Assessment of Fibula Flap Skin Perfusion in Patients Undergoing Oromandibular Reconstruction: Comparison of Clinical Findings, Fluorescein, and Indocyanine Green Angiography

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IMPORTANCE Complications of partial flap necrosis contribute substantially to morbidity in patients who undergo head and neck reconstructive surgery.

OBJECTIVE To assess the usefulness of clinical findings, intraoperative fluorescein angiography, and intraoperative indocyanine green angiography (ICGA) for evaluation of flap skin paddle perfusion in patients undergoing oromandibular reconstruction who are at high risk of partial skin paddle necrosis.

DESIGN, SETTING, AND PARTICIPANTS Retrospective medical record review from May 21, 1996, to May 27, 2015, at a tertiary care academic medical center. Participants were 73 patients who underwent reconstruction of through-and-through defects of the mucosa, mandible, and skin using fibula free flaps that contained large bilobed skin paddles.

MAIN OUTCOMES AND MEASURES The rates of partial skin paddle necrosis and revision reconstructive surgery.

RESULTS The rates of partial flap necrosis were 8% (n = 2) among 25 patients in whom the skin paddle was trimmed based on ICGA and 33% (n = 16) among 48 patients in whom the skin paddle was trimmed according to clinical findings (P = .02). The rates of revision reconstructive surgery were 20% (5 of 25) when flap skin paddles were trimmed using ICGA and 42% (20 of 48) when trimmed per clinical findings (P = .06).

CONCLUSIONS AND RELEVANCE The use of ICGA may reduce the risk of partial skin flap necrosis in free flaps used in patients undergoing head and neck reconstruction who are at high risk of developing flap necrosis. Indocyanine green angiography imaging should be considered in any flap in which skin paddle viability is uncertain based on clinical findings and in patients in whom the skin paddle extends beyond the primary and adjacent angiosomes.

LEVEL OF EVIDENCE 3.
Partial necrosis of a flap skin paddle is a complication of head and neck reconstructive surgery that can have substantial consequences. Even in minor cases of partial flap necrosis that are amenable to conservative treatment using local wound care, wound healing occurs by secondary intention and is delayed. Such morbidity can be associated with impaired quality of life, aesthetic results, and functional outcomes and possibly delay the initiation of adjuvant therapy. The consequences of partial flap necrosis may be severe in certain situations. For example, patients who develop partial flap necrosis after undergoing reconstruction of the mucosa of the oral cavity, pharynx, larynx, or cervical esophagus are at risk of developing wound infections and salivary fistulas. These complications can lead to delayed oral intake and life-threatening conditions, including mediastinitis, sepsis, and carotid blowout syndrome. Finally, partial flap necrosis may result in prolonged hospitalization and the need for revision reconstructive surgical procedures, which can increase the cost of treatment.

When the cutaneous portion of a flap extends beyond the perfusion limits of a flap's vascular blood supply, arterial insufficiency can occur, leading to partial necrosis of the flap skin paddle. Clinical findings that are commonly used during oromandibular reconstruction to determine flap viability include skin color, turgor, capillary refill, and dermal bleeding of the skin edge. In some cases, areas with poor arterial flow are obvious, as evidenced by a dusky color, absent turgor and capillary refill, and a lack of dermal bleeding. However, areas of borderline perfusion are much more difficult to assess. Clinically, the skin color may be pale, while turgor, capillary refill, and dermal bleeding may be present but reduced. In such patients, accurate prediction of the ultimate fate of the threatened skin may be difficult even in the hands of an experienced surgeon, and the final outcome may not be certain for 2 to 3 weeks.

In addition to clinical findings that suggest flap skin viability, specialized imaging modalities may be used during surgery to assess tissue perfusion. These include indocyanine green angiography (ICGA) and fluorescein angiography (FA), which have been used previously in patients undergoing breast reconstruction to assess the risk of skin flap necrosis. Indocyanine green dye remains in the blood vessels by rapidly binding to plasma proteins and is distributed throughout the body's intravascular compartment. It is detected by exposure to light in the infrared spectrum and has a short half-life of 150 to 180 seconds. The medical uses of indocyanine green include assessment of cardiac output, liver function, and blood volume, as well as tissue and organ perfusion studies. Fluorescein dye is used for intraoperative angiography in a fashion similar to ICGA. However, it is detected by exposure to UV light and has the disadvantage of a long half-life, limiting how often it can be used during a procedure.

