



How to Secure Pedicled Flaps Using Perioperative Indocyanine Green Angiography: A Prospective Study about 10 Cases

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Abstract

Background: The aim of this study is to report our experience in the evaluation of the intraoperative use of indocyanine green angiography to secure pedicled flaps.

Methods: We used an intraoperative indocyanine green angiography to assess the perfusion of ten pedicled flaps performed between January 2021 and March 2021. After harvesting the flap, a clinical evaluation of its color was made and complemented by intravenous injection of indocyanine green. The flap's perfusion was precisely evaluated using a near-infrared camera and, if needed, the surgeon could reduce the size of the skin paddle, position the flap differently or make any change aiming at improving perfusion.

Results: Nine patients who underwent reconstructive surgery using pedicled flaps (n=10) between the 6th of January and the 24th of February 2021 in the Department of Plastic and Reconstructive Surgery of Rennes's University Hospital were prospectively included. Intraoperative analysis of the flap's perfusion allowed confirmation of a satisfactory clinical aspect in two cases, complementary actions due to an overall lack of perfusion in five cases and modification or removal of the skin paddle in four cases. There was no complication secondary to the intravenous injection of indocyanine green.

Conclusion: Indocyanine green can prove extremely useful to the surgeon during the harvesting of pedicled flaps and should be widely used to reduce the vascular complications of these flaps.

Keywords: Indocyanine green; Intraoperative angiography; Flap; Pedicled flap; Reconstructive surgery

Background

Indocyanine green laser angiography has been used in ophthalmology since the 1970s [1] to diagnose choroidal neovascularization [2]. It precisely evaluates the perfusion of tissues and, being a dynamic technique, it has been developed in the study of blood flow and liver functional test [3,4]. More recently, the technique has been used for the preoperative assessment of free flaps [5] in particular for breast reconstruction (mainly Deep Inferior Epigastric artery Perforator – DIEP flap [6]), as well as for the intraoperative detection of sentinel node in abdominal and gynecological surgery [7,8]. A near-infrared camera detects the arterial, arteriolar and capillary migration of indocyanine green, which is an injectable fluorescent coloring, from the intravenous region to the skin. Indocyanine green is a coloring which absorption's spectrum is at its highest around 805 nm with a radiating around 835 nm. A better evaluation of the flap's perfusion can help the surgeon improve the approach. Here we examined the use of indocyanine green angiography in the intraoperative evaluation of pedicled flap's perfusion at the recipient site. We report the operative technique, the results and we discuss the interest of this intraoperative angiographic control for the overall surgical management.

Methods

Preoperative planning

Between January 2021 and March 2021, we carried out a prospective study in the Department

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of Plastic and Reconstructive surgery of the University Hospital of Rennes. Every patient undergoing reconstructive surgery with a pedicled flap was included. There were no exclusion criteria. Preoperative evaluation of the vessels through CT angiography or Doppler ultrasound was not systematic but only performed according to the vascular status and medical history of the patient. However, we systematically used an acoustic Doppler (8 MHz) preoperatively to precisely identify the perforating vessels of the region. All clinical investigations have been conducted according to the principles expressed in the Declaration of Helsinki. All the patients included had given oral consent.

