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Chapter

Scope of Real Time Fluorescence Imaging in Esophagectomy

Subramanyeshwar Rao Thammineedi, Srijan Shukla, Nusrath Syed, Ajesh Raj Saksena, Sujit Chyau Patnaik and Pratap Reddy Ramalingam

Abstract

Esophagectomy is a challenging surgery that is known to be associated with high rates of morbidity. Anastomotic leaks, pneumonia, conduit necrosis and chyle leaks are the commonly reported complications. Perfusion assessment and tissue injection based fluorescence guided surgery (FGS) are the newer clinical applications of fluorescent dyes. With the advent and integration of real time fluorescence imaging with the existing minimal access platforms, the esophageal surgeon can employ these techniques to potentially improve outcomes. During thoracic dissection, thoracic duct lymphography, fluorescence guided airway visualization, tracheal perfusion assessment and sentinel lymph node biopsy/dissection are the reported clinical applications. In the abdominal dissection, gastroepiploic arcade identification, gastric conduit perfusion assessment and proximal esophagus perfusion assessment have been described. Using the different routes of administration, the same dye can be used for different uses at separate points in a single esophagectomy surgery. The principles and evidence pertaining to these applications have been outlined.

Keywords: esophagectomy, indocyanine green, ICG, fluorescence imaging, near infrared, thoracic duct, gastric conduit

1. Introduction

Real time fluorescence imaging with indocyanine green (ICG) is a promising technology with a potential to resolve many challenges during esophagectomy including the assessment of gastric conduit vascularity, ICG-guided navigation surgery for an adequate lymphadenectomy, detection of sentinel nodes in early stage cancer, defining trachea and bronchial tree and in delineating thoracic duct anatomy and identification of chyle leaks during and after surgery [1]. It is also useful in identifying and safeguarding gastroepiploic arcade vital for gastric conduit creation, especially in obese patients where arcade detection could be challenging. This article provides an overview of the principles of fluorescence imaging, types of fluorescence dyes, indications of fluorescence-guided surgery (FGS) and summarizes the utility of FGS in relation to esophageal surgery.

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2. Near-infrared fluorescence- the physics

Intraoperative fluorescence utilizes the property of specific molecules which absorb light at a particular wavelength and emit light at a longer wavelength [2]. When stimulated by an external light source, these molecules are excited, and the emission occurs at a longer wavelength in the near-infrared range (NIR) (650–900 nm). The emitted light is captured using a camera equipped with specialized filters, and the visualization of the fluorescence signal is relayed to an external display providing real-time in vivo imaging.

The light emitted in the NIR spectrum cannot be seen by human eyes. The NIR fluorescent cameras selectively capture it. Also, NIR fluorescence has the advantages of low background autofluorescence from blood components (hemoglobin and water) and an excellent signal-to-background ratio, providing clear fluorescence visuals.

3. Fluorescent dyes- the chemistry

Fluorescein, 5-amino levulinic acid, indocyanine green (ICG), and methylene blue are fluorescent dyes used for in vivo fluorescent imaging. Indocyanine green, small diameter water soluble tricarbocyanine dye, exhibits fluorescence when activated by NIR light within the wavelength of 760 to 780 nm delivered by a near-infrared optical system. On excitation, ICG emits a fluorescence emission between 800 and 850 nm, which the NIR device captures [3]. The depth of tissue visualization varies between 0.5 and 1 cm. When injected intravenously, ICG is tightly bound to the plasma proteins and remains within the intravascular compartment. This property is helpful for angiography assessment of the gastric conduit or tissue perfusion. It rapidly washes out with a short half-life of 150–180 seconds. When injected submucosal or intranodal, ICG is distributed through the lymphatic system. ICG concentrates in the liver and is excreted through the biliary system, which helps delineate the biliary system for fluorescence cholangiography. ICG is relatively safe with a low risk of adverse effects at a dose of 0.1 mg to 0.5 mg/mL/kg for human use [4]. Methylene blue (MB) is a thiazine dye and has also shown to have fluorescent properties. It has an excitation peak of approximately 700 nm with less tissue penetration but more background tissue autofluorescence. It can be administered orally, subcutaneously, or intravenously. MB is excreted through the kidneys and is contraindicated in patients with renal insufficiency [5].