The present study was undertaken to assess the usefulness of clinical findings, intraoperative FA, and intraoperative ICGA for assessment of skin flap perfusion in patients undergoing oromandibular reconstruction who are at high risk of partial skin paddle necrosis. The main outcome measures were the rates of partial skin paddle necrosis and revision reconstructive surgery.

Methods

This retrospective medical record review was approved by the David Geffen School of Medicine at University of California, Los Angeles, institutional review board. Written informed consent was obtained from all participants. From May 21, 1996, to May 27, 2015, a total of 73 patients at tertiary care academic medical centers in Los Angeles (Ronald Reagan UCLA Medical Center, Harbor-UCLA Medical Center, and VA West Los Angeles Medical Center) underwent reconstruction of through-and-through defects of the mucosa, mandible, and skin using fibula free flaps that contained large bilobed skin paddles.

In 2010, we began intraoperative assessment of flap skin paddle perfusion using FA and ICGA. Patients with iodine allergy were excluded from ICGA analysis. In all patients, 2-team surgery was used for simultaneous tumor resection and flap reconstruction. Five milliliters of indocyanine green (ICG-PULSION; PULSION Medical Inc) was used at a concentration of 5 mg/5 mL and cost approximately $80 per use. The imaging systems (SPY Imaging System, LifeCell Corp; and SPY Elite Imaging System, Novadaq Technologies Inc) cost approximately $1200 per case. Five milliliters of fluorescein (AK-Fluor; Akorn Inc) was used at a concentration of 100 mg/I mL and cost $15 per use. A Wood lamp, which was used to image the fluorescein dye, can be purchased for approximately $1000. A description of the surgical technique that was used and a discussion of the indications and limitations of fibula flaps for reconstruction of through-and-through oromandibular defects can be found in a prior publication by our group. Because all flaps were harvested before completion of the tumor resection, flap designs incorporated skin paddles that were larger than the anticipated soft-tissue components of the defect. All flaps were elevated under tourniquet, and flap skin paddle perfusion was assessed by clinical findings (skin color, turgor, capillary refill, and dermal bleeding of the skin edge), FA, and ICGA at least 30 minutes after tourniquet release but before flap pedicle division. Sometimes, ICGA was performed more than once during a case, with at least 10 to 20 minutes between each imaging session to allow for washout of the contrast dye. The perfusion territories determined by clinical findings, FA, and ICGA were marked directly on the flap skin paddle using a surgical marking pen, and a percentage of flap skin paddle viability was estimated. Among patients in whom ICGA was used, the harvested flap skin paddle was trimmed and inset into the defect according to the perfusion territory established by ICGA.

The main outcome measured was percentage flap skin paddle viability as determined by clinical findings, FA, and ICGA. The rates of partial skin paddle necrosis and revision reconstructive surgery were also determined. Statistical analysis was performed using an Internet-based calculator (http://www.socscistatistics.com/tests/chisquare/default2.aspx), with significance defined as \( P < .05 \).
Results

Skin paddle perfusion was estimated by clinical findings in all 73 patients, by ICGA in 25 patients, and by FA in 8 patients. The 8 patients assessed by FA were also evaluated by ICGA, and the results are summarized in the Table. In 6 of 8 patients, ICGA detected at-risk areas that were not detected by clinical findings (Figure). In 4 of 8 patients, ICGA also detected at-risk areas that were not detected by FA. In one patient, FA detected at-risk areas that were not detected by ICGA. This flap was trimmed according to ICGA findings and did not develop partial necrosis, indicating that some FA findings may represent false-positive results.

Among 25 patients in whom the skin paddle was trimmed based on ICGA, ICGA findings agreed with clinical findings in 6 (24%). In 17 of 25 patients (68%), ICGA detected areas of hypoperfusion that were not detected by clinical findings. In 4 of 25 patients (16%), ICGA showed adequate perfusion in areas that were determined to be hypoperfused by clinical findings. These 4 patients underwent skin paddle trimming according to ICGA findings and did not develop partial flap necrosis.

