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The Role of Intraoperative Fluorescence Imaging During Esophagectomy

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Background

In recent years, advances in both technique and technology have aimed to minimize the morbidity associated with esophagectomy and improve oncologic outcomes. Most notably, the introduction of minimally invasive esophagectomy and the application of robotic surgical technology have offered the chance to improve perioperative and long-term results. However, despite these innovations, several stubborn challenges remain unresolved in the field of esophageal resection, including the assessment of conduit perfusion in preventing anastomotic leaks, adequate lymphadenectomy and prevention of thoracic duct injuries. Intraoperative fluorescence imaging (FI) is an emerging technology that may have the potential to address each of these challenges.

FI involves the injection of a small quantity of fluorescent dye into the patient at a specified time in the operation. Most often, a specialized camera is used with a separate FI light source and sensor. The FI light source emits light at a wavelength tuned to excite the fluorescent dye, which in turn releases a known wavelength of light back to the FI sensor (1). The image generated by the fluorescence can be viewed on its own or superimposed on a standard laparoscopic/thoracoscopic image, thus highlighting, in real-time, organ perfusion and areas of relevant anatomy, such as blood supply and lymphatic drainage. The dye most often used in esophageal surgery is indocyanine green (ICG). In the past, fluorescein was

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used in surgical applications because of the ability to see the emitted fluorescence with the naked eye, without the use of a specialized camera. However, ICG has the advantage of better visualization of deeper tissues than fluorescein (1) and has gained recent popularity. ICG is safe, approved for use in humans and has extensive history of use in ophthalmology, cardiac and vascular surgery, plastic and reconstructive surgery, oncologic surgery and cardiology (1). Adverse reactions may be possible in patients with allergies to iodine or shellfish (2). Several FI camera options for ICG exist on the market, including the SPY and Pinpoint systems from Novadaq (Novadaq, Ontario, Canada) and the HyperEye Medical System (Mizuho Ikakogyo Co, Tokyo, Japan) both of which combine a standard laparoscope/thoracoscope with an ICG camera, and the Da Vinci robotic surgical system (Intuitive Surgical, Sunnyvale, CA), which has built-in ICG imaging capabilities.

Assessment of Gastric Conduit Perfusion in Preventing Anastomotic Leaks

Chief among the challenges faced by esophageal surgeons is the risk of anastomotic leak, the most significant of the common complications after this operation. Leak rates remain a disappointingly high 10% or more, and are associated with increased perioperative mortality, morbidity and length of stay (3). The high rate of leaks relative to other types of anastomoses is related, at least in part, to the need to rely on a single arterial supply for the transposed stomach that originates distally, such that the area used for the anastomosis is by definition the most ischemic part of the conduit, perfused entirely by submucosal vascular channels.

Classically, assessment of the gastric conduit's perfusion has depended on fairly unreliable measures such as visual inspection of the stomach's color and the palpation of temperature and pulse. Even the use of Doppler ultrasound technology only provides information about the macro-circulation, while it is the micro-circulation that is truly critical to anastomotic healing. Intraoperative FI, on the other hand, provides qualitative and quantitative information about both micro and macro-circulatory health of the gastric conduit. FI dye can be administered intravenously either during conduit preparation in the abdominal phase of the operation, and/or prior to performing the anastomosis in the chest or neck. By observing the speed with which the conduit enhances as well as any areas of demarcation in the conduit, the overall perfusion can be assessed and an optimal location for performing the anastomosis can be selected. This is commonly done qualitatively, with a gross visual assessment of the fluorescence of the conduit, though quantitative measures can be performed. The speed of fluorescence flow can be measured and has been associated with anastomotic leak rates (4). External software (Luminview, Mizuho Ikakogyo Co., Tokyo, Japan) is also available which allows quantitative measurement of fluorescence intensity (5) and newer versions of FI camera systems now feature quantitative assessments built-in (Novadaq, Ontario, Canada).