4. Routes of administration- the biology

The versatility of fluorescent dyes has opened up many interesting clinical applications. The route of administration of the dye determines the drainage pathway of the dye. The resultant highlighted structures can help the surgeon make the intended surgical decisions (**Table 1**). The most commonly used route is the intravenous injection wherein the perfusion of the organ under interest has to be studied. ICG has been successfully studied in assessment of perfusion of anastomotic segments of colon, rectum and esophagus [6]. Because the predominant excretion of ICG happens via the biliary tract, delayed fluorescence imaging performed upto 15 hours after injection allows for cholangiography [7]. When ICG is injected directly into tissues, it gets drained by nearby lymphatic channels to the regional lymph node. This concept

Route of administration	Intended use	Clinical application
Intravenous	Perfusion assessment	Gastric conduit perfusion (esophagectomy), Flap perfusion (reconstructive surgery, Colon perfusion (Colectomy)
Intravenous	Biliary drainage	Cholangiography
Peritumoral	Lymph node mapping	Sentinel lymph node biopsy (Breast carcinoma, endometrial carcinoma)
Groin nodal injection	Lymphography	Chyle leak localization, Thoracic duct mapping
Aerosol inhalation/ nebulisation	Airway fluorescence	To be studied

Table 1.
Various routes of administration of fluorescence dyes and their clinical applications.

is utilized in sentinel lymph node biopsy (SLNB). Peritumoral ICG injection has been found to be a suitable alternative to other dyes in breast and endometrial carcinoma [8, 9]. Lymphatic system of retroperitoneum and thoracic duct can be imaged via ICG injection in groin lymph node. This has opened up a new avenue to visualize and manage thoracic duct and chyle leaks [10, 11]. Fluorescein aerosolization has been attempted and fluorescence confirmed on thoracoscopy [12]. Further studies are required to explore the administration of fluorescent dyes via airway.

5. Technology integration

Recent advances in esophagectomy include wide acceptance of minimal access surgery (MAS) approaches. MAS reduced the major morbidity associated with esophagectomy with equivalent oncological outcomes. With MAS came the advantages of magnification and better identification of surgical anatomy. To improve upon the previous iterations of camera systems, newer cameras have integrated fluorescence imaging capabilities. The first generation fluorescence integrated cameras required the surgeon to switch off white light and the fluorescent structure would get highlighted in a background of darkness. Second generation fluorescence integrated cameras overcame this by adding artificial intelligence to overlay the fluorescent structure over a well-lit background. This enabled interruption free instrumentation and accurate dissection. Portable handheld cameras with integrated fluorescence capabilities are also available now for open surgeries. With these modern adjuncts in the armamentarium, an esophageal surgeon stands at an advantage of having real time information pertaining to various critical steps of an otherwise complex procedure.

The technology has been increasingly utilized for real-time surgical decision-making. Various commercially available equipment for open, laparoscopic, and robotic platforms simultaneously provides high-definition fluorescence and white light images on the same screen. These systems have built-in NIR filters, a camera, and a visual processor for capturing high-definition fluorescent images. The fluorescence and white light modes can be conveniently toggled by clicking a button or using a foot pedal switch (**Table 2**) [5].

Open procedures	Thoracoscopy/Laparoscopy	Robotic platforms
• PDE- Neo II • Quest Spectrum • Stryker PINPOINT with SPY-PHI	• Karl Storz IMAGE 1 S™/ IMAGE 1 S™ Rubina • Quest Spectrum • Stryker 1688 AIM	• Da Vinci Surgical Systems with Firefly

Table 2.
Commercially available integrated fluorescence imaging platforms.

6. Challenges in esophagectomy

Esophagectomy is a complex surgery requiring the surgeon to master both technical and cognitive skills. MAS approaches have their own learning curves and learning curve associated complications have also been reported [13, 14]. The major challenges for a team managing esophagectomy patients include prevention and management of these postoperative complications. Pneumonia, anastomotic leaks, chylothorax, conduit necrosis are the most often reported complications [15]. Patients who experience major complications tend to have poorer overall survival as well [15]. Predictive factors for anastomotic leaks have been studied and apart from the medical comorbidities of the patient, technique of surgery has also been found to be a significant risk factor [16]. It is generally accepted that ensuring and improving adequate blood supply affects leak rates in esophageal anastomoses [17]. Visual assessment of gastric conduit perfusion is considered inadequate [18]. Fluorescence perfusion assessment offers opportunity to study real time blood supply to the anastomotic segments.

During thoracic dissection in esophagectomy, thoracic duct is a difficult structure to appreciate under white light. As radiation therapy before surgery is being increasingly used for locally advanced tumors, the tissue planes can get fused making identification of thoracic duct even harder. Chylothorax can be very debilitating and may increase length of stay and mortality rates [19]. Fluorescence lymphography is being explored for accurate intraoperative identification of thoracic duct [11, 20]. Newer morphological patterns of thoracic duct previously not described are also being reported [20].

7. Thoracic duct lymphangiography

Chylothorax after thoracic surgeries is an infrequent postoperative complication. Incidence of chylothorax ranges from 1.4% after transthoracic esophageal resection to 2.4% after transhiatal esophagectomy [21]. Thoracic duct injury is a serious complication after chest surgery and major neck dissections that significantly increases hospital stay, with high in-hospital mortality [22–25]. Chyle leak carries high morbidity up to 38% and mortality as high as 25% [26].