There were no complete flap failures among the study patients. The mean total flap skin paddle area in flaps trimmed according to clinical findings (271 cm²) was larger than the mean of those trimmed according to ICGA findings (231 cm²). The rates of partial flap necrosis were 8% (n = 2) among 25 patients in whom the skin paddle was trimmed based on ICGA and 33% (n = 16) among 48 patients in whom the skin paddle was trimmed according to clinical findings (P = .02). The rates of revision reconstructive surgery were 20% (5 of 25) when flap skin paddles were trimmed using ICGA and 42% (20 of 48) when trimmed per clinical findings (P = .06).

Two patients developed partial flap necrosis, despite their skin paddles being trimmed according to ICGA findings. In one patient, ICGA showed an area of skin paddle hypoperfusion that was excised; however, an immediately adjacent 3 × 2-cm area of the skin paddle developed partial necrosis, which subsequently healed by secondary intention. The other patient had 2 separate skin paddles that were used for reconstruction of a

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patient No.</th>
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<tbody>
<tr>
<td>Flap area, cm²</td>
<td>1 2 3 4 5 6 7 8</td>
</tr>
<tr>
<td>270</td>
<td>290</td>
</tr>
<tr>
<td>Flap viable portion, %</td>
<td>89</td>
</tr>
<tr>
<td>By clinical findings</td>
<td>82</td>
</tr>
<tr>
<td>By FA</td>
<td>79</td>
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| Abbreviations: FA, fluorescein angiography; ICGA, indocyanine green angiography.

The entire skin paddle appeared to be viable according to clinical findings. Using the quantification software that is available with the SPY Elite Imaging System (Novadaq Technologies Inc), a perfusion intensity of less than 33% of maximal perfusion was chosen as an indicator of hypoperfusion, and the flap was trimmed according to these findings. This line of demarcation corresponds to the black line. The flap did not develop partial necrosis. The percentages represent perfusion compared with the green 100, which was selected as the maximal area of perfusion in the flap.
through-and-through defect of the intraoral mucosa, lower lip, and chin skin. The skin paddle from the proximal leg was used for the cutaneous reconstruction and was supplied by one large perforator and one small perforator. It appeared to be well perfused when imaged by ICGA at the leg after tourniquet release. However, after flap insetting and revascularization, the skin paddle was pale and had diminished turgor, capillary refill, and dermal bleeding of the skin edge. This skin paddle was not reassessed by ICGA, and it subsequently developed 50% partial necrosis that required debridement and pectoralis major myocutaneous flap reconstruction. We believe that the larger of the 2 perforators to the lip and chin skin paddles may have been injured during flap contouring and insetting. In hindsight, the development of partial flap necrosis may have been identified and the need for revision surgery avoided by repeating ICGA when hypoperfusion was suspected based on clinical findings after flap revascularization.

Discussion

The risk of partial flap necrosis in head and neck reconstruction varies according to the method of reconstruction. For example, the cutaneous territory of axial pattern regional rotational flaps harvested from the trunk often lies entirely outside the primary angiosome of the flap's vascular blood supply and sometimes extends beyond the adjacent angiosome, resulting in substantial risk of partial flap necrosis for regional rotational flaps. Two large series that used pectoralis major myocutaneous flaps for head and neck reconstruction found that the rate of partial flap necrosis varied from 21% to 27%. For trapezius flaps, the risk of flap necrosis varied from 13% to 57%. The risk of partial necrosis of supraclavicular artery island flaps used for head and neck reconstruction has been reported to be as high as 18%. Large skin flaps with a random blood supply also have a considerable risk of partial flap necrosis. For instance, cervicofacial rotation flaps have a reported partial flap necrosis rate of 9%. Because free flaps have no arc of rotation, the skin paddle is typically centered within the primary angiosome of the flap's vascular pedicle, rendering the skin paddle reliable for most free flaps. In general, the risk of partial necrosis of free flaps used for head and neck reconstruction is only about 3%. However, when flaps contain large skin paddles that extend beyond their vascular pedicle’s primary and adjacent angiosomes, the risk of partial flap necrosis increases substantially.3

Our analysis showed a statistically significant reduction in the risk of partial skin paddle necrosis in fibula flaps used for through-and-through oromandibular defect reconstruction when flap skin paddle perfusion was assessed by ICGA rather than by clinical findings (8% [2 of 25] vs 33% [16 of 48], P = .02). Furthermore, we showed a 50% reduction in the need for revision reconstructive surgery in patients assessed by ICGA (5 of 25) compared with patients assessed by clinical findings (20 of 48), although this finding did not reach statistical significance (P = .06). The use of FA to assess flap skin paddle perfusion was generally disappointing because the results were often difficult to interpret, especially in patients with dark skin tone. Moreover, fluorescein has a long half-life, which means that FA can usually be used only once during a case. As a result of these issues, we decided to abandon the use of FA to analyze flap perfusion after just 8 cases. Similarly, Phillips et al1 found ICGA to be superior to FA in predicting mastectomy free skin flap necrosis.

