Case Report

Intraoperative Indocyanine Green Fluorescence Angiography during Minor Amputation of the Ischemic Foot: A Case Report

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ABSTRACT

Minor amputations for critical limb ischemia have been reported to confer an increased risk of postoperative skin necrosis or poor wound healing secondary to poor vascularity. Predicting wound healing in patients with critical limb ischemia is a focus of ongoing research. Indocyanine green fluorescence angiography is used to visualize tissue perfusion in various surgical fields. We sought to address this challenge and introduced indocyanine green fluorescence angiography during minor amputation in a patient with critical limb ischemia to evaluate perfusion of the wound tissue. Before wound closure, the parts of the skin flaps exhibiting fluorescence were preserved, while the non-fluorescent edges of the skin flaps were trimmed off. The trimmed skin was reused as a full-thickness skin graft. The postoperative course was uneventful. There was no wound dehiscence or flap necrosis, and the graft was completely incorporated. Indocyanine green fluorescence angiography was suggested to be effective for preventing postoperative wound dehiscence after minor amputation in a patient with critical limb ischemia.

Key words: critical limb ischemia, indocyanine green fluorescence angiography, minor amputation, tissue perfusion, wound healing

Introduction

Critical limb ischemia (CLI) is considered the most severe form of peripheral artery disease (PAD) and is typically characterized by chronic ischemic pain at rest, ulcerations, or gangrene that is attributed to occlusive PAD. Patients undergoing minor amputation for CLI have been reported to have an increased risk of postoperative skin necrosis or poor wound healing secondary to poor vascularity, which may lead to a second surgery or re-amputation. Predicting wound healing in patients with CLI is a focus of ongoing research. Recently, indocyanine green (ICG) fluorescence angiography has been used to visualize tissue perfusion intraoperatively in various surgical fields, including cardiac surgery, transplantation, and flap surgery¹⁻³. ICG fluorescence angiography has the potential to provide information on regional tissue perfusion. Therefore, we sought to address this challenge and

introduced ICG fluorescence angiography during minor amputation in a patient with CLI to evaluate perfusion of the wound tissue.

Materials and methods

Patient

A 67-year-old Japanese man with a 7-year history of diabetes mellitus and receiving hemodialysis was admitted to the hospital with ulcers of the left forefoot and great toe. He had been diagnosed with PAD and had previously undergone endovascular therapy several times. Left foot plain radiographs showed signs of osteomyelitis in the great toe. The skin perfusion pressure (SPP) in the left foot was 59 mmHg on the dorsum and 50 mmHg on the plantar aspect, as measured using a skin perfusion pressure system (SensiLase PAD 3000; Kaneka Medix Corp., Osaka, Japan). The patient had undergone multiple surgical debridements with subsequent

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Received: 28, February 2020 / Accepted: 5, April 2020

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Fig. 1. Preoperative view of the left foot and incision design.

Purulent discharge from the ulcer in the great toe was observed. The second metatarsophalangeal joint capsule was collapsed and exposed to the surrounding subcutaneous soft tissue necrosis.

disarticulation of the interphalangeal joint in the great toe and of the metatarsophalangeal joint in the third, fourth, and fifth toes. Purulent discharge from the ulcer due to osteomyelitis in the great toe was still observed. The second metatarsophalangeal joint capsule was collapsed and exposed with surrounding subcutaneous soft tissue necrosis. The wounds were subsequently left to heal under conservative treatment (Fig. 1). Although the skin of the great toe and second toe was not necrotic, it was difficult to preserve the phalanges of both toes. Disarticulation and toe fillet flap reconstruction was performed. All procedures were performed in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. All procedures were performed in accordance with the ethical standards of the institutional review board of Hokkaido University Hospital.

Surgical procedure and ICG fluorescence angiography

The surgical procedures were performed under general anesthesia. An incision was made around the nail and over the lateral aspect of the second toe, and a longitudinal incision that included the ulcerated area was made over the dorsal aspect of the great toe, exposing the phalanges (Fig. 1). After making the incisions, whole toe flaps were elevated in the phalangeal area. Disarticulation at the metatarsophalangeal joint was then performed, followed by trimming of the tendons and joint capsules. The elevated flap of the second toe was advanced laterally, covering the metatarsal bone and defect area (Fig. 2a). The skin flaps were not pale in color, but the bleeding from the edges was minimal. To prevent wound necrosis