The non-visualization of the thoracic duct with its proximity to the esophagus makes it prone to iatrogenic injury during surgery, leading to chylothorax. The diagnosis is considered in the presence of excessive pleural output and established by biochemical and physical characteristics of the fluid. Intraoperative identification of the thoracic duct can be difficult, especially during reoperation. Because traditional conservative treatment of thoracic duct injury has a high failure rate, intraoperative image guidance is essential for proper surgical management. Presently, lymphoscintigraphy and lymphangiography are available in preoperative setting to diagnose and recognize the site of thoracic duct injury; however, these procedures cannot accurately guide the surgeon during surgery [27, 28]. Oral administration of heavy cream before surgery is sometimes performed to visualize chyle leak [29].

Real time fluorescence imaging with ICG has the potential to solve all these issues. Thoracic duct NIR fluorescence imaging with ICG has been reported earlier for the recognition of site of chyle leak after esophageal and other thoracic surgeries in form of case reports [11, 30]. Using subcutaneous ICG injection at the inguinal area, Chang et al. identified and ligated chyle leak site through re-sternotomy in a 3-month-old infant with congenital heart disease who had refractory postoperative chylothorax despite multiple line of managements [31]. Kaburagi et al. performed successful mass ligation of thoracic duct at the level of the diaphragmatic crura following ICG injection in mesentery in a case of post esophagectomy chyle leak [32].

Vecchiato et al. reported their experience of minimally invasive esophagectomy with ICG injection in inguinal lymph nodes in 19 patients. The thoracic duct was identified in all patients after a mean of 52.7 minutes from injection time [11]. The protocol followed at the author's surgical unit is as follows. After induction of anesthesia, ICG is injected in groin node with ultrasound guidance. ICG is available as 25 mg powder (Aurogreen; Aurolabs, Madurai, India), which is reconstituted in 10 ml of sterile distilled water. One ml of the solution contains 2.5 mg of ICG. One ml is injected via ultrasound guidance in a groin node, one each on both sides. Generally, the node appears as an oval structure in ultrasound with central echoic and peripheral hypoechoic architecture. A successful administration is noted by tumescence of the node with loss of central hyperechoic architecture. Real time fluorescence lymphography is utilized at the time of thoracic dissection (**Figure 1**). Thoracic duct is visualized and safeguarded in all cases of esophagectomy, unless directly involved by the tumor (**Figure 2**) [1].

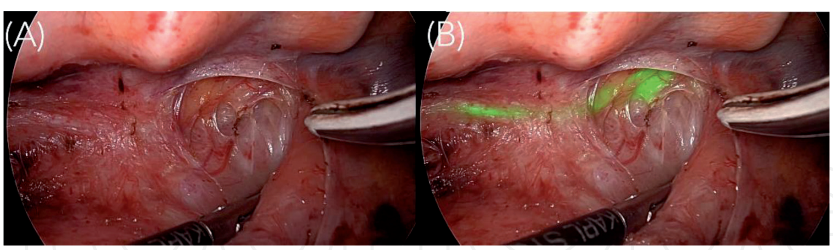

Figure 1.
Comparison of thoracic duct visualization without and with real time fluorescence lymphography. (A) White light thoracoscopy with esophagus retracted towards surgeon to stretch mesoesophagus to allow for visualization of thoracic duct. (B) Real time fluorescence lymphography turned on, thoracic duct along its course is highlighted.

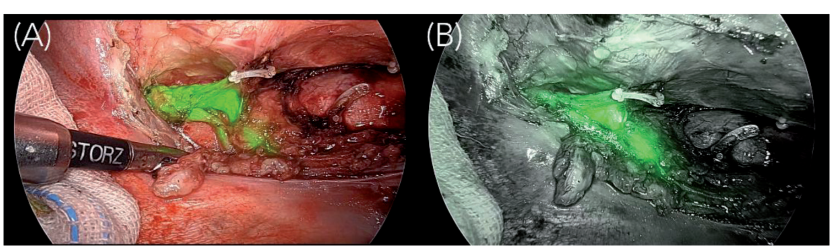

Figure 2.
Real time fluorescence lymphography depicting thoracic duct involvement by lower third esophageal carcinoma under different modes. (A) Overlay mode. (B) Color segmented fluorescence (CSF) mode.

8. Fluorescence nebulization for airway visualization

In locally advanced upper and mid thoracic esophageal cancers, the posterior plane of dissection is limited by the membranous trachea. Bulky subcarinal and hilar lymph nodes can also pose difficulty in dissection over posterior surface of right and left bronchi. The fear of injuring the tracheobronchial membrane makes this part of thoracic dissection in esophagectomy an extremely challenging task. Fluorescence guided airway visualization could be an adjunct in this regard.