Previously, ICGA has been reported to reduce the risk of partial flap skin necrosis in patients undergoing mastectomy and breast free flap reconstruction. Duggal et al13 reported a significant reduction in reoperation for perfusion-related complications and a lower incidence of mastectomy skin necrosis in patients undergoing postmastectomy breast reconstruction who were assessed by ICGA. Casey et al14 noted a significant reduction in partial flap skin and fat necrosis after ICGA assessment of deep inferior epigastric perforator flap perfusion in patients with a history of abdominal liposuction. Furthermore, Kanuri et al15 demonstrated the cost-effectiveness of using ICGA in high-risk patients, including reconstructions that required larger flaps.

To our knowledge, this study is the first case-control series to show a reduced risk of flap necrosis after ICGA evaluation in patients undergoing head and neck reconstruction. In our patients, the use of ICGA reduced but did not eliminate the risk of partial flap necrosis. For instance, in one patient an area of skin paddle hypoperfusion was identified by ICGA, but the true area of decreased perfusion was underestimated. This result points to the fact that, while ICGA provides a visual indication of perfusion, the findings are not truly an objective measure of tissue perfusion because the resulting images are open to subjective interpretation by the surgical team. With the quantification software that is available with the SPY Elite Imaging System, a perfusion intensity of less than 33% of maximal perfusion was chosen in this series as an approximate indicator of hypoperfusion. However, this practice likely represents an oversimplification of the physiology of skin flap perfusion, and other factors such as the rate of contrast inflow and outflow should also be considered. Moyer and Losken16 reported a gray area for ICGA interpretation, with a risk of mastectomy skin flap necrosis occurring between 25% and 45% of maximal skin perfusion.

Despite our promising results, it is important to recognize the limitations of our investigation. Our analysis was conducted among a small series of patients, so the study was not sufficiently powered to perform a multivariable analysis of other factors that may have affected the risk of partial flap necrosis. Indeed, our group’s prior publication on the use of fibula flaps for through-and-through mandible reconstruction reported that flap skin paddle area correlated with the risk of partial skin paddle necrosis.3 In the present study, skin flaps that were assessed and trimmed according to ICGA findings (231 cm2) were smaller than those assessed and trimmed solely based on clinical findings (271 cm2). While recognizing this limitation, it is also important to consider the relative rarity of this surgical indication, with only 73 patients being accrued over 19 years. This low frequency makes it unlikely that any single institution would be able to perform enough similar cases within a reasonable time frame to perform a multivariable analysis for factors that might affect the risk of partial flap necrosis. Despite the smaller skin
paddles trimmed according to ICGA findings, areas of hypoperfusion were detected in 68% (n = 17) of 25 patients who were assessed by ICGA, indicating that these flaps were at high risk of developing partial flap necrosis. The longitudinal nature of this study also diminishes the strength of the conclusions. The use of ICGA has been available at Ronald Reagan UCLA Medical Center only since 2010, so some of the improved results seen after the initiation of ICGA may have been due to a learning curve associated with this method of reconstruction rather than owing to ICGA findings. Finally, it is possible that ICGA underestimated the true perfusion territories of the flaps that were trimmed according to ICGA findings. While the use of ICGA resulted in a significantly reduced risk of partial skin paddle necrosis, some viable portions of the flaps assessed by ICGA may have been needlessly trimmed away.

Conclusions

The use of ICGA may reduce the risk of partial skin flap necrosis in free flaps used in patients undergoing head and neck reconstruction who are at high risk of developing partial flap necrosis. In particular, we demonstrate a reduced rate of partial skin necrosis in fibula free flap reconstructions requiring large bilobed skin paddles for through-and-through oromandibular reconstruction. In such patients and those with uncertain skin paddle viability based on clinical findings, ICGA should be considered to maximize flap viability. Likewise, there may be similar benefit among patients in whom the flap skin paddle extends beyond the primary and adjacent angiosomes of the supplying vessel.