Original Paper

Comparison of Intraoperative Indocyanine Green Angiography and Digital Subtraction Angiography for Clipping of Intracranial Aneurysms

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Key Words

Digital subtraction angiography · Indocyanine green angiography · Intracranial aneurysm · Aneurysm clipping · Microsurgical clipping

Abstract

Background: Residual aneurysm after microsurgical clipping carries a risk of aneurysm growth and rupture. Digital subtraction angiography (DSA) remains the standard to determine the adequacy of clipping. Intraoperative indocyanine green (ICG) angiography is increasingly utilized to confirm optimal clip positioning across the neck and to evaluate the adjacent vasculature. **Objective:** We evaluated the correlation between ICG and DSA in clipped intracranial aneurysms. **Methods:** A retrospective study of patients who underwent craniotomy and microsurgical clipping of intracranial aneurysms with ICG for 2 years. Patient characteristics, presentation details, operative reports, and pre- and postclipping angiographic images were reviewed to determine the adequacy of the clipping. **Results:** Forty-seven patients underwent clipping with ICG and postoperative DSA: 57 aneurysms were clipped; 23 patients (48.9%) presented with subarachnoid hemorrhage. Nine aneurysms demonstrated a residual on DSA not identified on ICG (residual sizes ranged from 0.5 to 4.3 mm; average size: 1.8 mm). Postoperative DSA demonstrated no branch occlusions. **Conclusion:** Intraoperative ICG is useful in the clipping of intracranial aneurysms to ensure a gross patency of branch vessels; however, the presence of residual aneurysms and subtle changes in flow in branch vessels is best seen by DSA. This has important clinical implications with regard to follow-up imaging and surgical/endovascular management.

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Introduction

Despite the introduction of several new and emerging endovascular techniques, surgical clipping remains an important tool for the management of ruptured or unruptured intracranial aneurysms [1]. The risk of recurrent subarachnoid hemorrhage after surgical clipping can result from either de novo aneurysm formation or regrowth/rupture of an incompletely clipped aneurysm [2, 3]. The incidence of residual neck filling of surgically clipped aneurysms has been reported to range from 3.9 to 12% [4–7]. Intraoperative or postoperative digital subtraction angiography (DSA) is the gold standard to determine the adequacy of clipping. Intraoperative indocyanine green (ICG) angiography is a method of intraoperative blood flow assessment introduced in 2003. ICG is an inert agent and it avoids contrast exposure. This method is simple, fast, reliable, and provides real time information [8, 9]. It has been increasingly utilized to confirm optimal clip positioning across the neck, to evaluate the patency of adjacent vasculature and potentially obviate the need for intraoperative DSA.

There have been several studies published showing the reliability and accuracy of ICG angiography [10–13]; however, several recent studies have demonstrated a poor correlation between ICG angiography compared to intraoperative/postoperative DSA. Ozgiray et al. [14] reported 4 cases in which ICG angiography failed to demonstrate the persistent flow in the aneurysm dome, and in 1 case, it missed a residual neck. Mery et al. [15] also reported similar inadequacies with intraoperative ICG angiography. Dashti et al. [9] reported a series of 239 clipped aneurysms in which intraoperative ICG was performed and a residual neck was seen in 6% of cases on postoperative imaging. Similarly, an unexpected branch occlusion was seen in 6% of these cases, while an incomplete occlusion of the aneurysm dome was not reported in any case [9].

In some cases, ICG angiography is used as an adjunct in addition to intraoperative or postoperative DSA, and in other cases, it is used as the sole method to confirm the complete obliteration of clipped intracranial aneurysms. Therefore, we conducted a retrospective chart analysis to evaluate the correlation between ICG and DSA in clipped intracranial aneurysms in which both modalities were utilized.

Methods

This is a retrospective study of patients who underwent craniotomy and microsurgical clipping of intracranial aneurysms with ICG between January 2010 and March 2013 at 2 tertiary care hospitals in Memphis, Tenn., USA (Baptist Memorial Hospital and Methodist University Hospital). A chart review was performed to obtain data describing age, sex, presentation, location and number of aneurysms as well as details of the operative reports of clipping. Pre- and postclipping angiographic images were reviewed to determine the adequacy of clipping. Postclipping DSA was evaluated by 2 neuroendovascular physicians who were not involved in the care of the patient; they looked for the presence of residual aneurysms and the patency of branch vessels/parent artery.

