



Near-infrared fluorescence imaging with indocyanine green to assess the blood supply of the reconstructed gastric conduit to reduce anastomotic leakage after esophagectomy: a literature review

Hiroyuki Kitagawa¹ · Keiichiro Yokota¹ · Akira Marui¹ · Tsutomu Namikawa¹ · Michiya Kobayashi² · Kazuhiro Hanazaki¹

Received: 20 July 2021 / Accepted: 9 January 2022 / Published online: 19 February 2022
© The Author(s) under exclusive licence to Springer Nature Singapore Pte Ltd. 2022

Abstract

The blood supply of the right gastroepiploic artery after esophagectomy with gastric tube reconstruction is essential for avoiding anastomotic leakage. Near-infrared fluorescence (NIRF) imaging with indocyanine green is widely used to assess the blood supply because it can visualize it in real-time during navigation surgery. However, there is no established protocol for this modality. One reason for this lack of protocol is that NIRF provides subjective information. This study aimed to evaluate NIRF quantification. We conducted a literature review of risk factors for anastomotic leakage after esophagectomy, NIRF procedures, NIRF quantification, and new methods to compensate for NIRF limitations. Major methods for the quantification of NIRF include measuring the blood flow speed, visualization time, and fluorescence intensity. The cutoff value for the blood flow speed is 2.07 cm/s, and that for the visualization time is 30–90 s. Although the time-intensity curve provided patterns of change in the blood flow, it did not show an association with anastomotic leakage. However, to compensate for the limitations of NIRF, new devices have been reported that can assess tissue oxygenation perfusion, organ hemoglobin concentration, and microcirculation.

Keywords Near-infrared fluorescent imaging · Indocyanine green · Anastomotic leakage · Esophagectomy

Introduction

Esophagectomy is the main curative treatment for esophageal cancer. To create anastomosis after esophageal resection, the stomach is commonly used as a reconstruction organ because it is easily pulled up and not easily necrotized because of the rich vascular networks in its wall [1] in comparison to the colon or jejunum. However, the incidence of anastomotic leakage (AL) after esophagectomy is higher than that after colon or jejunum surgery, with rates of > 10% even for minimally invasive esophagectomy using a thoracoscopic approach [2]. AL is not only a cause of prolonged

hospital stays but also a risk factor for a poor prognosis after esophagectomy [3, 4]. Although there are several risk factors for AL after esophagectomy, including the patient's comorbidities, surgical procedure, surgeon's experience, and tension at the site of anastomosis, the ischemic condition of the conduit might be the most important factor [5].

The right gastroepiploic artery (RGEA) supplies blood to the site of esophagogastric anastomosis, and its sufficiency has been evaluated with color or vessel pulsation of the conduit by an experienced surgeon [6]. Recently, near-infrared fluorescence (NIRF) imaging with indocyanine green (ICG) has come to be widely used for visualizing the blood flow in real-time during navigation-assisted esophagectomy, as well as liver resection and colon resection [7, 8]. Van Daele et al. reviewed 19 articles in which ICG perfusion was used to assess the gastric conduit after esophagectomy and found that AL was reduced with the ICG-guided procedure in comparison to when ICG guidance was not used (9.9 vs. 20.5%) [9]. However, there is no established NIRF imaging protocol for reducing the incidence of AL after esophagectomy.

✉ Hiroyuki Kitagawa
kitagawah@kochi-u.ac.jp

¹ Department of Surgery, Kochi Medical School, Kohasu-Okochi, Nankoku, Kochi 783-8505, Japan

² Department of Human Health and Medical Sciences, Kochi Medical School, Kohasu-Okochi, Nankoku, Kochi 783-8505, Japan

We, therefore, reviewed the relevant literature to address this issue.

We conducted an electronic search of the MEDLINE database using the search terms “indocyanine fluorescence” AND “blood flow” AND “esophagectomy”. Articles that did not report AL, Japanese articles and case reports were excluded. Of the 22 articles identified in 2021, 11 were selected for this study. Eight additional articles that included more than 20 cases were found by a manual hand search and selected for this study, resulting in a total of 19 articles [6, 8, 10–26] (Fig. 1); these are summarized in Table 1.

NIRF imaging with ICG to assess the blood supply to the gastric tube

NIRF imaging with ICG can visualize the blood flow in the arteries and perfusion in the intragastric wall arterial networks. Furthermore, it can be used for real-time surgical assessments during resection of the insufficient fluorescence area of the gastric tube [17], for the conversion of the anastomosis procedure from end-to-side to end-to-end to relieve tension at the site of cervical anastomosis [18], and for additional procedures such as super drainage [27]. NIRF can be used repeatedly and does not prolong the overall surgical

time [27]. Shimada et al. [10] evaluated the usefulness of NIRF using the Photodynamic Eye (Hamamatsu Photonics K. K., Tokyo, Japan) in 40 cases (38 McKeown procedures; two cervical esophagectomies) and reported that no AL occurred in patients when the small vessels in the reconstructed organ could be visualized, and that vein anastomosis could be performed for five patients using NIRF information.