Intraoperative indocyanine green angiography

We used a NOVADAQ system (Stryker, Michigan, USA), which was initially customized for coelioscopy. The cart is made of a wide LED screen, a white light generator and a near-infrared monochromatic laser with 806 nm wavelength detection. The system is connected to a « SPY-PHI » hand piece detection camera. There are three programs: A RGB white light program which is able to film in high definition (full HD 1080p) that we are going to call program 1, a fluorescent program with a black background (called “SPY fluorescent”) where fluorescence is shown in white that we are going to call program 2 and a white light fluorescence program (called “PINPOINT fluorescent”) where perfused areas are shown in green that we are going to call program 3. The anesthesia team prepares the indocyanine green solution (Infracyanine[®]) at a 2.5 mg for 1 mL dilution (25 mg/10 cc) intraoperatively. After harvesting and positioning the flap, a sterile plastic cover is placed upon the near-infrared camera for protection so it can be safely held above the flap. It is important to keep “healthy skin” in the field of view to compare the perfusion of adjacent tissues to the flap’s perfusion on the same image. The camera is set on the black background fluorescent program (program 2). The anesthesia team uses a peripheral direct intravenous injection to administer 2 mL (5 mg) of indocyanine green to the patient. After 15 sec to 30 sec, a white fluorescence can be seen at first at the donor site and progressively reaches the flap with more or less delay. If the flap’s perfusion is satisfying, the flap can be positioned and sutured safely. Otherwise, additional surgical gestures can be performed such as mobilization of the pedicle, use of a vasodilator like papaverine (40 mg/mL, SERB, Belgium) or hemodynamic optimization. The efficacy of the actions taken can be assessed with a second angiographic control using, like before, a 2 mL intravenous injection of indocyanine green. As indocyanine green has a 3.5 min plasma half-life [5], we chose to wait at least 10 min between 2 injections in order to obtain a full clearance of the visible fluorescence. The maximum cumulative dose that can be used is 0.5 mg/kg (12 mL/30 mg) which means it is possible to perform up to 6 injections of 2 mL of indocyanine green according to the marketing authorization.

Postoperative care

The patients were closely monitored after the surgery to check the color of the skin paddle after pressure (which is normally of 3 sec) and the overall color of the flap. To prevent edema the patients were asked to keep their limb raised when possible and to wear support stockings. We used low-molecular-weight heparin to prevent deep vein thrombosis until the patients recovered a normal walk.

Results

Characteristics of the patients

Between January and March 2021, we included 9 patients

prospectively in our Department of Plastic and Reconstructive Surgery of the University Hospital of Rennes. We performed 10 pedicled flaps: 3 medial plantar flaps, 1 tensor fascia latae perforator flap, 1 pedicled DIEP, 1 inguinal perforator flap, 1 Superficial Circumflex Iliac Perforator flap (SCIP), 1 dorsal intercostal artery perforator flap and 2 pedicled musculo-cutaneous gracilis flaps for the same patient. In 9 out of 10 cases there was a unique pedicle. The defects which needed to be covered were localized in various regions of the body: 3 on the foot, 3 in the perineal region, 1 on the thigh, 1 in the inguinal region and 1 in the median region of the back. Average size of the defect was 90.7 ± 109.1 cm² and ranged from 30 cm² to 380 cm². Average size of the skin paddle was 127 ± 139.8 cm² and ranged from 9.6 cm² to 420 cm². Donor sites required skin grafting in 40% of the cases while primary closure was possible for the remaining 60%. The characteristics of the patients and flaps are summarized in Table 1.

Intraoperative angiography

Mean number of intraoperative indocyanine green an injection was 1.5 ± 0.5 and patients received a mean amount of $7.5 \text{ mg} \pm 2.63$ mg of indocyanine green for each flap. The intraoperative angiographic control of the flap showed a satisfying perfusion in 2 cases (20%) (Figure 1), a distal perfusion defect in 3 cases (30%), which led to the reduction of the size of the skin paddle, and an overall lack of perfusion for 5 cases (50%), which led to complementary actions. A vascular spasm was successfully stopped using a local instillation of papaverine. After being positioned upon the defect, 2 flaps showed signs of compression on the pedicle and needed remobilization. The skin paddles of both gracilis flaps showed no sign of cutaneous perfusion whereas the muscular vascularization remained satisfying. Therefore, we decided to remove all the skin from the gracilis flaps and perform muscular flaps instead.

Postoperative care

There was no postoperative complication for 6 flaps (60%). The fascia latae perforator flap had a distal necrosis of the skin paddle. There was a postoperative hematoma of the SCIP flap which required surgical revision in the operation room and resulted in a partial



Figure 1: Patient 2: Acral lentiginous melanoma of the left heel with a medial plantar flap performed to cover the defect.

