Usefulness of blood supply visualization by indocyanine green fluorescence for reconstruction during esophagectomy

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Abstract
Background Adequate blood supply for the reconstructed organ is important for safe esophagogastric anastomosis during esophagectomy. Recently, indocyanine green (ICG) has been used for visualization of the blood supply when anastomosis is performed in vascular surgery. To visualize the blood supply for reconstruction, we employed ICG fluorescence during esophagectomy.

Methods From August 2008, 40 patients received cervical or thoracic esophagectomy. They consisted of 33 patients having esophagectomy for thoracic esophageal cancer, 3 being treated for cervical esophageal cancer, and 4 with double cancer of the thoracic and cervical regions. Before and after pulling up the reconstructed organ, 2.5 mg of ICG was injected as a bolus. Then ICG fluorescence was detected by a camera and recorded.

Results ICG fluorescence was easily detected in all patients at 1 min after injection. The vascular network was well visualized in the gastric wall, colonic grafts, and free jejunal grafts. In five patients, we also performed anastomosis between the short gastric vein and the external cervical vein or superficial cervical vein. The intraoperative and postoperative course of all patients was uneventful apart from three anastomotic leakages.

Conclusions ICG fluorescence can be employed to evaluate the blood supply to reconstructed organs and can be useful in selecting the patients who do not need additional vessel anastomosis. However, anastomotic leakage was not reduced, so the microcirculation detected by ICG fluorescence did not necessarily provide appropriate blood supply for a viable anastomosis.

Keywords Anastomotic leakage · Vessel anastomosis · Microcirculation

Introduction
Reconstruction of the gastrointestinal tract is still a major issue in patients with gastrointestinal malignancies. In esophageal cancer surgery, anastomotic leakage is one of the important causes of death [1], and the rate of anastomotic leakage ranges from 6.2 to 27% [2–8]. Among several causes of anastomotic leakage, ensuring an adequate blood supply is the most important point for performing anastomosis safely after esophagectomy. In 1986, we introduced the EEA stapler for esophago-gastrostomy after resection of part of the sternum following subtotal esophagectomy [9], and the average anastomotic leakage rates from 1994 to 2008 were 4.8% (20/416).

Although all of these patients recovered, a method for effective evaluation of the blood supply to the reconstructed organs would be useful.

To assess the blood supply in reconstructed organs, laser Doppler flowmetry has been used, but sufficiently reliable measurements are not obtained [10, 11]. Indocyanine green (ICG) has long been used for the evaluation of liver function. Recently, ICG fluorescence has also been used for the detection of sentinel lymph
nodes in breast cancer surgery, gastrectomy, or colorectal cancer surgery, and for visualization of the blood supply after anastomosis during vascular surgery [12–17]. To visualize the blood supply of reconstructed organs during esophagectomy, we started to use ICG fluorescence in July 2008. This study was done to evaluate the efficacy of ICG fluorescence based on our experience so far.

Methods

Patient characteristics

The patients consisted of 33 having esophagectomy for thoracic esophageal cancer, 3 who were treated for cervical esophageal cancer, and 4 with double cancer of the thoracic and cervical regions. (Table 1). There were 32 men and 8 women with an average age of 66 years (range 49–81 years). Ten patients received preoperative chemotherapy, one patient received preoperative chemo-radiotherapy, and two patients had received radiotherapy several years before surgery.

| Table 1 Characteristics of the patients |
|----------------------------------------|
| Number                                |
| Age 66 (49–81)                         |
| Sex                                    |
| Male 32                                |
| Female 8                               |
| Tumor location                         |
| PhMt 2                                 |
| CeMt 2                                 |
| Ce 3                                   |
| Ut 2                                   |
| Mt 19                                  |
| Lt 12                                  |
| TNM stagea                             |
| 1 10                                   |
| 2a 5                                   |
| 2b 5                                   |
| 3 18                                   |
| 4 2                                    |
| Preoperative treatment                 |
| Chemotherapy 10                        |
| Chemoradiotherapy 1                    |
| Radiotherapy 2                         |
| None 27                                |