Gastric tubes are classified based on width. A whole stomach tube is created by simple resection of the cardia. A narrow gastric tube, which is 3–5 cm wide, is created by resection of the lesser curvature of the stomach using a linear stapler. The whole stomach tube has the advantage of preserving the intra-wall vessels at the lesser curvature; however, with the narrow gastric tube, the blood flow to the tip depends on the connection of the left gastroepiploic artery (LGEA) and RGEA. Therefore, attention to these two factors is required during NIRF imaging with ICG. The presence of a connection between the RGEA and LGEA allows good perfusion to the top of the gastric tube; however, without this connection, perfusion depends on the intragastric wall arterial networks [11]. Based on the ICG fluorescence information obtained using the Photodynamic Eye, Kumagai et al. [11] divided the gastric tube into the following three

Fig. 1 Flowchart of the article selection process

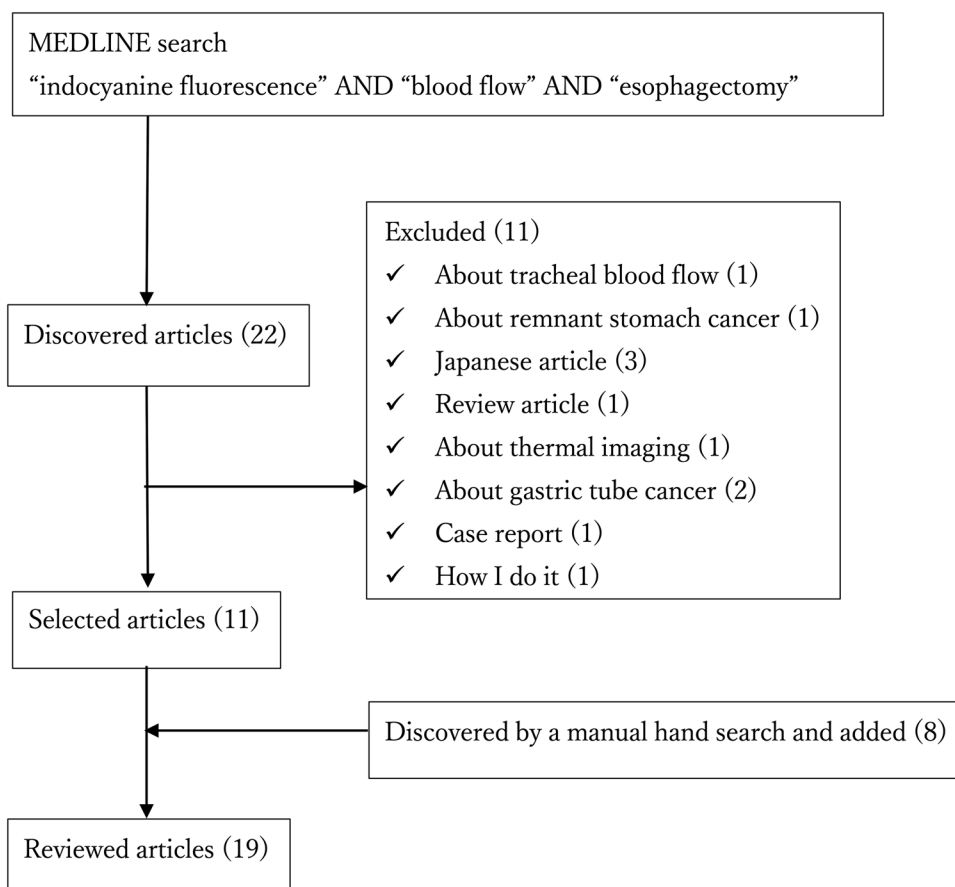


Table 1 Near-infrared fluorescence imaging with indocyanine green during esophagectomy and its effects on anastomotic leakage

References	Number of patients (type of esophagectomy)	ICG dose, system	Timing of ICG injection	Measurement or evaluation of the blood flow of the gastric tube	Change in anastomosis procedure	AL incidence (%)	Effects on AL
Shimada et al. [10]	40 (McKeown, 38; cervical esophagectomy, 2) (gastric tube, 36; gastric tube plus free jejunum, 1; free jejunum, 2; ileo-colic, 1)	2.5 mg, PDE	After creating the gastric tube	Vessel visualization	Vein anastomosis for 5 patients	3 (7.5)	No AL occurred in the patients whose small vessels could be visualized in the reconstructed organ
Kumagai et al. [11]	20 (McKeown)	2.5 mg, PDE	After creating the gastric tube	ICG visualization of the gastric tube	None	2 (10.0)	Preserving the left gastroepiploic vessels contributed to the blood supply to the further proximal side of the gastric tube
Rino et al. [12]	33	2.5 mg, PDE	After creating the gastric tube	ICG visualization of the gastric tube	None	5 (15.2)	The blood flow route was classified into 3 routes; gastric wall; greater curvature; and splenic hiatal
Zehetner et al. [6]	144 (McKeown, 88; Ivor Lewis, 26; MIE, 24)	2.5 mg, SPY	After creating the gastric tube	ICG visualization of the gastric tube	Anastomosis was placed near the good ICG perfusion area	24 (16.7)	AL was unlikely to occur when anastomosis was placed near the good ICG perfusion area
Campbell et al. [13]	30 (Ivor Lewis)	5 mg, SPY	After creating the gastric tube	ICG visualization of the gastric tube	Anastomosis was made within the relative 75% perfusion line	0	Incidence of AL was reduced in comparison to that of the 60 patients without NIRF (20%)
Yukaya et al. [14]	27 (McKeown)	0.1 mg/kg, HEMS	After creating the gastric tube	Pattern of change in luminance	None	9 (33.3)	No association between AL and the pattern of luminance change
Kitagawa et al. [15]	51 (McKeown)	5 mg, HEMS	After/before creating the gastric tube	Arterial network borders of the greater and lesser curvatures	Before creating the gastric tube, HEMS could visualize the arterial network borders (line marking method)	6 (11.8)	In comparison to the after creation of the gastric tube group, the incidence of AL decreased from 17.9 to 4.4%

