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Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jped surg

Operative Technique

Novel thoracoscopic navigation surgery for neonatal chylothorax using indocyanine-green fluorescent lymphography ^{☆,☆☆,★}

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ARTICLE INFO

Article history:

Received 5 October 2017

Received in revised form 31 December 2017

Accepted 24 January 2018

Key words:

Indocyanine green fluorescent lymphography

Near-infrared fluorescence imaging

Postoperative chylothorax

Thoracoscopic navigation surgery

Neonatal

Esophageal atresia

ABSTRACT

Background: Postoperative chylothorax after surgery for esophageal atresia/tracheoesophageal fistula (TEF) is a rare but serious complication, especially in neonates. This study aimed to identify the thoracic duct and ligate chylous leakage sites, using thoracoscopic navigation of an indocyanine-green (ICG)-based near-infrared (NIR) fluorescence imaging system.

Methods: From November 2014 to April 2017, thoracoscopic intraoperative ICG-NIR imaging was performed in 10 newborns (11 surgeries) with first TEF operation or with persistent postoperative chylothorax after TEF operation. NIR imaging was performed 1 h after an inter-toe injection of ICG. Thoracoscopic ligations against the NIR-detected leakage sites were performed with sutures.

Results: The thoracic duct or lymphatic leakage was directly visualized in each patient. In 8 surgeries with first thoracoscopic TEF operation, one case had suspected minor chylous leakage without postoperative chylothorax. Another case with no chylous leakage at the first operation resulted in chylothorax at postoperative day 11. In three neonates with postoperative chylothorax, leakage points were detected near the ablation site of the azygos vein during the first operation. These points were properly ligated, and postoperative chylous leakage ceased with no adverse events.

Conclusions: Thoracoscopic ICG-NIR imaging encourages the repair of refractory chylothorax and seems reliable.

Level of Evidence: IV

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Postoperative chylothorax is a rare but serious complication after surgery for esophageal atresia/tracheoesophageal fistula (TEF). It occurs after injury to the thoracic duct or in association with lymphatic or congenital anomalies [1]. Chylothorax is associated with a high morbidity and mortality in children and adults with high chyle leakage [2,3], and seems to be especially more severe in neonates.

Multidisciplinary therapies are often attempted to treat this condition including cessation of enteral feeding, total parental nutrition (TPN), and somatostatin analog administration [4–6], but they do not

Abbreviations: TEF, tracheoesophageal fistula; ICG, Indocyanine green; NIR, near-infrared; POD, postoperative day.

☆ **Acknowledgments:** None.

☆☆ **Conflicts of interest:** None

★ **Funding:** This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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<https://doi.org/10.1016/j.jpedsurg.2018.01.019>

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have a high success rate [2]. For refractory cases, surgical interventions are required such as ligation of the thoracic duct [7,8], pleurodesis with fibrin glue to putative sites [9–11], and pleuroperitoneal shunt [12,13]. Even with lymphoscintigraphy [14], detection of the exact site of chylous leakage or the thoracic duct is challenging, in reoperation and in neonates or infants. If intraoperative imaging guidance exists, the surgical management of chylothorax would be a promising alternative treatment, even in neonates.

Indocyanine green (ICG) fluorescence imaging is a safe and minimally invasive technique. ICG is commonly available and is a very safe compound that has been widely used for procedures such as ICG liver and cardiac function testing. ICG primarily binds to albumin, which drains into the lymphatic vessels. Currently, ICG lymphography is often used in sentinel lymph node biopsy and for navigation in many cancers (e.g.: breast, stomach, colon, melanoma, and so on [15]). Recently, ICG, used as a fluorophore, was introduced for the visualization in lymphography with a near-infrared (NIR) camera system [16]. Moreover, in some studies, detection of the chylous leakage site was attempted to repair a postoperative chylothorax after esophagectomy

[17,18]. Intraoperative real-time NIR imaging has been used in many areas of surgery to visualize, noninvasively, the surgical site anatomy and tissue function with a high spatiotemporal resolution [19–21].

We hypothesized that intraoperative NIR imaging might aid the assessment of the thoracic duct and detection of chylous leakage sites, even in neonates. If the NIR-ICG imaging technique is effective, surgical treatment for chylothorax would be possible. Thus, we performed thoracoscopic surgery with ICG-NIR imaging to detect sites of thoracic duct injury to treat postoperative chylothorax.

1. Methods

1.1. Study design

From November 2014 to April 2017, we performed thoracoscopic intraoperative NIR imaging for 10 neonates (4 female and 6 male, 11 surgeries), and retrospectively analyzed the data. Before this study was started, all protocols were approved by the ethics review board of Nagoya University Graduate School of Medicine (approval number: 2017-0098), and informed consent was obtained from patients and guardians regarding data usage for this report. All patients during this period who underwent this surgery were assigned to this study, and there were no exclusion criteria.