postoperatively, the ischemic parts of the flap were identified and trimmed off before the wound was closed. The flaps were then roughly closed using several 5-0 nylon sutures, and the blood supply to the skin flaps was checked using ICG fluorescence angiography (Fig. 2b). For this process, 25 mg of ICG (Diagnogreen™; Daiichi-Sankyo Pharmaceutical, Tokyo, Japan) was dissolved in 10 mL of distilled water, and 0.05 mg/kg of this solution was then administered via a peripheral intravenous line followed by flushing with 10 mL of saline. Fluorescence images were acquired immediately after ICG administration using an infrared camera system (PDE-Neo; Hamamatsu Photonics K. K., Hamamatsu, Japan), which activated the ICG using light emitted at a wavelength of 760 nm and light filtered out at a wavelength of < 820 nm. ICG was irradiated using a 760-nm light-emitting diode as the light source, with a charge-coupled camera as the detector. The camera system was placed at an approximately 30-cm distance from the skin of the foot, and real-time fluorescence imaging was displayed on a monitor. Fluorescence imaging showed the blood flow dynamics in succession as the dye traversed the microcirculation. About 1–3 min after ICG administration, perfusion of the skin flap was confirmed by ICG fluorescence imaging as a white stain. The parts of the skin flaps exhibiting fluorescence were preserved, while the edges of the skin flaps with non-fluorescence were trimmed off to prevent postoperative flap necrosis or wound dehiscence. After trimming, wound closure was performed using more 5-0 nylon sutures. The trimmed skin of the second toe fillet flap was reused as a full-thickness skin graft and applied onto the remaining skin

Fig. 2. Intraoperative view of the left foot.

- (a) The flap of the second toe was advanced laterally. Fillet flaps were closed roughly with nylon sutures. Non-fluorescent edges of the skin flaps were trimmed off at the dotted lines on the great toe and solid lines on the second toe.
- (b) Intraoperative fluorescent angiography image of the left foot. Gray dotted lines represent the wound edge. Asterisks represent the non-fluorescent area.

Fig. 3. View of the left foot immediately postoperatively. Trimmed skin of the second toe fillet flap was reused as a full-thickness skin graft and applied onto the remaining skin defect.

Fig. 4. Postoperative view of the left foot at the sixth month.

defect. The skin graft was then secured to the wound using 5-0 nylon sutures (Fig. 3).

Results

The postoperative course was uneventful. The sutures were removed 2 weeks postoperatively. The skin graft was completely incorporated. There was no obvious wound dehiscence or flap necrosis during the early postoperative period. No complication or recurrence of the ulcers was observed at the 12-month follow-up (Fig. 4).

Discussion

ICG is a widely used, water-soluble, tricarboyanine dye that has been used for assessing ophthalmic angiography data, cardiac output, and hepatic function for over 50 years¹⁻³. Intraoperative ICG fluorescent angiography is used in plastic surgery to assess skin perfusion for classical pedicled flaps and

pedicled perforator flaps and in vascular surgery to assess graft patency. Previously, we reported the use of ICG fluorescence angiography during inguinal lymph node dissection⁴. In another study, 53% of cases involved some degree of wound dehiscence, defined as poor wound healing with a measured defect of at least 1 cm⁵. In our study, we divided 17 patients into two groups⁴. In the first group, microcirculatory wound closure perfusion was not evaluated using ICG fluorescent angiography, and 89% of the patients developed wound dehiscence postoperatively. In the second group, we performed ICG fluorescent angiography and trimmed off the non-fluorescent areas of the wound edges; only 13% of these patients developed wound dehiscence postoperatively ($p = 0.003$). The use of ICG fluorescence angiography in amputations of ischemic lower extremities have been evaluated in some studies⁶⁻¹⁰. Zimmermann et al. evaluated tissue perfusion in 10 amputation stumps in patients with CLI within 72 h after major amputations (above and below the knee) using ICG fluorescence angiography⁷. Substantive perfusion deficits were noted in 3 stumps in the early postoperative period of ICG angiography, and all 3 patients developed wound necrosis

leading to re-amputation. Regarding minor amputations, Samies et al. and Joh et al. used ICG fluorescence angiography before incision to determine the area of debridement or level of amputation in necrotic or gangrenous feet in a case series^{9,10}. Therefore, we introduced ICG fluorescence angiography intraoperatively during minor amputation in a patient with CLI. Unlike the approaches reported previously, we used ICG fluorescence angiography intraoperatively after the flaps were elevated and roughly closed. Thin skin flaps and high tension in wound closure, as well as poor vascularity in patients with CLI may cause perfusion deficiency at the wound edges^{3,4}. We think it is important to evaluate perfusion after flap elevation and rough closure.

Clinical assessment of wound edge bleeding or skin coloration is the most commonly used method to evaluate wound perfusion^{4,8,10}. However, clinical assessment is highly subjective in many cases, and when used alone, is not always completely reliable^{8,10-12}. ICG fluorescence angiography is very useful to clearly distinguish between ischemic and non-ischemic areas⁴. Compared with other modalities for angiography such as X-ray, computed tomography, magnetic resonance imaging, and positron emission tomography, ICG fluorescent angiography can be easily and economically used intraoperatively². Ankle-brachial index (ABI), transcutaneous oxygen pressure (TcPO₂), and SPP are also used in the assessment of CLI¹³⁻¹⁵. ABI is used extensively in screening for PAD. It provides information on blood pressure at the ankle level, but may be falsely elevated due to medial arterial calcification, which is widely observed in patients with CLI or those receiving hemodialysis. TcPO₂ and SPP are established parameters reflecting cutaneous perfusion and are measures of the transfer of oxygen molecules to the skin surface and of the microcirculatory arterial pressure at the skin level, respectively. Both measures have been successfully used to determine the likelihood of wound healing in patients with CLI. However, evaluation of TcPO₂ or SPP during surgery is difficult. ICG angiography can be used as an intraoperative tool to visualize and obtain information about regional perfusion, determine the border between viable and non-viable ischemic tissue, and predict the likelihood of healing.