Table 1 (continued)

References	Number of patients (type of esophagectomy)	ICG dose, system	Timing of ICG injection	Measurement or evaluation of the blood flow of the gastric tube	Change in anastomosis procedure	AL incidence (%)	Effects on AL
Koyanagi et al. [16]	40 (McKeown)	2.5 or 1.25 mg, PDE	After creating the gastric tube	ICG flow speed	None	7 (17.5)	Delayed ICG flow speed in the gastric tube wall was a risk factor for AL, and its cutoff value was 1.76 cm/s
Dalton et al. [17]	20 (Ivor Lewis)	SPY		ICG visualization of the gastric tube	No perfusion area of the gastric tube tip was resected for 6 (30%) patients	2 (10.0)	No AL in the non-ICG group
Karampinis et al. [8]	35	7.5 mg, PIN	After creating the gastric tube	Anastomosis zone of optimal ICG perfusion (“optizone”)	Anastomosis could not be made in the “optizone” of 2 patients and AL occurred	3 (8.6)	AL was reduced when anastomosis was made in the “optizone” (3%) in comparison to the historical 55 patients without ICG (18%)
Ohi et al. [18]	59 (unknown)	2.5 mg, PDE	After creating the gastric tube	ICG visualization time	Superdrainage	1 (1.7)	40 s rule AL occurred in 1.7% of the ICG group and 14.7% of the non-ICG group
Kumagai et al. [19]	70 (McKeown)	2.5 mg, PDE	After creating the gastric tube	ICG visualization time	For 18 cases, anastomosis site was decided and the gastric tube tip was excised	1 (1.4)	90 s rule
Noma et al. [20]	68 (McKeown)	12.5 mg, PDE	After creating the gastric tube	ICG visualization time	Further mobilization of the gastric tube or supercharge/drainage	6 (8.8)	30 s rule
Ishige et al. [21]	20 (McKeown)	1.25 mg, VIS	Before/after creating and after pulling up the gastric tube	Pattern of change in fluorescence intensity	None	None	The maximum intensity was decreased and the time to reach the maximum intensity was extended after creating and pulling-up the gastric tube
Kitagawa et al. [22]	66 (McKeown, 55; PLE, 5; bypass, 6)	5 mg, LV	Before creating and after pulling up the gastric tube	ICG visualization time	Change from end-to-side circular stapler anastomosis to end-to-end hand-sewn	10 (15.2)	36 s in AL patients vs. 28 s in non-AL patients

Table 1 (continued)

References	Number of patients (type of esophagectomy)	ICG dose, system	Timing of ICG injection	Measurement or evaluation of the blood flow of the gastric tube	Change in anastomosis procedure	AL incidence (%)	Effects on AL
Talavera-Urquijo et al. [23]	100 (Ivor Lewis)	0.3 mg/kg, VIS	Before and after creating the gastric tube	ICG flow speed	None	32 (32.0)	The lower ICG speed measured in the abdominal cavity (before creating the gastric tube) was associated with AL (4.23 ± 0.33 s vs. 2.93 ± 0.26 cm/s; $P = 0.003$)
Slooter et al. [24]	84 (Ivor Lewis, 67; McKeown, 17)	0.05 mg/kg, PIN or SPY	Before anastomosis	ICG visualization time	Change from end-to-side anastomosis to end-to-end	12 (14.3)	63 s in AL patients vs. 45 s in non-AL patients The cut off value was 98 s
Koyanagi et al. [25]	109 (McKeown)	1.25 mg, PDE	After creating the gastric tube	ICG flow speed	None	15 (13.8)	2.07 cm/s or less and SMA calcification predicted AL
Yamaguchi et al. [26]	129 (McKeown)	2.5 mg, PDE	After creating the gastric tube	ICG visualization time	Anastomosis was made at the point where visualization occurred within 90 s	4 (3.1)	AL occurred in 2.4% of patients with visualization within 60 s and in 33.3% with visualization within 60 to 90 s ($P = 0.09$)

