Intra-Arterial Injection of Indocyanine Green in Cerebral Arteriovenous Malformation Surgery

Serebral Arteriyovenöz Malformasyon Cerrabisinde İntraarteriyel İndosiyanin Yeşil Enjeksiyonu

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ABSTRACT
Surgical microscope-integrated intraoperative angiography with intra-venous injection of indocyanine green (ICG) has been widely used during bypass or aneurysm surgery. Instead of intra-venous injection of ICG, we describe a case of intraoperative video angiography with intra-arterial injection of ICG in cerebral arteriovenous malformation (AVM) surgery. During the surgery, we injected ICG through a catheter placed in the internal carotid artery in each step. The technique was feasible and useful to distinguish feeders from normal arteries and to observe changes in flow dynamics. Intra-arterial injection of ICG had better phase contrast than intra-venous injection of ICG and better spatial resolution than digital subtraction angiography. Therefore, this technique can be helpful in cerebral AVM surgery.

KEYWORDS: Cerebral arteriovenous malformation, Indocyanine green video angiography, Intra-arterial injection

INTRODUCTION
Raabe et al. (3) described a neurosurgical technique for indocyanine green (ICG) video angiography in which the fluorescent camera is integrated into the operating microscope. ICG angiography is quick and inexpensive and requires no additional personnel or equipment. Many publications have reported its usefulness in aneurysm or bypass surgery (4, 6). However, almost all the reports are about intra-venous injection of ICG. A few reports described intra-arterial injection of ICG, all of which were about spinal arteriovenous fistulas (1, 7). In this report, we show the detailed method and the efficacy of intra-arterial injection of ICG in cerebral arteriovenous malformation (AVM) surgery.

CASE REPORT
A 58-year-old woman presented with acute headache. A cerebral angiogram disclosed a Spetzler-Martin Grade III AVM in the left frontal lobe. The diameter of a nidus was 36mm; it was fed by the pericallosal artery, the lenticulostriate artery, the middle cerebral artery (MCA), and the posterior pericallosal artery, and drained into cortical veins. There was an unruptured aneurysm at the left pericallosal artery (Figure 1A-D). The patient underwent clipping of the unruptured aneurysm and excision of the AVM. We used a video-integrated microscope (Carl Zeiss Co., Oberkochen, Germany). After induction of general anesthesia, two 4-French sheaths were introduced into bilateral femoral arteries. A 4-French catheter was placed in the left common carotid artery and the other one was placed in the right vertebral artery. Both catheters were irrigated with heparinized saline during the surgery. At each session, we performed ICG angiography with intra-venous injection or intra-arterial injection through each catheter. In case of intra-arterial injection, ICG was injected through each catheter as a bolus (0.02 mg dose dissolved in 5 ml of heparinized saline). Figures 2B-D show ICG angiography with intra-arterial injection through the left common carotid artery. ICG angiography with intra-arterial injection made it possible to distinguish feeders from normal arteries because of better phase contrast than intra-venous injection. Figure 3A,B shows time density curves at a feeder, a normal artery, a draining vein, and a normal vein.
Only intra-arterial ICG injection showed the different curves between the feeder and the normal artery. Although these time density curves were obtained after the surgery in order to investigate the quantitative differences between intra-arterial and intra-venous injections, it was possible to find these differences in real-time ICG angiography during the surgery. Therefore, we could cut only feeders determined by intra-arterial ICG angiography and preserve normal arteries in the operation. In addition, we repeatedly performed intra-arterial ICG angiography in a short time to review flow patterns because ICG was cleared in approximately 15 seconds. The repeated ICG angiography enabled us to confirm the identification of feeders. In case of intra-venous injection, since ICG was cleared in approximately 15 minutes, we had to wait for the next injection of ICG. Therefore, repeated intra-venous ICG injection was not practical.

We also performed ICG angiography with intra-arterial injection through the right vertebral artery. The angiography showed only draining veins and normal veins. The feeders were not observed because they originated from the posterior pericallosal artery and ran not superficially but deeply. ICG angiography showed only views under the microscope and did not clarify vessels underneath the surgical view. The excision of AVM was successfully performed. No complications occurred.