Ph pharynx, Ce cervical esophagus, Ut upper thoracic esophagus, Mt middle thoracic esophagus, Lt lower thoracic esophagus, Ae abdominal esophagus

Results

Twenty-three patients underwent thoracoscopic-assisted right thoracotomy in the left lateral position, 1 patient...
received left thoracotomy because of a right aortic arch. 14 patients had esophagectomy in the prone position, and 2 patients received cervical esophagectomy in the supine position. With regard to the method used for reconstruction of the esophagus, a gastric tube was employed in 36 patients, a gastric tube plus free jejunal graft in 1 patient, a free jejunal graft in 2 patients, and an ileo-colonic graft in 1 patient. In 2 patients, reconstruction was done via the posterior mediastinal route, while 5 patients were treated by the subcutaneous route, and the retrosternal route was used in 31 patients (Table 2).

Fluorescence of the reconstructed esophagus was easily detected in all patients at 1 min after ICG injection. Both arteries and veins were effectively visualized (Fig. 2a, b). Furthermore, microvessels of the gastric wall were well visualized about 2 min after ICG injection (Fig. 3a, b). The blood supply of the free jejunal grafts was also well visualized (Fig. 4a, b). In five patients, an anastomosis was added between the short gastric vein and vessels in the neck based on the ICG fluorescence findings. Subsequently, one patient required re-anastomosis because poor circulation was revealed by ICG fluorescence (Fig. 5a, b). We could also effectively visualize blood flow in the colonic graft (Fig. 6a, b).

During this study we evaluated ICG fluorescence using the detection of microcirculation; however, retrospective re-evaluation of the fluorescence status after the period of this study revealed that small vessels were observed in the stump of the reconstructive organ’s wall in 22 cases, (Table 3).

There were no severe complications in this series, but two minor and one major anastomotic leakage. In all of the leakage patients, the subcutaneous route was used for reconstruction. Retrospective analysis revealed that there was no anastomotic leakage in the cases where we could observe small vessels in the reconstructive organ’s wall. On the other hand, in 15 out of 18 cases in which we could not observe small vessels in the organ’s wall, anastomotic leakage did not occur. (Table 3).

**Discussion**

Although surgical techniques have improved in recent decades and the incidence of anastomotic leakage has decreased to less than 10%, leakage is still one of the factors that influences the postoperative course and

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**Table 2** Summary of the operative procedures

| Reconstruction method      | Number |
|---------------------------|--------|
| Gastric tube              | 36     |
| Free jejunal graft + gastric tube | 1     |
| Free jejunal graft         | 2     |
| Ileo-colonic graft         | 1     |
| Reconstruction route       |        |
| Retrosternal               | 31     |
| Posterior mediastinal      | 2     |
| Subcutaneous               | 5     |
| Cervical                   | 2     |
| Additional vascular anastomosis |  |
| Yes                        | 5     |
| No                         | 35    |
| Surgical position          |        |
| Lateral                    | 24    |
| Prone                      | 14    |
| Supine                     | 2     |

**Fig. 1** Near-infrared camera system

**Fig. 2** ICG fluorescence image of a gastric tube before anastomosis. Blood flow in the arteries and veins is well visualized. a The gastric tube. b ICG fluorescence image. A closed arrow indicates an artery and an open arrow indicates a vein.
survival after en bloc resection of esophageal cancer [19]. Thus, in order to improve the outcome, reducing the occurrence of anastomotic leakage is a major issue in the field of esophageal surgery. The most important predictors of anastomotic leakage are ischemia of the gastric conduit and a low blood oxygen level [20]. Several reports have also suggested that tissue blood flow is worse during the intra-operative and postoperative periods among patients with leakage than those without leakage [10, 11]. Epidural anesthesia may improve blood flow to the gastric tube and reduce the occurrence of anastomotic leakage [20].