AL anastomotic leakage, *HEMS* HyperEye Medical System (Mizuho Ikkogyo, Japan), *ICG* indocyanine green, *LV LIGHT VISION* (Shimadzu Corporation, Kyoto, Japan), *MIE* minimally invasive esophagectomy, *PDE* Photodynamic Eye (Hamamatsu Photonics K. K., Tokyo, Japan), *PIN* PINPOINT (Stryker, Kalamazoo, MI, USA), *PLE* pharyngo-laryngo-esophagectomy, *SMA* superior mesenteric artery, *SPY* Spy-phi fluorescence imaging system (Stryker, Kalamazoo, MI, USA), *VIS* VISERA ELITE II (Olympus, Tokyo, Japan)

zones: zone 1, dominated by the RGEA; zone 2, dominated by the LGEA; and zone 3, dominated by short gastric vessels. Zones 2 and 3 (when the right and left gastroepiploic connections were absent) were perfused by the intra-wall microvessels. The median time of ICG visualization from the root of the RGEA to the most cranial branch of the LGEA was 27 s. Interestingly, there was no difference in the time with and without connections between the RGEA and LGEA. However, two patients had gastric tube necrosis in zone 3, and their ICG visualization time was > 100 s. Dalton et al. [17] compared 20 patients with and without NIRF imaging with ICG. Despite resection of the non-perfused area at the tip of the gastric tube in six (30%) patients in the NIRF group, AL occurred in two patients (10.0%); however, AL did not occur in the group without NIRF.

Color NIRF system

Various doses of ICG and NIRF systems are presented in Table 1. The association between these factors and AL reduction is unclear. Various instruments have been developed, including black and white, color, and high-vision systems. In comparison to the black and white system, the color system has advantages because it can be viewed and compared simultaneously and synchronously with the actual surgical field, and can be used with NIRF imaging with ICG during navigation surgery. The HyperEye Medical System (HEMS) [28] is the first color charge-coupled device system for intraoperative NIRF used for vessel anastomosis during cardiovascular surgery [29], sentinel lymph node navigation during breast cancer surgery [30], and preserving the non-ischemic bowel area during surgery for non-occlusive mesenteric ischemia [31]. Kubota et al. [32] reported that the HEMS is useful for detecting the blood flow to the esophageal substitute (the gastric tube or colon) with microvascular anastomosis or sentinel lymph node detection during esophagectomy for five cases of esophageal cancer. Kitagawa et al. [15] reported that the HEMS is useful for visualizing the intragastric wall arterial network borders between the blood flow from the greater and lesser curvatures of the stomach before the gastric tube is created to preserve the arterial networks on the greater curvature during esophagectomy (line marking method). Initially, the HEMS color system was not high-definition; however, it was later converted to high-definition. Unlike other bedside high-definition color systems, the HEMS is portable, which is advantageous. Recently, the NIRF imaging system has been adopted for laparoscopy and robotic surgery, in addition to laparotomy. However, it is difficult to determine the cutoff value for AL development and to establish a protocol for NIRF with ICG to reduce AL. Because the results obtained with NIRF assessment are subjective, several instruments, procedures, ICG doses, and measurements have been

developed. To address this issue, it is necessary to perform a quantitative assessment of NIRF imaging. We focused on ICG fluorescence time or the flow speed at which ICG reaches the tip of the gastric tube, and reviewed potential objective quantitative methods and their impact on reducing anastomotic leakage.

Quantification of NIRF

One of the quantitative methods used to assess NIRF is measuring the ICG perfusion speed in the stomach. Some researchers have attempted to determine a simpler cutoff value for the ICG visualization time. Ohi et al. [18] classified the gastric tube area using ICG visualization time information as follows: rapid perfusion area, visualized within 15–40 s from ICG injection (40 s rule); slow perfusion area; 40–60 s; and low perfusion area, not visualized within 60 s. The low perfusion area has been recognized as unsafe for anastomosis. AL occurred in 1.7% of the ICG group and in 14.7% of the non-ICG group. Noma et al. [20] demonstrated the significant benefits of ICG for reducing the severity and incidence of AL in comparison to not using ICG by performing propensity score matching. They performed ICG visualization of the gastric tube and marked the point where visualization occurred at 20 s and 30 s after ICG injection. After pulling-up the gastric tube to the neck, they created anastomosis at the level visualized within 30 s (30 s rule). When it was difficult to perform anastomosis at the level where visualization occurred within 30 s, they performed further mobilization of the gastric tube or supercharge/drainage. In the Clavien-Dindo grading of the anastomotic leakage, the ICG group had a significantly lower incidence of anastomotic complications than the non-ICG group. Kumagai et al. [19] performed end-to-side anastomosis at the point where visualization of the root of the RGEA occurred within 90 s (90 s rule) based on their previous experience with gastric tube necrosis patients in which > 100 s were required before visualization of the gastric tube tip occurred [11]. In addition, they resected the tip of the gastric tube visualized after more than 60 s in 50% of the patients; only one of 70 patients developed AL. With Noma's 30 s rule, the aim is to perform anastomosis in the area that ICG could reach within 30 s. In contrast, with Kumagai's 90 s rule, the aim is to prophylactically excise the tip of the gastric tube to avoid necrosis at sites that ICG does not reach within 90 s. Slooter et al. [24] performed NIRF imaging before anastomosis (Of the 84 patients, 67 underwent Ivor Lewis esophagectomy and the remaining 17 underwent McKeown esophagectomy. Ivor Lewis esophagectomy patients had NIRF imaging performed in the trathorac cavity) and demonstrated that the ICG visualization time for patients with AL was longer than that for patients without AL. Yamaguchi et al. [26] conducted a prospective, multicenter study and demonstrated