Thoracic surgeons have utilized ICG for determining the intersegmental plane in lung segmentectomies [33]. While intravenous ICG injection was studied initially, subsequently endobronchial injection has also been successfully attempted [34]. The authors have applied the same principle by performing nebulization of ICG for early visualization and accurate dissection of posterior membrane of trachea and bronchus in difficult tumors. Using the overlay mode of the NIR camera, esophagus and the lymph nodes can be safely separated from the highlighted membranous trachea and bronchus. **Figure 3** illustrates this technique. Fluorescence nebulization is being tested as a prospective study to standardize the application and evaluate the safety and potential advantages.

9. Sentinel nodal mapping and guided lymphadenectomy

Real time fluorescence imaging can be used for lymphatic mapping in esophageal cancer to better delineate the lymphatic pathways and to aid nodal dissection. Yuasa et al. determined the feasibility of sentinel lymph node (SLN) detection using intraoperative ICG fluorescence imaging navigated by preoperative computed tomographic lymphography (CTLG) in 20 superficial esophageal cancer patients. Preoperative CTLG localized the number and site of SLNs during computed tomography. Further, SLNs were identified intraoperatively, resulting in successful SLN navigation [35]. Schlottmann et al. and Hachey et al. demonstrated the feasibility of sentinel nodal mapping in patients with esophagogastric junction and mid third esophageal malignancies [36, 37]. Schlottmann et al. identified the pattern of nodal drainage by submucosal injection of 2.5 mg ICG via endoscopy in 4 peritumoral quadrants 15–20 minutes before surgery. Left gastric nodes were the first lymph node station to exhibit fluorescence in 8 out of 9 cases. Hachey et al. utilized ICG: human serum albumin (ICG: HSA) to better delineate nodes with near infrared indocyanine green (NIR-ICG). In order to improve fluorescence-guided sentinel lymph node

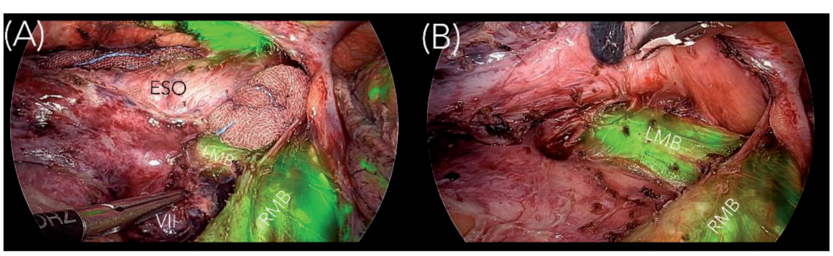

Figure 3.
Fluorescence nebulization and airway visualization. (A) Middle third esophageal tumor (ESO) with contiguous bulky subcarinal lymph node (VII). Right main bronchus (RMB) is dissected away. Left main bronchus (LMB) remains to be dissected, posterior surface is starting to come into view and is highlighted via fluorescence. (B) Subcarinal lymphadenectomy and ventral dissection of esophagus over LMB is complete.

biopsy, Kim et al., in an animal model, used a novel macrophage-targeting ICG bound to human serum albumin (ICG:MSA). This ICG:MSA compound when injected via endoscopy into esophageal tissue has provided promising results in sentinel lymph node detection in a porcine model [38].

10. Gastric conduit perfusion assessment

One of the most feared complications post esophagectomy is anastomotic leak (AL), occurring in 10–30% of patients [39]. While fashioning the gastric conduit, both left gastric and short gastric vessels are usually divided. The conduit solely relies on the right gastroepiploic artery for its blood supply. Inadequate perfusion at the tip of the gastric conduit is one of the most critical factors contributing to anastomotic leak. Conventional assessment techniques of the perfusion and viability of gastric conduit such as visual inspection of the gastric conduit color, warmth, pulsation of the arcade and bleed from the cut edges are considered unreliable. Accurate assessment of perfusion and selecting an appropriate anastomotic site are critical to reduce AL [40]. As a means of evaluating blood flow, indocyanine green (ICG) fluorescence angiography (FA) has recently been introduced to provide real-time assessment of the anastomotic area during esophagectomy [18]. ICG can be used as a vascular contrast agent for assessing perfusion of gastric conduit (**Figure 4**) [5].

A meta-analysis by Slooter et al. reported that ICG significantly decreases anastomotic leaks and graft necrosis after esophagectomy (OR 0.30, 95% CI: 0.14–0.63). The pooled change in management rate due to fluorescence angiography using ICG was 24.55%. Change in management included excision of the poorly perfused area of the gastric conduit and change in site of anastomosis. Despite the change in management, the pooled incidence of anastomotic leak and graft necrosis was as high as 14.08% [41]. Another meta-analysis by Degett et al. reported similar anastomotic leak rate (14%) in patients with esophageal anastomoses after intraoperative ICG fluorescence angiographic assessment [42].