- (A) Preoperative.
 (B) Proximally based medial plantar flap on its receiving site.
 (C) Peroperative indocyanine green angiography showing an adequate perfusion.
 (D) Postoperative outcome at 3 months.

Table 1: Characteristics of included patients, performed flaps, and outcomes.

Patient	Sex	Age (yr)	BMI (kg/m ²)	Defect	Flap	Complementary action	Complication
1	Male	44	28.7	Unstable scar of the right heel secondary to a degloving defect	Distally based medial plantar flap	Reduction of skin tension over the pedicle using loose stitches and a skin graft	None
2	Female	50	26.2	Acral lentiginous melanoma of the left heel, Breslow >2 mm	Distally based medial plantar flap	No	None
3	Male	65	31.4	Acral lentiginous melanoma of the right heel, Breslow >2 mm.	Distally based medial plantar flap	Papaverin impregnation and hemodynamic optimization	Major edema
4	Male	59	39.2	Pleomorphic sarcoma of the posterior region of the thigh	TFL flap	Additional excision of the distal part of the skin paddle	Distal necrosis of 2 cm
5	Male	37	31.0	Retracted skin graft of the right groin	DIEP flap	Incision of the tunnel above the pedicle	Hematoma
6	Male	37	24.3	Postoperative buried penis	Thin-SCIP flap	Additional excision of the skin paddle	Hematoma
7	Male	56	19.5	Median dorsal exposure of a spine osteosynthesis implant	DICAP flap	No	None
8	Female	63	18.5	Pelvic exenteration and vulvectomy for invasive squamous cell carcinoma.	Bilateral gracilis musculocutaneous flap	Removal of both skin paddles	None
9	Male	73	20	Scrotal and penile resection for advanced squamous cell carcinoma	Groin flap	Additional excision of the skin paddle	Infection with cutaneous fistula

suffering of the flap. Another patient presented with postoperative hematoma but did not required surgical revision. The patient who had an inguinal perforator flap developed a surgical site infection. There was no complication secondary to the injection of indocyanine green. There was no case of venous suffering in our series of patient.

Case presentation: Patient 1

A 44 year-old male presented with an unstable scar of the posterior region of the heel secondary to a degloving defect. Given that the scar was responsible for a functional impairment and chronic ulcerations, we decided to perform a debridement of the unstable area and cover the defect with a medial plantar flap. No difficulty occurred during the flap's harvesting and the perfusion was evaluated after positioning the flap over the defect of the heel. The indocyanine green angiography showed a complete lack of perfusion which was discordant with the satisfying clinical aspect of the flap. We decided to reduce the compression on the pedicle by changing the position of the flap and to reduce the cutaneous tension by using a thin skin graft over the pedicle. A second injection of indocyanine green confirmed the revascularization of the entire skin paddle. There was no postoperative complication; in particular there was no suffering of the flap. Wound healing was achieved at 6 weeks postoperatively.

Case presentation: Patient 4

A 59 year-old male presented with a large sarcoma of the posterior region of the thigh which was treated with neoadjuvant radiotherapy (Figure 2A). The surgical removal of the tumor resulted in a large defect and given the history of radiation we chose to perform a fasciocutaneous fascia latae perforator flap. Theoretically, the length of the flap must not exceed the junction between 2 superior thirds and one inferior third of the line between the antero-superior iliac spine and the lateral femoral condyle in order to reduce the risk of distal necrosis. However, in our case, the size of the defect and its extension at the internal side of the thigh required to enlarge the flap beyond that limit on about 8 cm. Peroperatively, the indocyanine green angiography showed no sign of distal perfusion on 3 cm and a lack of perfusion on and intermediate area of 3 cm (Figure 2B). We performed a resection of the most distal 3 cm of the flap before positioning it and doing a new angiographic control. The second angiography confirmed a remaining default of vascularization of the intermediate area as seen before and led to a new resection which could not take all the defective part of the flap away in order to allow closure without tension (Figure 2C). Postoperatively, the patient developed a hematoma which required a new surgery. The flaps'



Figure 2: Patient 5: Pleomorphic sarcoma of the posterior region of the right thigh with a Tensor Fascia Lata (TFL) fasciocutaneous flap. (A) Preoperative. (B) Peroperative indocyanine green angiography showing a distal perfusion defect. (C) Postoperative aspect after additional excision of the most distal part of the flap. (D) Postoperative distal necrosis of the very distal part of the flap.

evolution was marked by a necrosis of the edge of the flap (Figure 2D) which corresponded to the intermediate area seen on the angiography during the first surgery. This case proved the good reliability of this technique to evaluate the perfusion of pedicled flaps preoperatively.

