide neck		

No., number; ICG-V, indocyanine green video-angiography; F, female; M, male; IC, internal carotid; ATA, anterior temporal artery; Acom, anterior communicating artery; MCA bif., middle cerebral artery bifurcation; NR, neck remnant; DF, dome filling

		Incomplete	Complete
		N=6	N=93
Dome (mm)	maximum height	6.0	5.0
	maximum length	6.5	5.4
Neck (mm)	orthogonal direction	4.1	3.8
	parallel direction	6.6	4.1
Rate of wall thickness around the neck		66.7%	39.9%
Number of clips applied		1.5	1.9
Closure line (orthogonal)		75.8%	83.3%

Table 3 Characteristics of clipped aneurysms and clipping procedure for cases of complete and incomplete closure

Table 4 Summary of false-negative ICG-V cases

Patient no.	Age (years) Sex	Aneurysm Location	Size (mm)	Aneurysm Characteristics	Leakage after Puncture	Action Taken after Puncture
1	70 F	IC (Pcom)	7	Saccular Wide neck Neck calcification	Major	Another (3 rd) clip was added parallel to the 1 st clip through the entire length of the aneurysm
2	74 F	MCA bif.	7.1	Saccular Neck calcification	Major	Another (3 rd) clip was added parallel to the 2 nd clip through the partial length of the aneurysm
3	64 F	IC (Acho)	8.4	Large, wide neck Neck calcification	Minor	Another (3 rd) clip was added parallel to the 2 nd clip through the entire length of the aneurysm
4	60 F	IC (Pcom)	5.1	Saccular Neck calcification	Minor	Another (2 nd) clip was added parallel to the 1 st clip through the entire length of the aneurysm

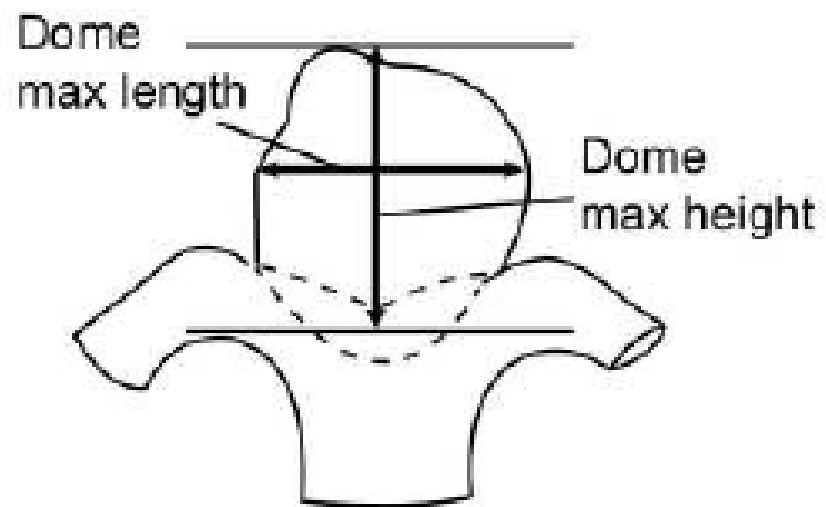
5	50 F	IC (top)	6.4	Multilobulated Neck calcification	Minor	Another (3 rd) clip was added parallel to the 2 nd clip through the entire length of the aneurysm
6	64 F	MCA bif.	5.1	Irregular shape Neck calcification	Minor	Natural hemostasis
7	81 F	MCA bif.	4	Small Neck calcification	Minor	Another (2 nd) clip was added parallel to the 1 st clip through the entire length of the aneurysm
8	72 F	MCA bif.	12.2	Large, Saccular Neck calcification	Minor	2 nd and 3 rd clips were added parallel to 1 st clip through the partial length of the aneurysm
9	68 F	MCA bif.	5.8	Saccular Neck calcification	Minor	3 rd and 4 th clips were added parallel to the 1 st clip through the entire length of the aneurysm

No., number; ICG-V, indocyanine green video-angiography; F, female; M, male; IC, internal carotid; Pcom, posterior communicating artery; Acho, anterior choroidal artery; Acom, anterior communicating artery; MCA bif., middle cerebral artery bifurcation

		False- Negative ICG-V N=9	True- Negative ICG-V N=56
Dome (mm)	maximum height	6.4	5.0
	maximum length	8.4	5.4
Neck (mm)	orthogonal direction	4.2	4.2
	parallel direction	4.5	4.7
Rate of wall thickness around the neck		100%	40%***
Number of clips applied		1.8	1.8
Closure line (orthogonal)		88.9%	88.0%