ICG is a non-radioactive and relatively non-toxic contrast agent, which is suitable for use in patients with CLI with renal dysfunction¹³. There are few adverse reactions to ICG after intravenous or intraarterial injection³. Adverse reactions to ICG most frequently include nausea and/or vomiting; rarely include discomfort, hot flush, sweating, or skin rash; and very rarely include anaphylactic shock. However, these are considered negligible compared to the benefits of its potential clinical utility¹.

Conclusions

We applied ICG fluorescence angiography during minor amputation in a patient with CLI. This procedure is safe and easy to perform and provides visual information about regional tissue perfusion. It can be used in the assessment of blood supply in ischemic feet. Further studies are necessary to help clarify the utility of ICG fluorescence angiography to predict the likelihood of wound healing and tissue necrosis.

Acknowledgments

None.

Sources of funding

None.

COI statement

There is no conflict of interest.

References

- 1) Burnier P, Niddam J, Bosc R, Hersant B, Meningaud JP: Indocyanine green applications in plastic surgery: a review of the literature. *J Plast Reconstr Aesthet Surg* 2017; 70: 814-27.
- 2) Alander JT, Kaartinen I, Laakso A, et al: A review of indocyanine green fluorescent imaging in surgery. *Int J Biomed Imaging* 2012; 2012: 940585.
- 3) Li K, Zhang Z, Nicoli F, et al: Application of indocyanine green in flap surgery: a systematic review. *J Reconstr Microsurg* 2018; 34: 77-86.
- 4) Furukawa H, Hayashi T, Oyama A, et al: Effectiveness of intraoperative indocyanine-green fluorescence angiography during inguinal lymph node dissection for skin cancer to prevent postoperative wound dehiscence. *Surg Today* 2015; 45: 973-8.
- 5) Chang SB, Askew RL, Xing Y, et al: Prospective assessment of postoperative complications and associated costs following inguinal lymph node dissection (ILND) in melanoma patients. *Ann Surg Oncol* 2010; 17: 2764-72.
- 6) van den Hoven P, Ooms S, van Manen L, et al: A systematic review of the use of near-infrared fluorescence imaging in patients with peripheral artery disease. *J Vasc Surg* 2019; 70: 286-97.
- 7) Zimmermann A, Roenneberg C, Wendorff H, Holzbach T, Giunta RE, Eckstein HH: Early postoperative detection of tissue necrosis in amputation stumps with indocyanine green fluorescence angiography. *Vasc Endovascular Surg* 2010; 44: 269-73.
- 8) Yang AE, Hartranft CA, Reiss A, Holden CR: Improving outcomes for lower extremity amputations using intraoperative fluorescent angiography to predict flap viability. *Vasc Endovascular Surg* 2018; 52: 16-21.

- 9) Samies JH, Gehling M, Serena TE, Yaakov RA: Use of a fluorescence angiography system in assessment of lower extremity ulcers in patients with peripheral arterial disease: A review and a look forward. *Semin Vasc Surg* 2015; 28: 190-4.
- 10) Joh JH, Park HC, Han SA, Ahn HJ: Intraoperative indocyanine green angiography for the objective measurement of blood flow. *Ann Surg Treat Res* 2016; 90: 279-86.
- 11) Perry D, Bharara M, Armstrong DG, Mills J: Intraoperative fluorescence vascular angiography: during tibial bypass. *J Diabetes Sci Technol* 2012; 6: 204-8.
- 12) Mothes H, Dönicke T, Friedel R, Simon M, Markgraf E, Bach O: Indocyanine-green fluorescence video angiography used clinically to evaluate tissue perfusion in microsurgery. *J Trauma* 2004; 57: 1018-24.
- 13) Forsythe RO, Hinchliffe RJ: Assessment of foot perfusion in patients with a diabetic foot ulcer. *Diabetes Metab Res Rev* 2016; 32: 232-8.
- 14) Bajwa A, Wesolowski R, Patel A, et al: Assessment of tissue perfusion in the lower limb: current methods and techniques under development. *Circ Cardiovasc Imaging* 2014; 7: 836-43.
- 15) Venermo M, Settembre N, Albäck A, et al: Pilot assessment of the repeatability of indocyanine green fluorescence imaging and correlation with traditional foot perfusion assessments. *Eur J Vasc Endovasc Surg* 2016; 52: 527-33.