One of the largest series reporting the use of FI in assessing conduit perfusion is by Zehetner, et al. (2). In this study, 150 consecutive esophagectomies with cervical esophago-gastric anastomosis were performed with ICG assessment of the conduit intraoperatively in the abdominal phase. An assessment was made as to whether the conduit had rapid and robust perfusion or evidence of a demarcation, with an area of poor perfusion. In cases with

poor perfusion a stitch was placed at the site of demarcation and an attempt was made to place the anastomosis proximal to the stitch (closer to the origin of the right gastroepiploic artery), though this was not always possible. 84 (66%) of patients had an area of demarcation with poor perfusion distally in the fundus noted. 29 of these patients had the anastomosis performed proximal to the demarcation (closer to the artery), 49 were performed distally (toward the fundus) and 6 had delayed reconstruction at a second phase. Patients with anastomosis placed distally had a higher risk of leak compared to anastomoses proximal to the demarcation and those with no demarcation noted (45% vs 2%, $p<0.0001$). In multivariate analysis, anastomosis in an area of poor graft perfusion was the only significant predictor of a leak. Similarly, Campbell, et al. noted a decrease in their anastomotic leak rate from 20% to 0% ($p=0.007$) after the introduction of both Doppler ultrasound and ICG FI to assess their gastric conduits (6).

ICG has also been used to help identify the route of the right gastroepiploic artery in order to better protect it during division of the greater omentum (7), as well as to visualize the intramural blood supply of gastric, colonic and jejunal conduits (8) or the vascularity of omental flaps used for anastomotic reinforcement (9). Our colleagues at Memorial Sloan Kettering Cancer Center noted that the use of ICG FI during robotic esophagectomy allowed improved visualization of the right gastroepiploic artery and the identification of “otherwise unvisualized small transverse vessels between the termination of the vascular arcade and the...short gastric arteries” (10). Kitagawa, et al. demonstrated a non-statistically significant decreased leak rate from 17.9% to 4.4 % ($p=0.2$) with the use of FI to denote intramural arterial arcade anatomy prior to the creation of the gastric conduit (11). Lastly, Kamyia, et al. used videos of ICG FI to retrospectively evaluate the perfusion of 26 free jejunal grafts and found that quantitative measures of poor perfusion were associated with the five patients in the series who had a venous anastomotic failure (12).

Sentinel Node Mapping

Another recalcitrant challenge in esophageal surgery relates to oncologic outcomes. Long-term survival rates with esophageal cancer are low even after tri-modality therapy (13). This is partly related to the widespread and often unpredictable distribution of lymph node metastases. This has led to interest in the use of sentinel node mapping techniques to improve the accuracy of lymphadenectomy. FI has been shown to be feasible in detecting lymph node drainage from the esophagus in several small series involving peritumoral injection of ICG (14–17). While still investigational, proponents of this technique have noted the potential to improve lymph node dissection either by allowing a more targeted, less morbid approach to node removal, or alternatively by ensuring a radical dissection encompasses all relevant nodal stations. Whether either approach will result in improved patient outcomes remains to be seen (18).

Prevention of Thoracic Duct Injuries

Lastly, thoracic duct injury remains an infrequent but persistent risk after esophagectomy (19). Though the duct has well-known anatomic landmarks it is frequently not visible in the operative field, especially in obese patients, making avoidance of injury difficult, as well as

repair once injury has occurred. FI has the potential to allow surgeons to prophylactically identify the thoracic duct intraoperatively and to ligate the duct for chyle leaks after esophagectomy, both in the chest (20) and in the abdomen (21, 22). In reported cases ICG was either injected into the small bowel mesentery or into the bilateral inguinal regions, which allowed surgeons to identify and ligate ducts that were otherwise impossible to precisely locate. Whether this targeted approach is more effective than traditional massligation based on anatomic landmarks is unknown at the present time.

How We Do It

We routinely use ICG FI to evaluate the perfusion of the gastric conduit and to select the optimal location for our anastomosis. Our standard approach is a fully minimally invasive Ivor Lewis esophagectomy (MIE), though our procedure for FI is the same when we use alternate approaches including minimally invasive McKeown esophagectomy and robotic or open approaches. In MIE the gastric conduit is tubularized in the abdomen but not completely divided from the specimen. At this point if there is any question about the viability of the conduit or the integrity of the right gastroepiploic artery blood supply, ICG may be administered to aid in the assessment. This step is not commonly needed, but administering ICG at this phase does not affect its use later in the operation as it is washed out of tissues within a matter of minutes.