Case presentation: Patient 5

A 39-year-old male presented with an ancient retracted thin skin graft of 5 cm × 10 cm in the right inguinal region which limited the flexion of his thigh. We used a contralateral pedicled DIEP to perform a resurfacing after removing the skin graft. The flap was initially tunneled between the donor and the recipient site and we performed an indocyanine green angiography after positioning the flap. The evaluation of the perfusion showed no perfusion of the skin paddle as opposed to a satisfying clinical aspect and color of the flap. After thorough examination we found a hematoma at the donor site. After removing the hematoma and using papaverine locally, we performed a second angiographic test which showed a progressive vascularization of the flap. It is highly likely that, without indocyanine green angiography, the reassuring clinical aspect of the flap would have led us to close without any complementary gesture and we

probably would have needed to perform a surgical revision at some point.

Discussion

Evaluation of a flap's vascularization by intraoperative indocyanine green angiography secures the surgical technique while presenting few risks. In 2017, Li et al. [9] published a review of literature about 73 articles which reported the safety of this technique to evaluate free or pedicled flaps. It is interesting to note that the most commonly used dose appears to be 12.5 mg of indocyanine green (which represents half the content of an ampoule of Infracyanine[®] (SERB laboratory, Brussels, Belgium)) although there is no consensus about it. Authors recommend using a total dose of 10 mg or 8 mL of product. Nevertheless, it is important to keep in mind that more or less severe allergic reactions can occur in about 1/45000 to 1/60000 cases according to the marketing authorization. In our series, we did not use more than 10 mg of product and no complication related to the injection occurred. As time goes by, plastic surgeons are confronted with more and more complicated cases of soft tissue defects and are constantly trying to find less invasive solutions to cover them. Perforator flaps appeared in this context and now represent a major technical breakthrough in reconstructive surgery. While they are an attractive option, they remain difficult to dissect and the skeletonizations of the pedicle make them more fragile than regular musculocutaneous flaps. One example is their use in breast reconstruction as free flaps [10]. At first, indocyanine green was used to improve the results of free flaps [11,12]. The technique was helpful to choose the size and position of the final skin paddle, as shown by Varela et al. [6] in DIEP flaps, and could also evaluate the vascular permeability of the pedicle after the anastomosis of the vessels [13]. As it showed interesting results in free flaps, indocyanine green was later used for intraoperative evaluation of pedicled flaps to increase the chances of success of the surgery and to prevent vascular complications [14].

As a matter of fact, Royer et al. [15] explained in 2014 that the use of indocyanine green could even change the surgeon's attitude during the operation. Indeed, in his article, he reports the case of a posterior tibial artery perforator flap for which the skin paddle was entirely reshaped during surgery compared to the initial preoperative drawing. Jakubietz et al. [16] report a series of patients undergoing a reconstruction with pedicled anterolateral thigh flap (3 cases) or propeller flap (2 cases) where indocyanine green angiography also proved valuable. Our series is in line with these findings, in particular given the 3 cases where indocyanine green analysis showed a problem of perfusion at the distal edge of the flap. In our fascia latae flap, partial resection of the intermediate area was not sufficient to prevent the apparition of a distal necrosis of the skin paddle. However, indocyanine green allowed us to harvest a larger flap than what is theoretically recommended. This case strengthened our faith in this technique and when a similar situation occurred during the bilateral gracilis flap surgery we did not hesitate and decided to sacrifice both skin paddles. In addition, in 2 cases, the angiography showed a complete lack of perfusion because of a compression on the pedicle when the flap was positioned over the defect which needed to be covered. It allowed us to instantly correct the position of the flap to relieve the pedicle from any compression and therefore no clinical sign of suffering was ever seen on these flaps. It should be noted that skeletonized pedicles are highly sensitive to compression which makes intraoperative indocyanine green angiography a valuable