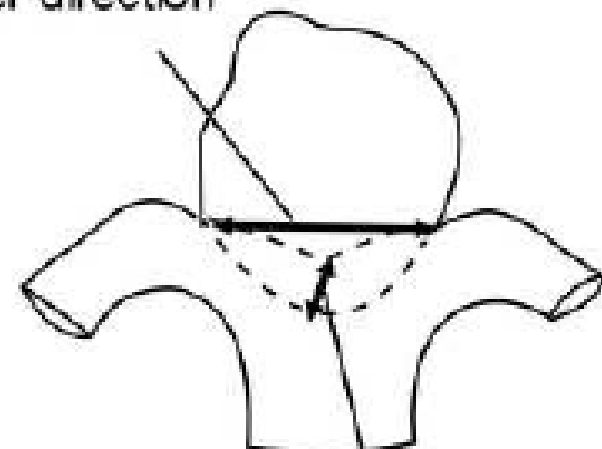
Table 5 Characteristics of clipped aneurysms and clipping procedure for cases in which negative and false-negative ICG-V findings were observed

ICG-V, indocyanine green video-angiography



a

Neck width
parallel direction



b

Neck width
orthogonal direction

Fig. 1

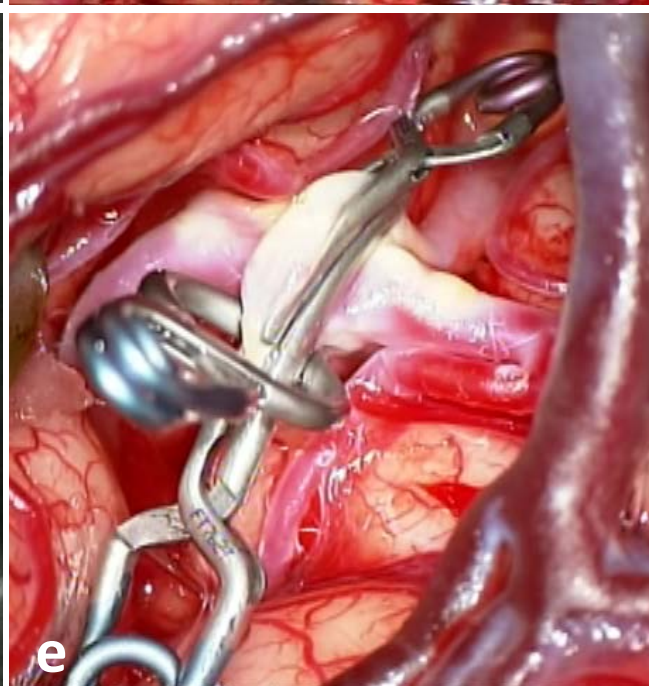
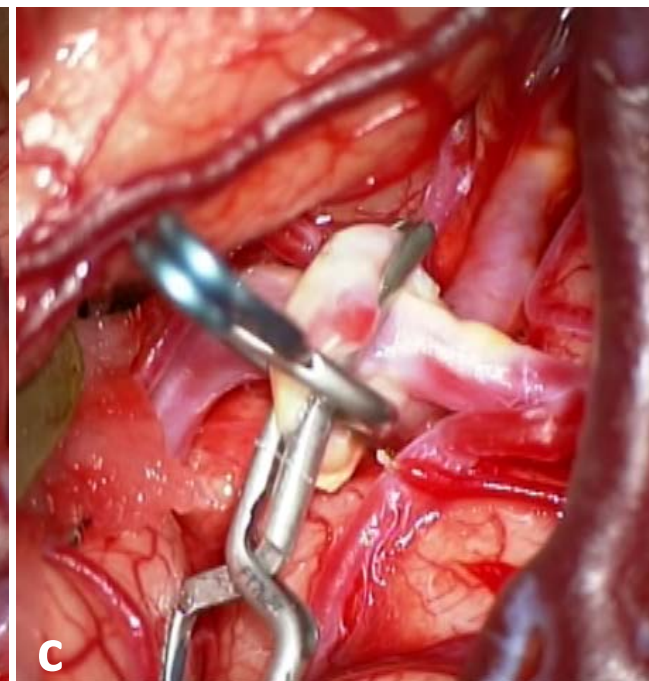
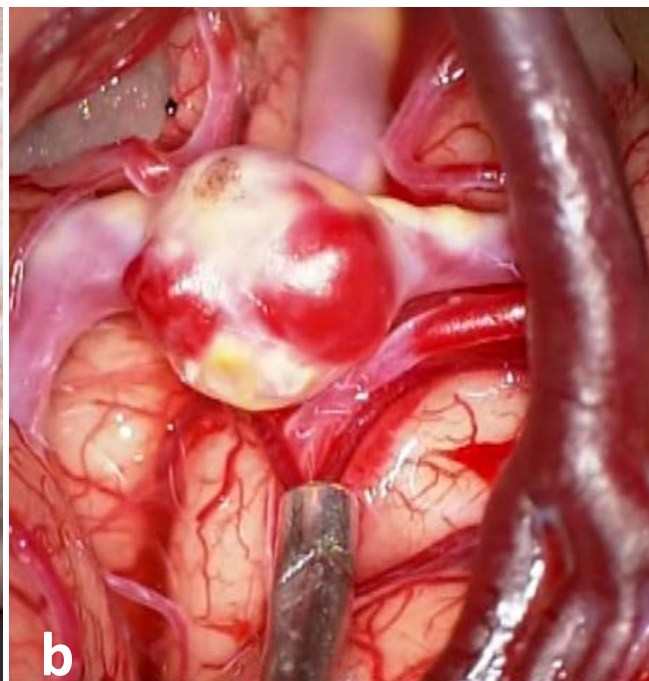
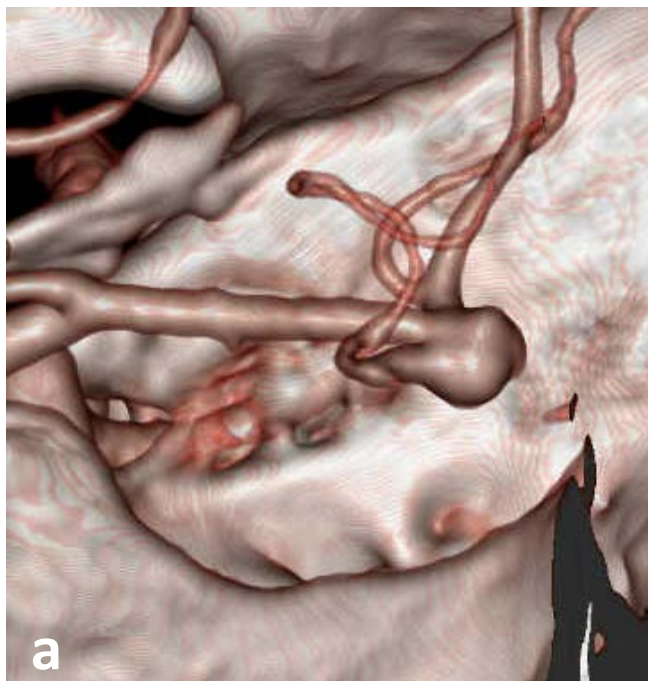