that incidence of AL was 2.4% for anastomoses created at the location visualized within 60 s and 33.3% for anastomoses created at locations visualized within 60–90 s ($P=0.09$). Based on these results, the creation of anastomosis at a location visualized within 60 s would effectively reduce the risk of AL. These studies differed in their methods of measuring the ICG visualization time. Kumagai counted the time from the initial fluorescence of the RGEA to visualization of the gastric tube, it might be suitable for measuring the blood flow velocity from the RGEA to the gastric tube. While Noma and Kitagawa counted the time from ICG injection to gastric tube visualization. It may be easier, although it included the time from the injection of ICG to the RGEA. Kumagai and Noma placed the gastric tube in front of the chest wall so that the entire gastric tube could be observed, while Kitagawa observed the tip of the gastric tube after pulling up the gastric tube through the posterior mediastinal route. Although it was difficult to observe the root of the RGEA and the tip of the gastric tube in the neck at the same time, it was able to observe congestion or ischemia at the tip of the gastric tube that occurred after pulling up the gastric tube to the neck.

Koyanagi et al. [16] first reported the association between the ICG flow speed and AL by performing ICG visualization of the gastric tube before pulling up to the neck, measuring the distance between the antrum and the top of the visualized ICG in the gastric tube wall or RGEA, and calculating each ICG flow speed. Based on the ICG flow speed, they created two classifications: the simultaneous group, in which the ICG flow speed of the gastric tube wall was the same as that of the gastroepiploic artery, and the delayed group, which had a slower ICG flow speed. Among 40 patients, 7 experienced AL; all 7 patients were in the delayed group. Furthermore, they determined a cutoff value of 1.76 cm/s (measured in the anterior chest wall). Koyanagi et al. [25] also reported that calcification of the superior mesenteric artery was associated with slow ICG speed in the gastric wall and AL. AL occurred in 15 of their 109 patients. The ICG speed in the RGEA was not associated with AL; however, the ICG speed in the gastric tube of AL patients (1.91 cm/s) was significantly lower than that in the non-AL patients (2.78 cm/s) ($P<0.001$). According to the receiver-operating characteristic curve, the cutoff value was 2.07 cm/s. Using this cutoff value in the multivariate analysis, the ICG speed was found to be an independent risk factor for AL. These results indicate that the ICG speed reflects the arterial blood flow speed, which could influence the arterial vascular condition and lead to sclerosis or calcification.

Talavera-Urquijo et al. [23] performed ICG visualization of the stomach in 100 patients who underwent laparoscopic/thoracoscopic Ivor-Lewis esophagectomy before the gastric tube was created laparoscopically with a near-infrared light source. They injected ICG and measured the visualization

time from the root of the RGEA to the tip of the stomach, measured the length of the stomach, and calculated the ICG speed (cm/s). They calculated the ICG speed in the abdominal cavity (before creating the gastric tube) and at the thoracic stage (after creating the gastric tube). They demonstrated that the lower ICG speed measured in the abdominal cavity was associated with AL (4.23 ± 0.33 vs. 2.93 ± 0.26 cm/s; $P=0.003$); however, AL was not associated with the ICG speed in the thoracic cavity (3.02 ± 0.20 vs. 2.51 ± 0.33 cm/s; $P=0.187$). Kitagawa et al. [22] measured the time of ICG visualization from the RGEA to the top of the stomach before creation and after pulling the gastric tube to the neck through the posterior-mediastinal route. The association between the delayed ICG visualization time and AL was recognized after pulling up the gastric tube rather than before the creation of the gastric tube. Koyanagi et al. [25] reported no correlation between the congestion of the gastric tube and the blood flow speed or AL assessed before pulling was performed. These results suggest that when the anastomosis was made in the neck, compression and congestion of the gastric tube tip because of the narrow size of the superior thoracic aperture (between the trachea and vertebra at the level of the sternum notch) [33] might affect the ICG speed, resulting in poor blood supply at the site of anastomosis and AL.

Another quantitative method used to assess NIRF is a measurement of the patterns of time and fluorescence intensity. Yukaya et al. [14] reported three patterns of luminance change at two points of the gastric tube: the last branch of the RGEA, and the 3 cm proximal point. They used the HEMS to create a time-luminance curve and determined that 13 of 27 patients (48%) had a normal pattern, 9 (33%) had an inflow-delayed pattern, and 5 (19%) had an outflow-delayed pattern. Eight patients with the inflow-delayed pattern lacked a connection between the RGEA and LGEA. However, there was no association between the changes in luminance and AL. Ishige et al. [21] quantified the fluorescence intensity and created a time-fluorescence intensity curve at three timepoints: before the creation of the gastric tube, after the creation of the gastric tube, and after pulling up the gastric tube (just before anastomosis). The maximum increase in fluorescence intensity was decreased, and the time to reach the maximum increase in fluorescence intensity was significantly extended after the creation and pulling up of the gastric tube in comparison to before the creation of the gastric tube. However, this result was not associated with AL because no AL occurred during the study.