Time to fluorescence is an important parameter which has been studied. The data pertaining to this aspect of the fluorescence angiography is heterogenous. Ishige et

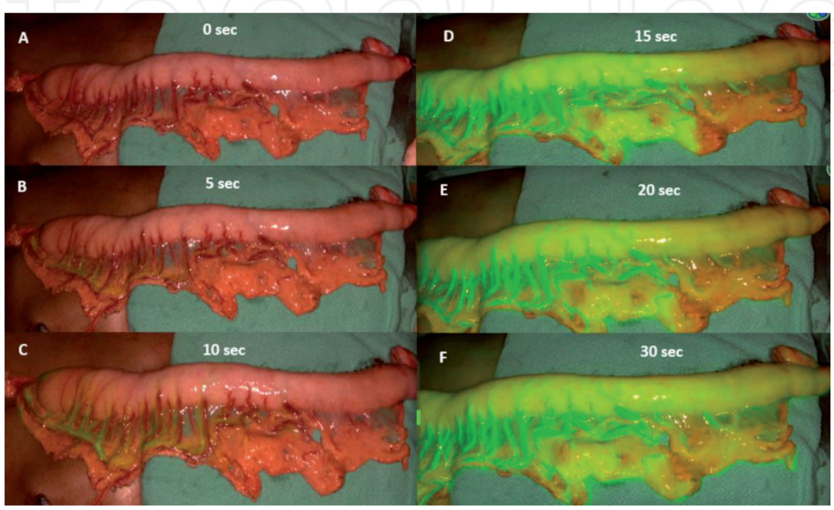

Figure 4.
Real time fluorescence perfusion assessment of gastric conduit. (A-F) fluorescence perfusion assessed at various time intervals after intravenous injection of indocyanine green (ICG) dye.

al. studied different patterns of time to fluorescence intensity curves. They found a "normal" pattern, characterized by a sharp high peak in fluorescence intensity in gastric tubes followed by rapid decline to plateau level, prior to division of perigastric vessels in 6 cases (30%). The other 14 cases showed a "gradual" pattern, characterized by an obtuse and low arterial inflow peak and slow increase in fluorescence intensity over time. However, no anastomotic leak occurred in both groups [43]. Yukaya et al. described three types of curves, normal, outflow delayed and an inflow delayed. Anastomotic leak occurred in 23.1% (3/13) in the normal type, 40% (2/5) in the outflow delayed type and 44.4% (4/9) in the inflow delayed type, with no significant difference among the three types [44]. Koyanagi et al. stratified patients into two groups according to ICG fluorescence flow speed: a simultaneous group with identical speed in gastric conduit wall and the greater curvature vessels, and a delayed group where the ICG fluorescence was slower in the gastric conduit wall in comparison to the greater curvature vessels. They calculated a threshold ICG flow speed of 1.76 cm/s in the gastric conduit predicting anastomotic leak. None of the patients developed anastomotic leak in the simultaneous group, while it occurred in 47% (7/15) patients in the delayed group [45]. Kumagai et al. proposed a 90-second rule wherein all anastomoses were to be reconstructed in the area that showed an enhancement within 90 seconds after initial enhancement at the root of the right gastroepiploic artery [19]. The tip needed revision in 50% (35/70), and in 18 of those 35 patients, a change in anastomotic site was needed. Anastomotic leak occured in 1 out of 70 cases (1.4%) [46]. Slooter et al. reported that the time between ICG injection and enhancement of tip was not significantly prolonged in patients with an anastomotic leak versus no leak (63 vs. 45 seconds) (P = 0.066) and time to fluorescence from base of conduit to the planned anastomosis was significantly increased in patients with a postoperative anastomotic stricture (13 vs. 7 seconds [47].

Nakashima et al. described outcomes of fluorescence angiography assessment of the pedicled omental flap performed to reinforce the esophagogastric anastomosis. Poorly perfused omental tissue was excised on the demarcation line. Anastomotic leak and stricture occurred in 1/38 (2.6%) and 2/38 (5.3%) patients respectively [48]. The importance of proximal esophageal stump revision has been emphasized by Thammineedi et al. where 5 out of 13 patients (38.46%) underwent revision of proximal esophageal stump after ICG assessment [18]. Randomized controlled trials are warranted to prove the exact benefit of ICG fluorescence angiography in reducing anastomotic leaks and strictures in esophagectomy.

11. Future directions

Fluorescent dyes have been around for more than 40 years [3]. In the past decade interest has grown especially after incorporation of fluorescence capable MAS platforms. Most studies of fluorescence guided surgery have been single center experiences. Multicenter trials with better study designs are needed. International collaborations between societies can lead to standardization of techniques and uniform reporting of outcomes.