tool especially for tunneled flaps. However, this technique does not replace the clinical evaluation of the surgeon by the cutaneous recoloring after hand pressure, the overall color of the flap and the skin's temperature. It should be used as an additional support to react sooner to any problem during surgery that clinical exam or surgical experience missed. It is also interesting to pair it with the preoperative use of an acoustic ultrasound Doppler as it is very precise for the evaluation of the full skin paddle. Our series showed that a peroperative hypoperfusion seen with the angiography can have significant consequences like a resection of the skin paddle or even the removal of all skin in the case of musculocutaneous flaps. Other actions are better positioning the flap, reducing the skin tension over the pedicle, using a local vasodilator or optimizing the general hemodynamic status. What is particularly interesting here is that the surgeon can respond before the first clinical signs of failure of the flap appear. It means that indocyanine green analysis prevents major vascular complication like partial or complete necrosis of the flap which require additional surgeries. By increasing the chances of success of the flap, this technique lowers the risks for reoperation under general or locoregional anesthesia which have important consequences on the patient's health. In conclusion it improves the overall patient care. We concede that adopting this technique represents an expensive investment and is not always possible. However, we believe that, given the multiple indications of this device, it is possible to mutualize its acquisition between several departments of surgery in the same hospital like plastic surgery, gynecological surgery or oncodermatological surgery. One of the limits of this technique, as we explained it, lies in the fact that it requires the evaluation of perfusion according to the fluorescence's intensity. We estimated that perfusion was satisfying if the fluorescence of the flap was comparable to the fluorescence of surrounding tissues but was not if there was an important difference between the two structures. This subjective analysis is well illustrated by the 4th case report where an intermediate area was partly preserved by the surgical team even though it was less fluorescent than healthy tissue around and where a necrosis occurred in the postoperative outcomes. It would be very interesting to develop a fluorescence scale to objectify the evaluation of the perfusion and increase the vascular safety of the flap. Philips and Al. [17] then Munabi and Al. [18] published their early experience of such a scale. Software is currently under development by a biomedical European company (QUEST Innovations, Middenmeer, Netherlands) and scientific progress in this field will probably be very valuable. Another limit is the fact that even though the angiography confirms there is a good arterial flow in the flap it does not prevent venous complications which are commonly seen in perforator flaps. New innovations in this field could be interesting although it seems difficult to imagine injecting a coloring to evaluate the quality of the venous return. Finally, another limit is the small size of this series even if patients were included prospectively. Over our small sample of patients, indocyanine green angiography was useful in 80% of cases in the surgical intraoperative decision-making. It seems important to us to develop the use of this device in order to increase the number of patients in published series and enhance the validity of the technique in the years ahead. It would be interesting also to do a randomized trial with a group of patients where indocyanine green would not be used peroperatively. In plastic surgery, this technique looks very promising in the field of perforator flaps especially with multiple pedicles. If used while doing a clamping test peroperatively, this technique could guide the surgeon towards the dissection and the conservation of the pedicle which seems to better irrigate the flap.

Conclusion

Intraoperative indocyanine green angiography associated with a near-infrared camera appears to be a reliable and reproducible technique. It brings a benefit onto the surgical technique, it secures the flap and it reduces vascular complications. This preliminary study shows that this technique is particularly interesting as it can change the surgical strategy peroperatively.

Video

An additional video showing the intraoperative angiography of case 3 is available. It shows the first angiography which revealed a large distal perfusion defect, followed by the additional excision of the most distal part of the flap in the bottom right corner. The video finally shows the second angiography with the remaining distal perfusion defect. (<https://youtu.be/vZQuC2uE5Zc>).

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