Results

Forty-seven patients (76.5% female, mean age: 51.6 years) underwent the clipping of intracranial aneurysms with ICG and had postoperative DSA. In all cases, the operative reports indicated the complete clipping of all aneurysms without any compromises of the branch vessels (fig. 1). Postoperative DSA was performed in a follow-up, ranging from 1 day to 6 months.

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Fig. 1. Open surgical exposure of a ruptured middle cerebral artery aneurysm before (a) and after clipping (b). The same aneurysm with ICG angiography – before (c) and after clipping (d) – demonstrated patent vessels as well as a secured aneurysm.

Fig. 2. a-c DSA (posterior-anterior, lateral, magnified oblique) of a ruptured right A2 bifurcation aneurysm. d-f Postoperative DSA (PA, lateral, magnified oblique) showing a flow-limiting stenosis at the origin of the callosal marginal branch.

Fifty-seven aneurysms were clipped, 23 patients (48.9%) presented with subarachnoid hemorrhages. Forty-two aneurysms were located in the anterior circulation (average size: 7.1 mm) and 15 in the posterior circulation (average size: 6.3 mm). Ten patients had 2 aneurysms clipped in the same setting. Out of the 57 aneurysms treated, 9 demonstrated residual aneurysms on DSA not identified on ICG. The residual sizes ranged from 0.5–4.3 mm, with an average size of 1.8 mm. Five aneurysms were in the anterior, 4 in the posterior circulation, and 6 were ruptured at presentation. Postoperative DSA demonstrated no branch occlusions; however, 3 patients demonstrated a slow flow due to clip impingement on a branch vessel – 2 in the posterior communicating artery, and 1 in the callosal marginal artery (fig. 2). There was no compromise of the parent vessel in any cases. In our series, the calculated specificity of the ICG angiography was 100%, while sensitivity was only 26.65%.

Fig. 3. DSA (a) and 3-D angiography (b) of a ruptured 5-mm posterior communicating artery aneurysm. DSA (c) and unsubtracted images (d) demonstrating clip placement and residual aneurysm. 3-D angiography (e) with dual volume reconstruction helps to further define significant 3.3-mm residual aneurysm. DSA (f) and unsubtracted (g) images demonstrating coil occlusion of the residual aneurysm.

Discussion

Compared to previously reported studies, our study shows higher discrepancies between ICG angiography and postoperative DSA results (21.07%). Washington et al. [16] described discordance between ICG and intraoperative angiography in 14.3% (7 of 49) cases. Three of 7 clipped aneurysms showed residuals, and the remaining 4 showed a branch compromise. Three out of 7 were ruptured at presentation. Similarly, Fischer et al. [17] showed inadequacies with ICG angiography in 10% of the clipped aneurysms.

Interestingly, in our study, postoperative DSA did not show any evidence of major branch occlusions or incomplete occlusions of the aneurysm domes. This finding seems to support the utility of ICG angiography in microsurgical clipping to ensure the gross patency of major arteries of the Circle of Willis and branch vessels at the neck of the aneurysms; however, postoperative DSA still seems to be necessary to evaluate the presence of a residual neck aneurysm and to be certain that there is no flow limitation compromise of smaller arteries. These subtle findings may influence the postoperative management of blood pressure in patients with subarachnoid hemorrhage who are vulnerable to vasospasm (fig. 2). Since the mortality rate with recurrent subarachnoid hemorrhage is very high [18], it is important to identify and manage these remnants diligently and ensure appropriate follow-up (fig. 3).

Although intraoperative DSA is not usually performed at our center, it is important to discuss it. Intraoperative DSA can be performed in a hybrid suit with a low complication rate and minimal morbidity [19]. The routine use of intraoperative DSA following ICG angiography can obviate the postoperative discovery of residual aneurysms or branch vessel occlusions. This technique is highly useful in cases of multiple aneurysms where ICG angiography is performed after each clipping, and intraoperative DSA only once at the end of all clippings. Few authors have raised concerns about its regular application considering radiating exposure [20] and high rates of false negatives (5–8%) compared to postoperative DSA [21, 22].