Conflict of interest

The authors declare no conflict of interest.

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Author details

Subramanyeshwar Rao Thammineedi, Srijan Shukla*, Nusrath Syed,
Ajesh Raj Saksena, Sujit Chyau Patnaik and Pratap Reddy Ramalingam
Department of Surgical Oncology, Basavatarakam Indo American Cancer Hospital and Research Institute, Hyderabad, India

*Address all correspondence to: shuklasrajan@gmail.com

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References

[1] Thammineedi SR, Patnaik SC, Reddy P, Saksena AR, Bollineni N, Nusrath S. The emerging role of ICG fluorescence during minimally invasive Esophagectomy. Indian Journal of Surgical Oncology. 2021;**12**(3):635-636

[2] Weissleder R, Pittet MJ. Imaging in the era of molecular oncology. Nature. 2008;**452**(7187):580-589

[3] Benson RC, Kues HA. Fluorescence properties of indocyanine green as related to angiography. Physics in Medicine and Biology. 1978;**23**(1):159-163

[4] Alander JT, Kaartinen I, Laakso A, Pätilä T, Spillmann T, Tuchin VV, et al. A review of indocyanine green fluorescent imaging in surgery. International Journal of Biomedical Imaging. 2012;**2012**:940585

[5] Thammineedi SR, Saksena AR, Nusrath S, Iyer RR, Shukla S, Patnaik SC, et al. Fluorescence-guided cancer surgery—A new paradigm. Journal of Surgical Oncology. 2021;**123**(8):1679-1698

[6] Blanco-Colino R, Espin-Basany E. Intraoperative use of ICG fluorescence imaging to reduce the risk of anastomotic leakage in colorectal surgery: A systematic review and meta-analysis. Techniques in Coloproctology. 2018;**22**(1):15-23

[7] Tsutsui N, Yoshida M, Nakagawa H, Ito E, Iwase R, Suzuki N, et al. Optimal timing of preoperative indocyanine green administration for fluorescent cholangiography during laparoscopic cholecystectomy using the PINPOINT® endoscopic fluorescence imaging system. Asian Journal of Endoscopic Surgery. 2018;**11**(3):199-205

[8] Grischke EM, Röhm C, Hahn M, Helms G, Brucker S, Wallwiener D. ICG fluorescence technique for the detection of sentinel lymph nodes in breast cancer: Results of a prospective open-label clinical trial. Geburtshilfe und Frauenheilkunde. 2015;**75**(9):935-940

[9] Rossi EC, Kowalski LD, Scalici J, Cantrell L, Schuler K, Hanna RK, et al. A comparison of sentinel lymph node biopsy to lymphadenectomy for endometrial cancer staging (FIRES trial): A multicentre, prospective, cohort study. The Lancet Oncology. 2017;**18**(3):384-392

[10] Shimajiri H, Egi H, Yamamoto M, Kochi M, Mukai S, Ohdan H. Laparoscopic management of refractory chylous ascites using fluorescence navigation with indocyanine green: A case report. International Journal of Surgery Case Reports. 2018;**49**:149-152

[11] Vecchiato M, Martino A, Sponza M, Uzzau A, Ziccarelli A, Marchesi F, et al. Thoracic duct identification with indocyanine green fluorescence during minimally invasive esophagectomy with patient in prone position. Diseases of the Esophagus. 2020;**33**(12):doaa030

[12] Noppen M, Dekeukeleire T, Hanon S, Stratakos G, Amjadi K, Madsen P, et al. Fluorescein-enhanced autofluorescence thoracoscopy in patients with primary spontaneous pneumothorax and normal subjects. American Journal of Respiratory and Critical Care Medicine. 2006;**174**(1):26-30

[13] Prasad P, Wallace L, Navidi M, Phillips AW. Learning curves in minimally invasive esophagectomy: A systematic review and evaluation of

benchmarking parameters. Surgery. 2022;**171**(5):1247-1256

[14] van Workum F, Stenstra MHBC, Berkelmans GHK, Slaman AE, van Berge Henegouwen MI, Gisbertz SS, et al. Learning curve and associated morbidity of minimally invasive Esophagectomy: A retrospective multicenter study. Annals of Surgery. 2019;**269**(1):88-94

[15] Booka E, Takeuchi H, Nishi T, Matsuda S, Kaburagi T, Fukuda K, et al. The impact of postoperative complications on survivals after Esophagectomy for esophageal cancer. Medicine (Baltimore). 2015;**94**(33):e1369

[16] Kassis ES, Kosinski AS, Ross P, Koppes KE, Donahue JM, Daniel VC. Predictors of anastomotic leak after esophagectomy: An analysis of the society of thoracic surgeons general thoracic database. The Annals of Thoracic Surgery. 2013;**96**(6):1919-1926