Based on these results, arterial blood perfusion and venous return at the site of anastomosis were influenced by the occurrence of AL. However, NIRF imaging cannot discriminate between the intensities of arterial perfusion or venous return and the congestion of the pulled-up gastric tube. NIRF with ICG can assess the patency of

venous anastomosis, and this procedure can be repeated. However, when vascular permeability is increased, such as when ischemia is present, albumin seeps into the tissue and remains; therefore, ICG bound to albumin also remains and fluorescence does not disappear completely, resulting in blurred images. Therefore, it is difficult to quantitatively evaluate the degree of venous congestion with NIRF using ICG. Additionally, the fluorescence intensity is affected by several factors, including the distance or angulation between the target tissue and the camera and the brightness of the operating room. Because of these limitations of NIRF imaging, another method is necessary.

New instrument that compensates for the limitations of NIRF

Recently, new modalities that compensate for the limitations of NIRF have been reported. Hyperspectral imaging can assess physiological parameters, including tissue oxygenation perfusion, organ hemoglobin, and the tissue water index, that are used to detect the demarcation line during liver resection [34] or the ischemic status of the gastric tube during esophagectomy [35]. This modality may improve the assessment of the risk of AL and provide additional physiological information that would not be obtained by NIRF alone [36]. Tsutsumi et al. [37] reported the usefulness of a multispectral imaging device—which can evaluate the tissue oxygen saturation and hemoglobin level—in the evaluation of 39 esophageal cancer patients. They used this device before the creation of esophagogastric anastomosis and classified the gastric tube into four types: good circulation, ischemic, congested, and mixed type (ischemic and congested), based on the values and patterns of O₂ saturation and hemoglobin levels. AL occurred in 2 of 39 patients with the mixed-type gastric tube with oxygen saturation < 85%. This method is non-invasive and allows for real-time quantitative navigation surgery. Jansen et al. [38] evaluated the intraoperative gastric tube microcirculation using sidestream darkfield microscopy for 22 patients (20 Ivor-Lewis procedures and 2 McKeown procedures). They demonstrated that perfusion was decreased and vasodilation occurred toward the fundus area rather than the watershed area. Three patients developed AL (one died). The average capillary velocity, microvascular flow index, perfusion vessel density, and proportion of perfused vessels were decreased in the watershed area in comparison to the fundus area. However, patients with AL experienced the opposite effect. They considered that venous congestion resulted in high pressure and slow flow in the capillaries and resulted in poor arterial perfusion. Milstein et al. [39] reported the effects of laser speckle contrast imaging, which has high temporal and spatial resolution and provides an index of the blood flow over large surface areas. They demonstrated that laser

speckle contrast imaging could measure the changes in tissue perfusion at different regions of interest in the gastric tube, especially around anastomosis of the LGEA and RGEA at three different time points (before creating the gastric tube, after creating the gastric tube, and in the reverse Trendelenburg position) and created an overview and mapping of the microvascular flow at different time points during surgery.

We are still concerned about what the response should be when ICG fluorescence is poor around the anastomotic site. Changing the method of anastomosis from end-to-side to end-to-end might be useful and easy [15]. Arterial reconstruction is an option for increasing the blood flow to the anastomotic site. However, the operative time would increase by approximately 40 min [40]. Saeki et al. [41] reported that super drainage reduced blood congestion and microcirculation of the colon conduit in 21 patients with esophageal cancer. Seven (33.3%) patients underwent arterial anastomosis because of arterial blood flow insufficiency: AL occurred in five (23.8%) patients and no patients had colon necrosis. Fujioka et al. [42] compared 20 patients with additional venous anastomosis and nine patients without venous anastomosis for esophageal or hypopharyngeal cancer. The venous anastomosis group had lower rates of AL (5.0 vs. 33.3%) and anastomotic strictures (0 vs. 66.7%). Kitagawa et al. [27] reported a case of super drainage at the neck using ICG fluorescence in esophageal cancer patients with right gastroepiploic vein injury at the root. NIRF was able to visualize the venous flow and AL could be avoided. Venous anastomosis may be a useful option for shortening the operative time in comparison to the arterial anastomosis and could reduce the risk of serious complications, such as conduit necrosis. Kono et al. reported that transient bloodletting of the short gastric vein improved the microcirculation of the gastric tube [43]; therefore, it may be possible to evaluate improvements in congestion by increasing the fluorescence intensity of the gastric tube by transient bloodletting.

Conclusion

NIRF imaging with ICG has been used during esophagectomy to avoid postoperative AL. It can visualize blood flow during real-time navigation surgery and provide information about the suitable gastric tube location for anastomosis. Arterial supply to the anastomotic site is essential. Furthermore, congestion caused by poor venous return is a risk factor for AL. NIRF is limited because of its subjective information and difficulty assessing venous return; however, these limitations are compensated by objective measurements of the blood flow speed, fluorescence intensity, and tissue oxygenation in the gastric tube.

Acknowledgements We would like to thank Editage (www.editage.com) for editing the English language of this article.

Declarations

Conflict of interest The authors declare no conflicts of interest in association with the present study.

Ethical approval Because this is a literature review article, IRB approval was not required; however, informed consent was obtained for the case presented in the figures.