No correlation was observed between missing residual neck aneurysms on ICG angiography and the location and size of clipped aneurysms. In this series, residual aneurysms undetected by ICG were more prevalent in patients presenting with ruptured aneurysms, as two thirds (6/9) of the patients presented with hemorrhage. Our study had a higher percentage of ruptured aneurysms in the group with discordant ICG and DSA findings compared to similar studies. Also, in our study, the group with discordant ICG and DSA had an average age of 46 years, with an average aneurysm size of 6.7 mm. Washington et al. [16] reported an average age of 54 years and an average aneurysm size of 8.4 mm. Including recent rupture, a younger group and smaller aneurysm size may account for our higher discrepancy rate.

A recent case series by Caplan et al. [23] reported discordance between ICG angiography and intraoperative DSA in 10.8% of cases. The authors also demonstrated that the rate of postoperative DSA clip adjustment did not vary significantly whether ICG angiography was performed or not. The results of this study again support the fact that the use of ICG angiography has not replaced the conventional intraoperative or postoperative DSA, and future randomized trials are warranted.

One possible explanation for missing a residual neck aneurysm with ICG angiography could be a diminished image contrast resulting from slow clearance of dye with an intravenous injection. Intra-arterial injection of dye has been reported to provide a brighter and clearer image contrast [24]. More studies with intra-arterial injection are required to investigate whether inadequacies with ICG angiography can be mitigated with this technique.

Conclusion

Intraoperative ICG is useful in the microsurgical clipping of intracranial aneurysms and to ensure the gross patency of branch vessels as well as to evaluate the completeness of clipping; however, the presence of residual aneurysms and subtle changes in flow in branch vessels is best seen by DSA. This has important clinical implications in immediate postoperative management, the need for delayed follow-up imaging and the decisions to re-treat incompletely clipped aneurysms. Additional studies of intra-arterial injections of ICG dye will help to better define the role of this technology as an adjunct to DSA. Currently, we believe that the combination of intraoperative ICG angiography and postoperative DSA should be used to ensure a complete obliteration of clipped aneurysms.