To assess the blood supply of reconstructed organs, several studies have employed laser Doppler flowmetry [10, 11, 21]. Recent progress has led to intraoperative fluorescent imaging (IFI) using the SPY system, which allows the evaluation of coronary artery bypass graft patency intraoperatively based on the detection of indocyanine green (ICG) fluorescence [15, 22–24].

In the gastrointestinal field, ICG fluorescence has already been used for navigation surgery and for...
| Patient no. | Age/ gender | Stage | Tumor location | Reconstruction method | Pull-up route | Method of thoracotomy | Preoperative treatment | Associated conditions | Vascular anastomosis | Anastomotic leakage | ICG (microcirculation in the stump) | ICG (small vessel in the stump) |
|------------|-------------|-------|----------------|----------------------|--------------|----------------------|-----------------------|----------------------|-------------------|----------------|-----------------------------|-----------------------------|
| 1          | 59/M        | T3N0M0 stage 2a | Mt | G | R | L | – | – | – | – | – | Observed | Observed |
| 2          | 59/M        | T3N1M0 stage 3 | Mt | G | P | L | FP × 2 | Funnel chest | – | – | – | Observed | Observed |
| 3          | 66/M        | T3N0M0 stage 2a | Lt | G | R | L | – | Obesity (BMI 30) | – | – | – | Observed | Observed |
| 4          | 70/M        | T1N0M0 stage 1 | PhMt | G | R | L | – | Pharyngeal cancer, DM | – | – | – | Observed | Observed |
| 5          | 62/M        | T1N1M0 stage 2b | Lt | G | R | L | – | Renal failure | + | – | – | Observed | Not observed |
| 6          | 70/M        | T3N1M0 stage 3 | Mt | G | R | L | FP × 2 | – | – | – | Observed | Not observed |
| 7          | 76/F        | T3N1M0 stage 3 | Mt | G | R | L | FP + 40 Gy | – | – | – | Observed | Not observed |
| 8          | 58/M        | T3N1M0 stage 3 | Lt | G | R | L | – | – | – | – | – | Observed | Not observed |
| 9          | 70/M        | T3N1M0 stage 3 | Lt | G | S | L | – | Colon cancer | + | + | + | Observed | Not observed |
| 10         | 78/M        | T3N1M0 stage 3 | Mt | G | R | L | – | – | – | – | – | Observed | Not observed |
| 11         | 56/F        | T4N1M0 stage 3 | Mt | G | R | L | – | – | – | – | – | Observed | Observed |
| 12         | 76/M        | T1N0M0 stage 1 | Ce | J | – | – | 60 Gy (9 years before) | – | + | + | Observed | Observed |
| 13         | 56/F        | T2N0M0 stage 2a | Ce | J | – | – | FP | – | + | – | Observed | Observed |
| 14         | 68/M        | T1N1M0 stage 2b | Mt | G | R | L | FP | – | – | – | Observed | Observed |
| 15         | 62/M        | T1N1M0 stage 2b | PhMt | G + J | R | L | FP | Pharyngeal cancer | + | – | – | Observed | Observed |
| 16         | 71/M        | T2N0M0 stage 2a | Mt | G | S | R | – | Right aortic arch | – | + | – | Observed | Not observed |
| 17         | 81/M        | T3N1M0 stage 3 | Lt | G | R | L | – | – | – | – | – | Observed | Observed |
| 18         | 67/M        | T4N1M0 stage 3 | CeMt | G | R | L | – | – | – | + | – | Observed | Not observed |
| 19         | 54/M        | T1N0M0 stage 1 | Mt | G | R | L | – | – | – | – | – | Observed | Observed |
| 20         | 67/M        | T1N0M0 stage 1 | Mt | C | S | L | – | – | – | – | – | Observed | Observed |
| 21         | 76/M        | T1N1M0 stage 2b | Mt | G | R | L | – | – | – | – | – | Observed | Observed |
| 22         | 79/M        | T2N0M0 stage 2a | Mt | G | R | L | – | Lung cancer | – | – | – | Observed | Not observed |
| 23         | 61/F        | T1N0M0 stage 1 | Mt | G | R | L | – | – | – | – | – | Observed | Observed |
| 24         | 60/M        | T1N1M1 stage 4 | CeMt | G | R | L | 60 Gy | – | + | – | Observed | Not observed |
| 25         | 67/M        | T1N0M0 stage 1 | Ce | G | P | L | – | – | – | + | – | Observed | Not observed |
| 26         | 64/M        | T2N1M0 stage 2b | AeLt | G | R | L | – | – | – | – | – | Observed | Not observed |
| 27         | 58/M        | T3N1M0 stage 3 | Lt | G | R | P | – | – | – | – | – | Observed | Observed |
| 28         | 74/M        | T1N0M0 stage 1 | Mt | G | R | P | – | – | – | – | – | Observed | Not observed |
| 29         | 68/F        | T1N0M0 stage 1 | AeLt | G | R | P | – | – | – | – | – | Observed | Observed |
intraoperative detection of hepatocellular carcinoma [18, 25, 26]. In addition, Sekijima et al. [27] introduced ICG fluorescence for organ transplantation. However, detection of the microcirculation in gastrointestinal organs has not been studied much so far [28, 29].