References

- Akiyama H, Miyazono H, Tsurumaru M, Hashimoto C, Kawamura T. Use of the stomach as an esophageal substitute. *Ann Surg.* 1978;188:606–10.
- Takeuchi H, Miyata H, Gotoh M, Kitagawa Y, Baba H, Kimura W, et al. A risk model for esophagectomy using data of 5354 patients included in a Japanese nationwide web-based database. *Ann Surg.* 2014;260:259–66.
- Biere SS, van Berge Henegouwen MI, Maas KW, Bonavina L, Rosman C, Garcia JR, et al. Minimally invasive versus open oesophagectomy for patients with oesophageal cancer: a multicentre, open-label, randomised controlled trial. *Lancet.* 2012;379:1887–92.
- 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:e1369.
- Markar SR, Arya S, Karthikesalingam A, Hanna GB. Technical factors that affect anastomotic integrity following esophagectomy: systematic review and meta-analysis. *Ann Surg Oncol.* 2013;20:4274–81.
- Zehetner J, DeMeester SR, Alicuben ET, Oh DS, Lipham JC, Hagen JA, et al. Intraoperative assessment of perfusion of the gastric graft and correlation with anastomotic leaks after esophagectomy. *Ann Surg.* 2015;262:74–8.
- Ishizawa T, Saiura A, Kokudo N. Clinical application of indocyanine green-fluorescence imaging during hepatectomy. *Hepatobiliary Surg Nutr.* 2016;5:322–8.
- Karampinis I, Ronellenfitsch U, Mertens C, Gerken A, Hetjens S, Post S, et al. Indocyanine green tissue angiography affects anastomotic leakage after esophagectomy. A retrospective, case-control study. *Int J Surg.* 2017;48:210–4.
- Van Daele E, Van Nieuwenhove Y, Ceelen W, Vanhove C, Braeckman BP, Hoorens A, et al. Near-infrared fluorescence guided esophageal reconstructive surgery: a systematic review. *World J Gastrointest Oncol.* 2019;11:250–63.
- Shimada Y, Okumura T, Nagata T, Sawada S, Matsui K, Hori T, et al. Usefulness of blood supply visualization by indocyanine green fluorescence for reconstruction during esophagectomy. *Esophagus.* 2011;8:259–66.
- Kumagai Y, Ishiguro T, Haga N, Kuwabara K, Kawano T, Ishida H. Hemodynamics of the reconstructed gastric tube during esophagectomy: assessment of outcomes with indocyanine green fluorescence. *World J Surg.* 2014;38:138–43.
- Rino Y, Yukawa N, Sato T, Yamamoto N, Tamagawa H, Hasegawa S, et al. Visualization of blood supply route to the reconstructed stomach by indocyanine green fluorescence imaging during esophagectomy. *BMC Med Imaging.* 2014;14:18.
- Campbell C, Reames MK, Robinson M, Symanowski J, Salo JC. Conduit vascular evaluation is associated with reduction in anastomotic leak after esophagectomy. *J Gastrointest Surg.* 2015;19:806–12.
- 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. *J Am Coll Surg.* 2015;221:e37–42.
- Kitagawa H, Namikawa T, Munekage M, Akimori T, Kobayashi M, Hanazaki K. Visualization of the stomach's arterial networks during esophageal surgery using the HyperEye medical system. *Anticancer Res.* 2015;35:6201–5.
- 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:e4386.
- Dalton BGA, Ali AA, Crandall M, Awad ZT. Near infrared perfusion assessment of gastric conduit during minimally invasive Ivor Lewis esophagectomy. *Am J Surg.* 2018;216:524–7.
- Ohi M, Toiyama Y, Mohri Y, Saigusa S, Ichikawa T, Shimura T, et al. Prevalence of anastomotic leak and the impact of indocyanine green fluorescein imaging for evaluating blood flow in the gastric conduit following esophageal cancer surgery. *Esophagus.* 2017;14:351–9.
- 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. *Dis Esophagus.* 2018. <https://doi.org/10.1093/dote/doy052>.
- Noma K, Shirakawa Y, Kanaya N, Okada T, Maeda N, Ninomiya T, et al. Visualized evaluation of blood flow to the gastric conduit and complications in esophageal reconstruction. *J Am Coll Surg.* 2018;226:241–51.
- 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. *J Surg Res.* 2019;234:303–10.
- Kitagawa H, Namikawa T, Iwabu J, Yokota K, Uemura S, Munekage M, et al. Correlation between indocyanine green visualization time in the gastric tube and postoperative endoscopic assessment of the anastomosis after esophageal surgery. *Surg Today.* 2020;50:1375–82.
- Talavera-Urquijo E, Parise P, Palucci M, Olivari G, Turi S, Cossu A, et al. Perfusion speed of indocyanine green in the stomach before tubulization is an objective and useful parameter to evaluate gastric microcirculation during Ivor-Lewis esophagectomy. *Surg Endosc.* 2020;34:5649–59.
- 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. *Dis Esophagus.* 2021;34:doaa100. <https://doi.org/10.1093/dote/doaa100>.
- Koyanagi K, Ozawa S, Ninomiya Y, Oguma J, Kazuno A, Yatabe K, et al. Association between indocyanine green fluorescence blood flow speed in the gastric conduit wall and superior mesenteric artery calcification: predictive significance for anastomotic leakage after esophagectomy. *Esophagus.* 2021;18:248–57.
- Yamaguchi K, Kumagai Y, Saito K, Hoshino A, Tokairin Y, Kawada K, et al. The evaluation of the gastric tube blood flow by indocyanine green fluorescence angiography during esophagectomy: a multicenter prospective study. *Gen Thorac Cardiovasc Surg.* 2021;69:1118–24.
- Kitagawa H, Namikawa T, Iwabu J, Hanazaki K. Gastric tube reconstruction with superdrainage using indocyanine green fluorescence during esophagectomy. *In Vivo.* 2017;31:1019–21.