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References

- 1 Spetzler RF, McDougall CG, Albuquerque FC, Zabramski JM, Hills NK, Partovi S, Nakaji P, Wallace RC: The Barrow Ruptured Aneurysm Trial: 3-year results. *J Neurosurg* 2013;119:1642–1644.
- 2 Wermer MJ, Greebe P, Algra A, Rinkel GJ: Incidence of recurrent subarachnoid hemorrhage after clipping for ruptured intracranial aneurysms. *Stroke* 2005;36:2394–2399.
- 3 Tsutsumi K, Ueki K, Morita A, Usui M, Kirino T: Risk of aneurysm recurrence in patients with clipped cerebral aneurysms: results of long-term follow-up angiography. *Stroke* 2001;32:1191–1194.
- 4 Thornton J, Bashir Q, Aletich VA, Debrun GM, Ausman JI, Charbel FT: What percentage of surgically clipped intracranial aneurysms have residual necks? *Neurosurgery* 2000;46:1294–1298.
- 5 Stellar S: Intraoperative angiography in cerebral aneurysm surgery: a prospective study of 100 craniotomies. *Neurosurgery* 1997;40:1108.
- 6 Feuerberg I, Lindquist C, Lindqvist M, Steiner L: Natural history of postoperative aneurysm rests. *J Neurosurg* 1987;66:30–34.
- 7 Rauzzino MJ, Quinn CM, Fisher WS 3rd: Angiography after aneurysm surgery: indications for 'selective' angiography. *Surg Neurol* 1998;49:32–40.
- 8 Raabe A, Beck J, Gerlach R, Zimmermann M, Seifert V: Near-infrared indocyanine green video angiography: a new method for intraoperative assessment of vascular flow. *Neurosurgery* 2003;52:132–139.
- 9 Dashti R, Laakso A, Niemela M, Porras M, Hernesniemi J: Microscope-integrated near-infrared indocyanine green videoangiography during surgery of intracranial aneurysms: the Helsinki experience. *Surg Neurol* 2009;71:543–550.
- 10 Wang S, Liu L, Zhao Y, Zhang D, Yang M, Zhao J: Evaluation of surgical microscope-integrated intraoperative near-infrared indocyanine green videoangiography during aneurysm surgery. *Neurosurg Rev* 2010;34:209–215.
- 11 Ma CY, Shi JX, Wang HD, Hang CH, Cheng HL, Wu W: Intraoperative indocyanine green angiography in intracranial aneurysm surgery: microsurgical clipping and revascularization. *Clin Neurol Neurosurg* 2009;111:840–846.
- 12 Imizu S, Kato Y, Sangli A, Oguri D, Sano H: Assessment of incomplete clipping of aneurysms intraoperatively by a near-infrared indocyanine green-video angiography (Niicg-Va) integrated microscope. *Minim Invasive Neurosurg* 2008;51:199–203.
- 13 Bruneau M, Sauvageau E, Nakaji P, Vandesteene A, Lubicz B, Chang SW, Baleriaux D, Brotchi J, De Witte O, Spetzler RF: Preliminary personal experiences with the application of near-infrared indocyanine green videoangiography in extracranial vertebral artery surgery. *Neurosurgery* 2010;66:305–311.
- 14 Ozgiray E, Akture E, Patel N, Baggott C, Bozkurt M, Niemann D, Baskaya MK: How reliable and accurate is indocyanine green video angiography in the evaluation of aneurysm obliteration? *Clin Neurol Neurosurg* 2012;115:870–878.
- 15 Mery FJ, Amin-Hanjani S, Charbel FT: Is an angiographically obliterated aneurysm always secure? *Neurosurgery* 2008;62:979–982.
- 16 Washington CW, Zipfel GJ, Chicoine MR, Derdeyn CP, Rich KM, Moran CJ, Cross DT, Dacey RG Jr: Comparing indocyanine green videoangiography to the gold standard of intraoperative digital subtraction angiography used in aneurysm surgery. *J Neurosurg* 2013;118:420–427.
- 17 Fischer G, Stadie A, Oertel JM: Near-infrared indocyanine green videoangiography versus microvascular Doppler sonography in aneurysm surgery. *Acta Neurochir (Wien)* 2010;152:1519–1525.
- 18 Johnston SC, Dowd CF, Higashida RT, Lawton MT, Duckwiler GR, Gress DR: Predictors of rehemorrhage after treatment of ruptured intracranial aneurysms: the Cerebral Aneurysm Rupture After Treatment (CARAT) study. *Stroke* 2008;39:120–125.
- 19 Chalouhi N, Theofanis T, Jabbour P, Dumont AS, Fernando Gonzalez L, Starke RM, Dalyai RT, Hann S, Rosenwasser R, Tjoumakaris S: Safety and efficacy of intraoperative angiography in craniotomies for cerebral aneurysms and arteriovenous malformations: a review of 1,093 consecutive cases. *Neurosurgery* 2012;71:1162–1169.
- 20 Derdeyn CP, Moran CJ, Eichling JO, Cross DT 3rd: Radiation dose to patients and personnel during intraoperative digital subtraction angiography. *AJNR Am J Neuroradiol* 1999;20:300–305.
- 21 Tang G, Cawley CM, Dion JE, Barrow DL: Intraoperative angiography during aneurysm surgery: a prospective evaluation of efficacy. *J Neurosurg* 2002;96:993–999.
- 22 Klopfenstein JD, Spetzler RF, Kim LJ, Feiz-Erfan I, Han PP, Zabramski JM, Porter RW, Albuquerque FC, McDougall CG, Fiorella DJ: Comparison of routine and selective use of intraoperative angiography during aneurysm surgery: a prospective assessment. *J Neurosurg* 2004;100:230–235.
- 23 Caplan JM, Sankey E, Yang W, Radvany MG, Colby GP, Coon AL, Tamargo RJ, Huang J: Impact of indocyanine green videoangiography on rate of clip adjustments following intraoperative angiography. *Neurosurgery* 2014;75:437–443.
- 24 Kuroda K, Kinouchi H, Kanemaru K, Nishiyama Y, Ogiwara M, Yoshioka H, Horikoshi T: Intra-arterial injection fluorescein videoangiography in aneurysm surgery. *Neurosurgery* 2013;72:141–150.