[17] Reavis KM. The esophageal anastomosis: How improving blood supply affects leak rate. Journal of Gastrointestinal Surgery. 2009;**13**(9):1558-1560

[18] Thammineedi SR, Patnaik SC, Saksena AR, Ramalingam PR, Nusrath S. The utility of Indocyanine green angiography in the assessment of perfusion of gastric conduit and proximal esophageal stump against visual assessment in patients undergoing Esophagectomy: A prospective study. Indian Journal of Surgical Oncology. 2020;**11**(4):684-691

[19] Miao L, Zhang Y, Hu H, Ma L, Shun Y, Xiang J, et al. Incidence and management of chylothorax after esophagectomy. Thoracic Cancer. 2015;**6**(3):354-358

[20] Tokumaru S, Kitazawa M, Nakamura S, Koyama M, Soejima Y. Intraoperative visualization of morphological patterns of the thoracic duct by subcutaneous inguinal injection of indocyanine green in esophagectomy for esophageal cancer. Annals of Gastroenterological Surgery. 2022;**00**:1-7. DOI: 10.1002/ags3.12594

[21] Hulscher JB, Tijssen JG, Obertop H, van Lanschot JJ. Transthoracic versus transhiatal resection for carcinoma of the esophagus: A meta-analysis. The Annals of Thoracic Surgery. 2001;**72**(1):306-313

[22] Brinkmann S, Schroeder W, Junggeburth K, Gutschow CA, Bludau M, Hoelscher AH, et al. Incidence and management of chylothorax after Ivor Lewis esophagectomy for cancer of the esophagus. The Journal of Thoracic and Cardiovascular Surgery. 2016;**151**(5):1398-1404

[23] Lapp GC, Brown DH, Gullane PJ, McKneally M. Thoracoscopic management of chylous fistulae. American Journal of Otolaryngology. 1998;**19**(4):257-262

[24] Wurnig PN, Hollaus PH, Ohtsuka T, Flege JB, Wolf RK. Thoracoscopic direct clipping of the thoracic duct for chylopericardium and chylothorax. The Annals of Thoracic Surgery. 2000;**70**(5):1662-1665

[25] Fahimi H, Casselman FP, Mariani MA, van Boven WJ, Knaepen PJ, van Swieten HA. Current management of postoperative chylothorax. The Annals of Thoracic Surgery. 2001;**71**(2):448-450 discussion 450-451

[26] Schild HH, Strassburg CP, Welz A, Kalff J. Treatment options in patients with chylothorax. Deutsches Ärzteblatt International. 2013;**110**(48):819-826

[27] Kotani K, Kawabe J, Higashiyama S, Shiomi S. Lymphoscintigraphy with

single-photon emission computed tomography/computed tomography is useful for determining the site of chyle leakage after esophagectomy. Indian Journal of Nuclear Medicine: IJNM: The Official Journal of the Society of Nuclear Medicine. 2012;**27**(3):208-209

[28] Sachs PB, Zelch MG, Rice TW, Geisinger MA, Risius B, Lammert GK. Diagnosis and localization of laceration of the thoracic duct: Usefulness of lymphangiography and CT. AJR. American Journal of Roentgenology. 1991;**157**(4):703-705

[29] Shen Y, Feng M, Khan MA, Wang H, Tan L, Wang Q. A simple method minimizes chylothorax after minimally invasive esophagectomy. Journal of the American College of Surgeons. 2014;**218**(1):108-112

[30] Bibas BJ, Costa-de-Carvalho RL, Pola-dos-Reis F, Lauricella LL, Pêgo-Fernandes PM, Terra RM. Video-assisted thoracoscopic thoracic duct ligation with near-infrared fluorescence imaging with indocyanine green. Jornal Brasileiro de Pneumologia. 2019;**45**(4):e20180401

[31] Chang TI, Chen YS, Huang SC. Intraoperative indocyanine green fluorescence lymphography to detect chylous leakage sites after congenital heart surgery. The Journal of Thoracic and Cardiovascular Surgery. 2014;**148**(2):739-740

[32] Kaburagi T, Takeuchi H, Oyama T, Nakamura R, Takahashi T, Wada N, et al. Intraoperative fluorescence lymphography using indocyanine green in a patient with chylothorax after esophagectomy: Report of a case. Surgery Today. 2013;**43**(2):206-210

[33] Pischik VG, Kovalenko A. The role of indocyanine green fluorescence for intersegmental plane identification during video-assisted thoracoscopic surgery segmentectomies. Journal of Thoracic Disease. 2018;**10**(Suppl. 31): S3704-S3711