28. Handa T, Katare RG, Nishimori H, Wariishi S, Fukutomi T, Yamamoto M, et al. New device for intraoperative graft assessment: HyperEye charge-coupled device camera system. *Gen Thorac Cardiovasc Surg.* 2010;58:68–77.
29. Yamamoto M, Orihashi K, Nishimori H, Wariishi S, Fukutomi T, Kondo N, et al. Indocyanine green angiography for intra-operative assessment in vascular surgery. *Eur J Vasc Endovasc Surg.* 2012;43:426–32.
30. Hokimoto N, Sugimoto T, Namikawa T, Funakoshi T, Oki T, Ogawa M, et al. A novel color fluorescence navigation system for intraoperative transcutaneous lymphatic mapping and resection of sentinel lymph nodes in breast cancer: comparison with the combination of gamma probe scanning and visible dye methods. *Oncology.* 2018;94:99–106.
31. Nitori N, Deguchi T, Kubota K, Yoshida M, Kato A, Kojima M, et al. Successful treatment of non-occlusive mesenteric ischemia (NOMI) using the HyperEye Medical System™ for intraoperative visualization of the mesenteric and bowel circulation: report of a case. *Surg Today.* 2014;44:359–62.
32. Kubota K, Yoshida M, Kuroda J, Okada A, Ohta K, Kitajima M. Application of the HyperEye medical system for esophageal cancer surgery: a preliminary report. *Surg Today.* 2013;43:215–20.
33. Mine S, Watanabe M, Okamura A, Imamura Y, Kajiyama Y, Sano T. Superior thoracic aperture size is significantly associated with cervical anastomotic leakage after esophagectomy. *World J Surg.* 2017;41:2598–604.
34. Sucher R, Athanasios A, Köhler H, Wagner T, Brunotte M, Lederer A, et al. Hyperspectral Imaging (his) in anatomic left liver resection. *Int J Surg Case Rep.* 2019;62:108–11.
35. Köhler H, Jansen-Winkel B, Maktabi M, Barberio M, Takoh J, Holfert N, et al. Evaluation of hyperspectral imaging (HSI) for the measurement of ischemic conditioning effects of the gastric conduit during esophagectomy. *Surg Endosc.* 2019;33:3775–82.
36. Barberio M, Felli E, Seyller E, Longo F, Chand M, Gockel I, et al. Quantitative fluorescence angiography versus hyperspectral imaging to assess bowel ischemia: a comparative study in enhanced reality. *Surgery.* 2020;168:178–84.
37. Tsutsumi R, Ikeda T, Nagahara H, Saeki H, Nakashima Y, Oki E, et al. Efficacy of novel multispectral imaging device to determine anastomosis for esophagogastrostomy. *J Surg Res.* 2019;242:11–22.
38. Jansen SM, de Bruin DM, van Berge Henegouwen MI, Bloemen PR, Strackee SD, Veelo DP, et al. Quantitative change of perfusion in gastric tube reconstruction by sidestream dark field microscopy (SDF) after esophagectomy, a prospective in-vivo cohort study. *Eur J Surg Oncol.* 2021;47:1034–41.
39. Milstein DMJ, Ince C, Gisbertz SS, Boateng KB, Geerts BF, Hollmann MW, et al. Laser speckle contrast imaging identifies ischemic areas on gastric tube reconstructions following esophagectomy. *Medicine (Baltimore).* 2016;95:e3875.
40. Yoshimi F, Asato Y, Ikeda S, Okamoto K, Komuro Y, Imura J, et al. Using the supercharge technique to additionally revascularize the gastric tube after a subtotal esophagectomy for esophageal cancer. *Am J Surg.* 2006;191:284–7.
41. Saeki H, Morita M, Harada N, Egashira A, Oki E, Uchiyama H, et al. Esophageal replacement by colon interposition with microvascular surgery for patients with thoracic esophageal cancer: the utility of superdrainage. *Dis Esophagus.* 2013;26:50–6.
42. Fujioka M, Hayashida K, Fukui K, Ishiyama S, Saijo H, Taniguchi K. Venous superdrained gastric tube pull-up procedure for hypopharyngeal and cervical esophageal reconstruction reduces postoperative anastomotic leakage and stricture. *Dis Esophagus.* 2017;30:1–6.
43. Kono K, Sugai H, Omata H, Fujii H. Transient bloodletting of the short gastric vein in the reconstructed gastric tube improves gastric microcirculation during esophagectomy. *World J Surg.* 2007;31:780–4.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.