Our results revealed that ICG fluorescence could detect organ blood flow before reconstruction and assist in evaluating the appropriate anastomatic sites. However, the incidence of anastomatic leakage was not reduced. Thus, the microvessels detected by ICG fluorescence did not always provide enough blood for a viable anastomosis. On the other hand, retrospective re-analysis revealed that there was no anastomatic leakage in cases in which we could observe small vessels in the stump of the reconstructive organ’s wall. Thus, observation of microcirculation and small vessels indicates an appropriate organ for anastomosis. However, we could observe microcirculation and small vessels in only about half of our series.

Intraoperative prostaglandin E1 treatment is also not effective for preventing anastomotic insufficiency [10]. Furthermore, gastric perfusion of less than 70% can predict the occurrence of anastomotic stricture but does not predict leakage [21]. Factors other than perfusion may also influence the process of anastomotic healing [21]. Thus, not only the blood supply, but also factors such as the route of anastomosis (retrosternal vs. posterior mediastinal or subcutaneous), the type of gastric tube (narrow or wide), the method of anastomosis (hand sewing, circular stapler, or triangulating stapling) and the tension at the anastomotic site may influence the healing of an anastomosis [10, 11, 20, 30–32].

In our series, the subcutaneous route was used in five patients because of the condition of the gastric tube or various anatomical problems, and three of these five patients had leakage. Thus, the need to employ the subcutaneous route may be one of the risk factors for anastomotic leakage [7].

With regard to additional microvascular anastomosis, a significant increase of tissue blood flow was observed after additional venous anastomosis (mean 19%) and also after combined arterial and venous anastomosis (mean 43%) [33]. Thus, additional anastomosis between the short gastric vessels and vessels in the neck resulted in the reduction of anastomotic leakage [34]. We had a good outcome in the present series, so ICG fluorescence may provide useful information to the surgeon about whether patients require additional microvascular anastomosis or not.

Finally, imaging with the photodynamic eye has the following benefits. First, ICG is almost completely washed out within 20 min after injection, so ICG fluorescence can be assessed several times during surgery. Second, we can detect the microcirculation of a target organ as well as the adjacent organs. Third, we can select the patients who do not need additional vessel anastomosis.
In conclusion, imaging of ICG fluorescence can be used to evaluate the blood supply of reconstructed organs and can be useful in selecting the patients who do not need additional vessel anastomosis. However, the microcirculation detected by ICG fluorescence does not necessarily provide enough blood flow to maintain a viable anastomosis. In order to establish more detailed and appropriate ICG fluorescence criteria, an additional and larger study is needed.

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