1.2. Thoracoscopic detection and repair of the chylothorax using ICG-NIR imaging

Thoracoscopic TEF surgery and thoracoscopic repair of chylothorax were performed using the same three ports (5 mm, 1 port; 3 mm, 2 ports) and a 5-mm 30° angled rigid scope under a 4–8 mmHg pneumothorax, according to previously reported techniques [22,23]. The thoracoscopic imaging system used was the IMAGE 1 SPIES Camera system (Karl Storz GmbH & CO. KG, Tuttlingen, Germany), and the D-Light P system (Karl Storz) was the white light and xenon-based NIR light source. The surgeons could easily switch, using a foot pedal, between the white and NIR lights. When intraoperative NIR imaging was performed, we used an ICG-specific filter-mounted Hopkins® rigid scope of 5.8 mm diameter (8710AGA, Karl Storz) or a 10-mm Hopkins® rigid scope (26003BGA, Karl Storz) having a camera port with a range of 5 to 12 mm. In these systems, emitted light at a wavelength of 760 nm was used and the scope filtered out light below 830 nm by the excitation of light at a wavelength of 830 nm. NIR imaging, which revealed the thoracic duct and chylous leakage, was performed 1 h after the inter-toe (between the first and second toes) injection of 0.025 mg of ICG (Diagnogreen®, Daiichi-Sankyo Pharma, Tokyo, Japan). During the reoperation, the NIR-detected leakage sites, including the detected thoracic duct and its branches or small lymphatic vessels, were sutured using 5-0 absorbable monofilament under white-light thoracoscopy.

2. Results

2.1. Patient cohort

We performed 25 cases of thoracoscopic TEF surgeries during the study period. In 8 of the 11 surgeries (median age at surgery: 2.0 days (range, 1–10 days), median weight: 2616 g (range, 2014–3396 g)), ICG-NIR imaging was performed to detect the thoracic duct, and not the lymphatic leakage, at the first thoracoscopic tracheoesophageal fistula (TEF) repair in operator's preference. For the other 3 surgeries (median age at surgery: 18 days (range, 13–25 days), median weight: 2676 g (range, 1710–2838 g)), ICG-NIR imaging was performed to detect the chylous leakage points, as postoperative chylothorax after thoracoscopic surgery for TEF was noted. These patients had prolonged high-volume lymphatic chylous leakage (≥ 100 ml/kg/day) or severe coagulation deficiency owing to massive loss of serum proteins. Multidisciplinary conservative treatment was administered, including the cessation of enteral feeding, total parental nutrition, intravenous coagulation factor XIII administration [24], and subcutaneous/intravenous somatostatin analog administration [4–6], which was increased in a stepwise fashion to a maximum dose of 40 μ g/kg/day. However, the conservative treatment was ineffective. Thus, these 3 patients underwent thoracoscopic ligation of the chylous leakage sites in a repeat surgery.

2.2. Confirmation of the thoracic lymph duct at the first thoracoscopic TEF repair

In 8 surgeries, thoracoscopic ICG-NIR imaging was performed at the first thoracoscopic TEF repair. Only one case had suspected minor chylous leakage, and the chylous leakage point was sutured. This case did not have postoperative chylothorax. There was no leakage at the end of the procedure in any of the cases. In the other 7 cases, chylous leakage was not detected. In one of the 7 cases (Case 3), we could not detect the chylous leakage point during the first operation. In this case, chylous leakage of 100 ml per day was noted at postoperative day (POD) 11. A small laceration might have occurred at the first operation, which expanded over time. We confirmed an uninterrupted or uninjured thoracic duct in 3 cases (Fig. 1). The detected thoracic duct passed over the azygos vein, near the point at which the vein joined the superior vena cava.

2.3. Postoperative refractory chylothorax cases were treated by ligating the injured thoracic duct using ICG-NIR imaging

In the other 3 cases, thoracoscopic NIR imaging was performed to detect the presence of injury in the thoracic duct. Chylous leakage ranging from 100 to 500 ml per day was noted from POD 2 to 11 (Table 1). Owing to the nonresponse to multidisciplinary conservative therapies, from POD 13 to 25, we attempted to ligate the chylous leakage points with NIR imaging. In each case, thoracoscopic “white light” observation detected only fluid collection. However, thoracoscopic NIR imaging



Fig. 1. Intraoperative near-infrared (NIR) image of the tracheoesophagus and thoracic duct (white arrows) with NIR fluorescence, from the upper diaphragm (left in image) to the azygos vein (white dashed arrow) during an esophageal elongation procedure. The gray dashed arrows show the mobilized distal esophagus. This image was generated from the original video.

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