The Role of Intraoperative Fluorescence Imaging During Esophagectomy

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KEYWORDS

• Esophagectomy • Esophageal cancer • Fluorescence imaging • Indocyanine green • Perfusion • Anastomotic leak • Sentinel node • Chylothorax

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, although 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.

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 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 used in surgical applications because of the ability to see the emitted fluorescence with the naked eye,

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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 macrocirculation, while it is the microcirculation that is truly critical to anastomotic healing. Intraoperative FI, on the other hand, provides qualitative and quantitative information about both micro- and macrocirculatory health of the gastric conduit. FI dye can be administered intravenously either during conduit preparation in the abdominal phase of the operation and/or before 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, although 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 and colleagues.[2] In this study, 150 consecutive esophagectomies with cervical esophagogastric 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), although this was not always possible. Eighty-four (66%) patients had an area of demarcation with poor perfusion distally in the fundus noted. Twenty-nine 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 with anastomoses proximal to the demarcation and those with no demarcation noted (45% vs 2%, $P<.0001$). In multivariate analysis, anastomosis in an area of poor graft perfusion was the only significant predictor of a leak. Similarly, Campbell, and colleagues[6] noted a decrease in their anastomotic leak rate from 20% to 0% ($P = .007$) after the introduction of both Doppler ultrasound and ICG FI to assess their gastric conduits.

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] The authors' 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 and colleagues[11] demonstrated a nonstatistically significant

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