Next, during the thoracic phase of the operation, the esophagus and surrounding tissues are dissected from the level of the hiatus to above the azygous vein and a mediastinal lymphadenectomy is performed. The conduit is then brought into the chest and laid in the proper orientation. The perfusion of the conduit is grossly assessed by observing its color and palpating for tissue turgor. At this point we assess every conduit using FI. The standard thoracoscope used for the operation is swapped out for the Novadaq Pinpoint camera (although with the recent technological improvements the entire operation can be done using the newest Pinpoint camera). One vial (25 mg) of ICG is diluted by the anesthesiologist in 10 mL of water and 3 mL of this solution are injected intravenously and flushed in with saline. The Pinpoint monitor allows simultaneous visualization of a standard white light image, the fluorescence image and a composite image (Figure 1). The speed of fluorescent enhancement is observed qualitatively, and note is made of any demarcated areas of poor perfusion toward the fundus. The process can be repeated after a few minutes if there is any doubt. An end to side anastomosis is performed using a circular EEA stapler with an orally placed anvil (OrVil, Medtronic, Minneapolis, MN). Every effort is made to construct a tension-free anastomosis in an area of brisk enhancement, resecting any demarcated and poorly perfused portion of the conduit distal to the anastomosis.

In the uncommon event that there is globally poor perfusion of the conduit or it is not possible to construct a tension-free anastomosis in an area of robust perfusion, several options exist. In otherwise low risk patients the anastomosis may be completed with a buttress of omental fat and widely drained. The patient is kept NPO for up to several weeks and the NG tube is kept in place longer than normal to minimize the risk of leak. However, in high risk patients with multiple factors predisposing to a leak or multiple comorbidities such that they would not tolerate a leak, the safest option may be to delay reconstruction

until a later time. Lastly, the gastric conduit can be abandoned altogether in favor of an alternate conduit such as the colon or the jejunum. Thankfully the need for any of these approaches is rare.

Conclusion

The complex nature of esophageal surgery and considerable risk for serious complications encourage surgeons to consider taking advantage of new available tools that offer the potential to mitigate these challenges. Intraoperative fluorescence imaging is a straightforward technique with minimal risk that may reduce anastomotic leaks. We have incorporated this technique as part of our standard approach to evaluating the gastric conduit and constructing the esophagogastric anastomosis. Other groups have reported the use of FI to aid in sentinel lymph node mapping and to help prevent and treat thoracic duct injuries. Further research will hopefully help to demonstrate the impact of these approaches on perioperative and oncologic outcomes, but at the current time they remain promising additions to the armamentarium of the esophageal surgeon.

References

- 1). Alander JT, Kaartinen I, Laakso A, et al. A review of indocyanine green fluorescent imaging in surgery. *Int J Biomed Imag* 2012; 2012: 1–26.
- 2). Zehetner J, DeMeester SR, Alicube ET, et al. Intraoperative assessment of perfusion of the gastric graft and correlation with anastomotic leaks after esophagectomy. *Ann Surg* 2015; 262: 74–8. [PubMed: 25029436]
- 3). Kassis ES, Kosinski AS, Ross P, et al. Predictors of anastomotic leak after esophagectomy: An analysis of the Society of Thoracic Surgeons General Thoracic Database. *Ann Thorac Surg* 2013; 96: 1919–26. [PubMed: 24075499]
- 4). Koyanagi K, Ozawa S, Oguma J, et al. Blood flow speed of the gastric conduit assessed by indocyanine green fluorescence. New predictive evaluation of anastomotic leakage after esophagectomy. *Med* 2016; 96: 30.
- 5). Yukaya T, Sacki H, Kasagi Y, et al. Indocyanine green fluorescence angiography for quantitative evaluation of gastric tube perfusion in patients undergoing esophagectomy. *J Am Coll Surg*. 2016; 222: e67–9. [PubMed: 27113525]
- 6). Campbell C, Reames MK, Robinson M. Conduit vascular evaluation is associated with reduction in anastomotic leak after esophagectomy. *J Gastrointest Surg* 2015; 19: 806–12. [PubMed: 25791907]
- 7). Rino Y, Yukawa N, Sato T, et al. Visualization of blood supply route to the reconstructed stomach by indocyanine green fluorescence imaging during esophagectomy. *BMC Med Imag* 2014; 14: 18.
- 8). Shimada Y, Okumura T, Nagata T, et al. Usefulness of blood supply visualization by indocyanine green fluorescence for reconstruction during esophagectomy. *Esoph* 2011; 8: 259–66.
- 9). Nakashima Y, Saeki H, Yukuya T, et al. Blood flow assessment with indocyanine green fluorescence angiography for pedicled omental flap on cervical esophagogastric anastomosis after esophagectomy. *J Am Coll Surg* 2016 222; e67–9. [PubMed: 27113525]
- 10). Sarkaria IS, Bains MS, Finley DJ, et al. Intraoperative near-infrared fluorescence imaging as an adjunct to robotic-assisted minimally invasive esophagectomy. *Innov* 2014; 9: 391–3.
- 11). Kitagawa H, Namikawa T, Munekage M, et al. Visualization of the stomach's arterial network during esophageal surgery using the HyperEye Medical System. *Anticancer Res* 2015; 25: 6201–6.
- 12). Kamiya K, Unno N, Miyazaki S, et al. Quantitative assessment of the free jejunal graft perfusion. *J Surg Res* 2015; 194: 394–9. [PubMed: 25472574]