**DISCUSSION**

In this study, we demonstrated that intra-arterial ICG injection in AVM surgery was feasible and helpful to identify feeders because of better phase contrast than intra-venous injection. Recently, ICG video angiography has been used in neurosurgical field. Especially, it is useful to see bypass patency or preservation of arteries during aneurysm surgery (4, 6). Killory et al. (2) stated that it is also useful during AVM surgery and complements digital subtraction angiography (DSA). Takagi et al. (5) showed ICG video angiography is helpful in resecting residual cerebral AVM. However, almost all the reports are about intra-venous injection of ICG. A few

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**Figure 1:** Preoperative cerebral angiograms. The angiograms showed the arteriovenous malformation in the left frontal lobe. (A) The anteroposterior view of the left internal carotid artery (ICA) angiogram at the arterial phase identified the left lenticulostriate artery (arrow) and the distal middle cerebral arteries as feeders. (B) The lateral view of the left ICA angiogram at the arterial phase revealed the left pericallosal artery (arrow) and an unruptured aneurysm at the pericallosal artery (arrow head). (C) The lateral view of the left ICA angiogram at the late arterial phase showed that the drainers were cortical veins. (D) The lateral view of the right vertebral artery angiogram showed the left posterior pericallosal artery as another feeder (arrow).
reports described intra-arterial injection of ICG, all of which were about spinal arteriovenous fistulas (1, 7). To the best of our knowledge, we are the first to report the efficacy of intra-arterial ICG angiography in AVM surgery.

There are three methods of intra-operative angiography; DSA, intra-venous ICG angiography, and intra-arterial ICG angiography. We compare these methods in terms of advantage and disadvantage. First, DSA and intra-arterial ICG angiography need a catheter insertion and placement in an artery. This takes some time and has risk of thromboembolic complications. To avoid this risk, we irrigated two catheters with heparinized saline during the surgery. However, we cannot diminish this risk. On the other hand, a catheter insertion makes it possible to perform selective angiography. This will give you better contrast views than intra-venous injection of ICG. Second, DSA and intra-arterial ICG angiography can be repeatedly performed in short time while you have to wait for approximately 15 minutes to clear ICG in case of intra-venous ICG injection. The repeated angiography enables us to confirm identification of feeders and review changes in flow dynamics. Third, only superficial vessels under a microscope can be observed in intra-arterial and intra-venous ICG injections while deep vessels underneath a surgical view can be observed only in DSA. On the other hand, spatial resolution is much better in ICG injections than DSA. Small arteries with approximately 0.1 mm of diameter could be observed in ICG injections (Figures 2B-G). In addition, comparisons of surgical view and ICG view are easy because of

**Figure 2.** Intraoperative indocyanine green (ICG) angiography. (A) Microscopic surgical view after dural incision showed normal arteries (dashed white arrow), feeders (dashed black arrow), normal veins (solid white arrow), and draining veins (solid black arrow). Regions of these vessels (black and white circles) were determined to investigate changes in density during ICG injection. ICG was injected intra-arterially through a catheter placed in the left common carotid artery. Time count was set at 0.00 sec when cortical arteries become to appear first. (B) The feeders (arrow) and normal arteries appeared at 0.86 sec. (C) At 2.92 sec, the draining veins (black arrow) appeared. The normal arteries (white arrow) remained while the feeders disappeared. (D) Finally, only normal veins (arrow) were observed at 10.05 sec. (E) ICG was injected intra-venously. The time count was set as described above. The feeders and normal arteries appeared at 0.86 sec. (F) At 5.01 sec, draining veins (black arrow) appeared. All the arteries (white arrow) still remained. (G) At 15.91 sec, cortical veins appeared. All the other vessels were still observed. Background density was higher than in case of intra-arterial injection of ICG.
Figure 3. The graphs of time density curves. (A) The time density curves of vessels determined in Figure 2A are shown in case of intra-arterial injection. The peak of the feeder (dashed black arrow) came faster than that of the normal artery (solid black arrow). The washout was also faster in the feeder than the normal artery. The draining vein (dashed gray arrow) appeared and disappeared much earlier than the normal vein (solid gray arrow). In addition, when the draining vein appeared, the feeder, the normal artery, and the draining vein disappeared completely. These different features of the curves made it possible to discriminate feeders and drainers from normal arteries and veins. (B) The time density curves are shown in case of intra-venous injection. The feeder and the normal artery showed similar features of time density curves. Therefore, it was difficult to distinguish the feeder from the normal artery. The draining vein appeared earlier than the normal vein. Even at the late phase, the feeder, the normal artery, and the draining vein did not disappear and were still observed. Namely, the density of these vessels did not return to the initial level.

the same surgical view under the microscope. In case of DSA, it may be necessary to place a small radiopaque instrument near a target vessel in order to confirm whether the vessel is the presumed one or not. Fourth, it takes some time to set up to perform DSA while ICG injection is quick to perform. To perform DSA, a microscope has to be removed to place a C-arm near the surgical field. In summary, intra-arterial ICG angiography has advantages in better spatial and temporal resolution, which enables identifying feeders. This will be of great help for surgeons in AVM surgery.

Although intra-arterial ICG injection is not mentioned in the FDA approval, we believe injecting a small amount of ICG (i.e. 1/250 times compared with intra-venous ICG injection) should be accepted. More cases are necessary to elucidate the validation and safety of this technique. However, we present the detailed method of intra-arterial ICG video angiography in this article so that others can use this technique and improve the method of this technique.

REFERENCES