Fig. 2

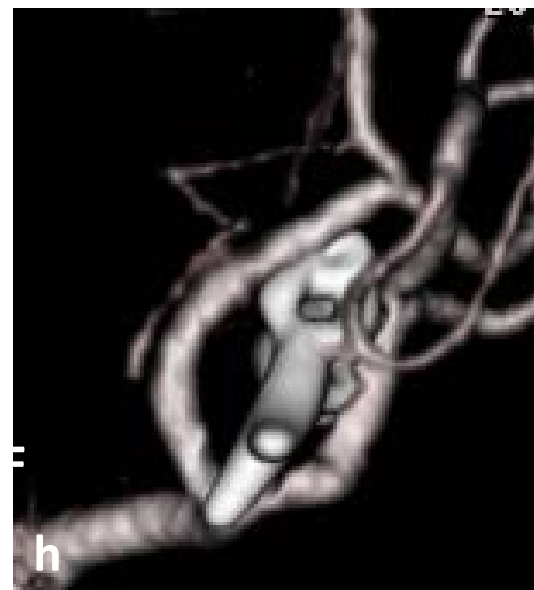
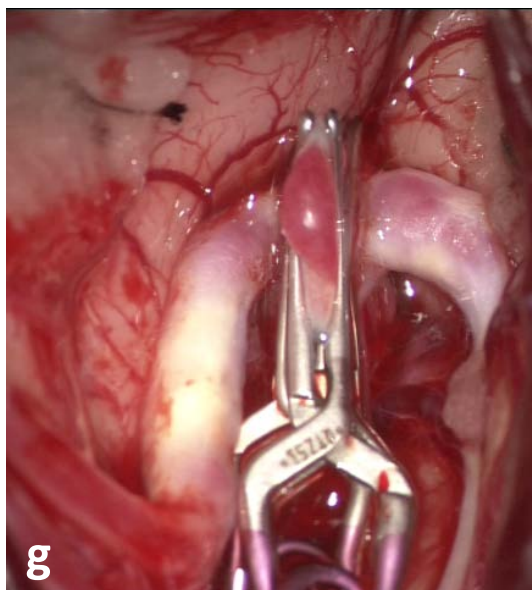
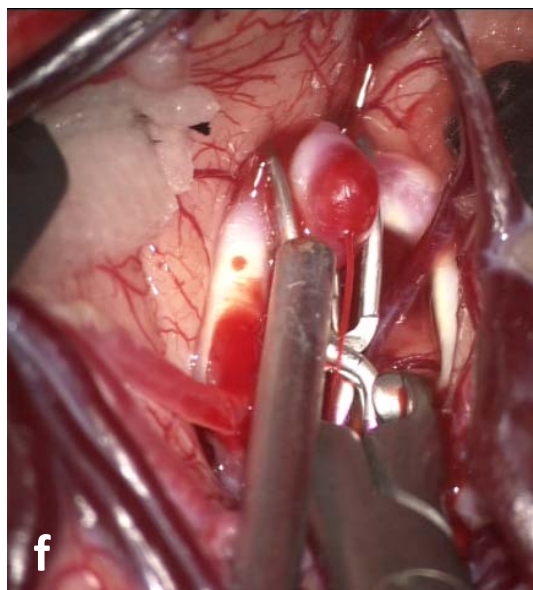
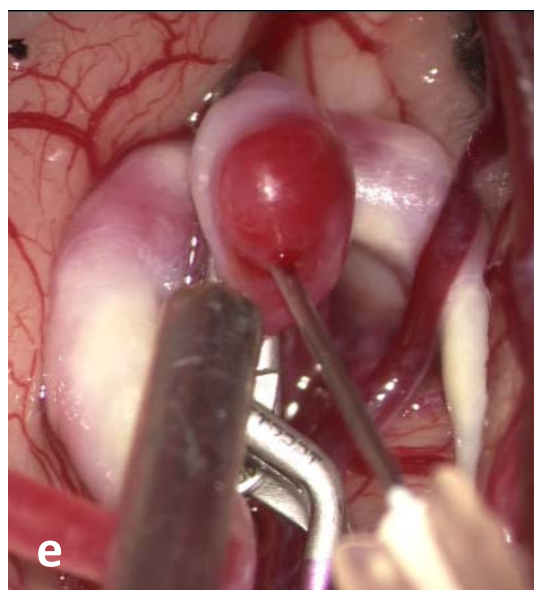
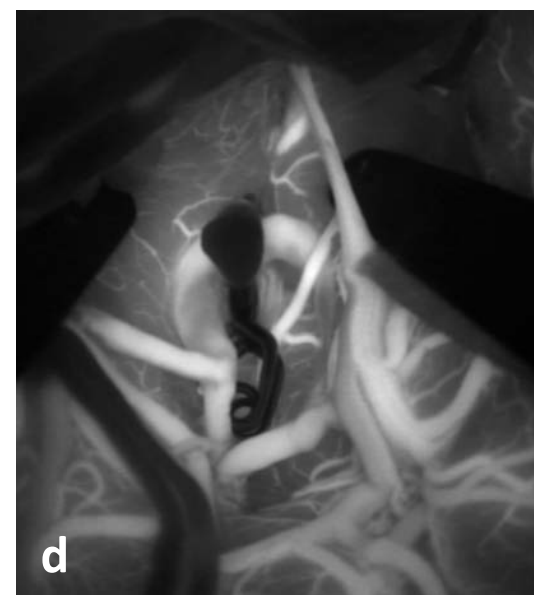
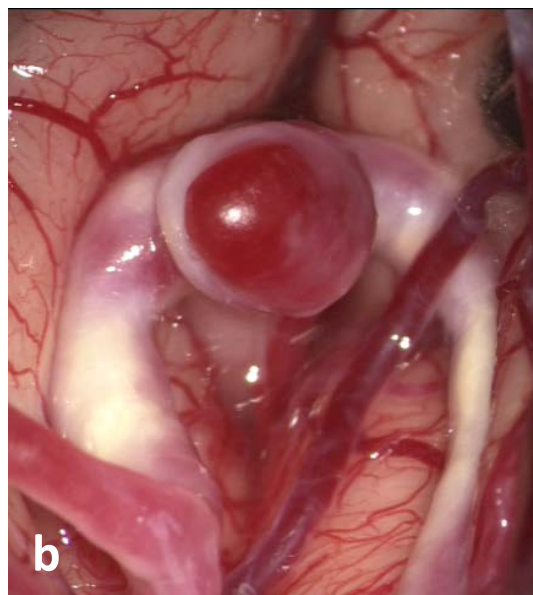


Fig. 3