[34] Wada H, Yamamoto T, Morimoto J, Sakairi Y, Suzuki H, Nakajima T, et al. Near-infrared-guided pulmonary Segmentectomy after endobronchial Indocyanine green injection. The Annals of Thoracic Surgery. 2020;**109**(2):396-403

[35] Yuasa Y, Seike J, Yoshida T, Takechi H, Yamai H, Yamamoto Y, et al. Sentinel lymph node biopsy using intraoperative indocyanine green fluorescence imaging navigated with preoperative CT lymphography for superficial esophageal cancer. Annals of Surgical Oncology. 2012;**19**(2):486-493

[36] Schlottmann F, Barbetta A, Mungo B, Lidor AO, Molena D. Identification of the lymphatic drainage pattern of esophageal cancer with near-infrared fluorescent imaging. Journal of Laparoendoscopic & Advanced Surgical Techniques. Part A. 2017;**27**(3):268-271

[37] Hachey KJ, Gilmore DM, Armstrong KW, Harris SE, Hornick JL, Colson YL, et al. Safety and feasibility of near-infrared image-guided lymphatic mapping of regional lymph nodes in esophageal cancer. The Journal of Thoracic and Cardiovascular Surgery. 2016;**152**(2):546-554

[38] Kim HK, Quan YH, Oh Y, Park JY, Park JH, Choi Y, et al. Macrophage-targeted Indocyanine green-Neomannosyl human serum albumin for intraoperative sentinel lymph node mapping in porcine esophagus. The Annals of Thoracic Surgery. 2016;**102**(4):1149-1155

[39] van Hagen P, Hulshof MCCM, van Lanschot JJB, Steyerberg EW, van Berge

Henegouwen MI, Wijnhoven BPL, et al. Preoperative chemoradiotherapy for esophageal or junctional cancer. The New England Journal of Medicine. 2012;**366**(22):2074-2084

[40] Karliczek A, Harlaar NJ, Zeebregts CJ, Wiggers T, Baas PC, van Dam GM. Surgeons lack predictive accuracy for anastomotic leakage in gastrointestinal surgery. International Journal of Colorectal Disease. 2009;**24**(5):569-576

[41] Slooter MD, Eshuis WJ, Cuesta MA, Gisbertz SS, van Berge Henegouwen MI. Fluorescent imaging using indocyanine green during esophagectomy to prevent surgical morbidity: A systematic review and meta-analysis. Journal of Thoracic Disease. 2019;**11**(Suppl 5):S755-S765

[42] Degett TH, Andersen HS, Gögenur I. Indocyanine green fluorescence angiography for intraoperative assessment of gastrointestinal anastomotic perfusion: A systematic review of clinical trials. Langenbeck's Archives of Surgery. 2016;**401**(6):767-775

[43] Ishige F, Nabeya Y, Hoshino I, Takayama W, Chiba S, Arimitsu H, et al. Quantitative assessment of the blood perfusion of the gastric conduit by Indocyanine green imaging. The Journal of Surgical Research. 2019;**234**:303-310

[44] Yukaya T, Saeki H, Kasagi Y, Nakashima Y, Ando K, Imamura Y, et al. Indocyanine green fluorescence angiography for quantitative evaluation of gastric tube perfusion in patients undergoing Esophagectomy. Journal of the American College of Surgeons. 2015;**221**(2):e37-e42

[45] Koyanagi K, Ozawa S, Oguma J, Kazuno A, Yamazaki Y, Ninomiya Y, et al. Blood flow speed of the gastric conduit assessed by indocyanine green fluorescence: New predictive evaluation of anastomotic leakage after esophagectomy. Medicine (Baltimore). 2016;**95**(30):e4386

[46] Kumagai Y, Hatano S, Sobajima J, Ishiguro T, Fukuchi M, Ishibashi KI, et al. Indocyanine green fluorescence angiography of the reconstructed gastric tube during esophagectomy: Efficacy of the 90-second rule. Diseases of the Esophagus: Official Journal of International Society Diseases of the Esophagus. 2018;**31**(12). DOI: 10.1093/dote/doy052. PMID: 29897432

[47] Slooter MD, de Bruin DM, Eshuis WJ, Veelo DP, van Dieren S, Gisbertz SS, et al. Quantitative fluorescence-guided perfusion assessment of the gastric conduit to predict anastomotic complications after esophagectomy. Diseases of the Esophagus: Official Journal of International Society Diseases of the Esophagus. 2021;**34**(5):doaa100

[48] Nakashima Y, Saeki H, Yukaya T, Tsutsumi S, Nakanishi R, Sugiyama M, et al. Blood flow assessment with Indocyanine green fluorescence angiography for Pedicled omental flap on cervical Esophagogastric anastomosis after Esophagectomy. Journal of the American College of Surgeons. 2016;**222**(5):e67-e69