- 13). van Hagen P, Hulshof MC, van Lanschot JJ, et al. Preoperative chemoradiotherapy for esophageal or junctional cancer. *New Eng J Med* 2012; 366: 2074–84. [PubMed: 22646630]
- 14). Schlottmann F, Barbetta A, Mungo B, et al. Identification of the lymphatic drainage pattern of esophageal cancer with near-infrared fluorescent imaging. *J Laparoendoscopic Adv Surg Tech A* 2017; 27: 268–71.
- 15). Hachey KJ, Gilmore DM, Armstrong KW, et al. Safety and feasibility of near-infrared imageguided lymphatic mapping of regional lymph nodes in esophageal cancer. *J Thorac Cardiovasc Surg* 2016; 152:546–54. [PubMed: 27179838]
- 16). Kubota K, Yoshida M, Kuroda J. Application of the HyperEye Medical System for esophageal cancer surgery: A preliminary report. *Surg Today* 2013; 43: 215–220. [PubMed: 22782594]
- 17). Yusua Y, Seike J, Yoshida T, et al. Sentinel lymph node biopsy using intraoperative indocyanine green fluorescence imaging navigated with preoperative CT lymphography for superficial esophageal cancer. *Ann Surg Onc* 2012; 19: 486–93.
- 18). Sarkaria IS, Luketitch JD. Seeing green...augmentation of lymph node assessment with near-infrared imaging in esophageal cancer resections. *J Thorac Cardiovasc Surg* 2016; 152: 555–6. [PubMed: 27423840]
- 19). Rao DV, Chaca SP, Sahni P, Chattopadhyay TK. Thoracic duct injury during esophagectomy; 20 years experience at a tertiary care center in a developing country. *Dis Esoph* 2004; 17: 141–5.
- 20). Kamiya K, Unno N, Konno H. Intraoperative intraoperative indocyanine green fluorescence lymphography, a novel imaging technique to detect a chyle fistula after an esophagectomy: Report of a case. *Surg Today* 2009; 39: 421–424. [PubMed: 19408081]
- 21). Kaburagi T, Takeuchi H, Oyama T, et al. Intraoperative fluorescence lymphography using indocyanine green in a patient with chylothorax after esophagectomy: report of a case. *Surg Today* 2013; 43: 206–10. [PubMed: 23108512]
- 22). Matsutani T, Hirakata A, Nomura T. Transabdominal approach for chylorrhea after esophagectomy by using fluorescence navigation with indocyanine green. *Case Report Surg* 2014; 2014: 464017.

Key Points:

- Fluorescence imaging, commonly with indocyanine green (ICG) has the potential to address several challenges encountered in esophagectomy
- Intravascular injection of ICG allows visualization of conduit vascular supply and assessment of perfusion to potentially reduce anastomotic leaks
- Peritumoral injection of ICG may allow identification of sentinel nodes in esophagectomy, though the oncologic value of this technique is unknown
- Intralymphatic injection of ICG allows the visualization of the thoracic duct which may allow preservation of the duct and easier ligation for duct injuries

Brief Synopsis:

Intraoperative fluorescence imaging (FI) with indocyanine green has several potential uses during esophagectomy. Intravascular injection for enhancing the visualization of conduit vascularity and assessing macro and microperfusion has the most literature support and may help reduce anastomotic leaks. Peritumoral injection has been reported for use in identifying sentinel nodes during lymphadenectomy and intralymphatic injection may be used to help preserve or ligate the thoracic duct. Our own technique of FI for conduit assessment is described. We routinely use this strategy to guide anastomosis placement and reduce leaks.

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Figure 1. Different views of conduit perfusion assessment using indocyanine green fluorescence imaging. An area of poor perfusion at the tip of the conduit is identified. White arrow-demarcation between well and poor perfused areas. Black arrow-site for anastomosis.