Safe management of laparoscopic endoscopic cooperative surgery for superficial non-ampullary duodenal epithelial tumors

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Background and study aims
Endoscopic submucosal dissection (ESD) for duodenal tumors results in a high delayed perforation rate due to the thinness of the duodenal wall. In most cases with perforation after duodenal ESD, additional surgery is needed due to severe peritonitis. A newly developed procedure, laparoscopic endoscopic cooperative surgery for duodenal tumors (D-LECS), may help to avoid perforation after ESD. In our institution, patients with superficial non-ampullary duodenal epithelial tumors (SNADET) smaller than 50 mm which could not have en-bloc resection by endoscopic mucosal resection were treated with D-LECS. After a laparoscopic exposure of anterior duodenal wall of second portion, ESD was performed. Laparoscopic suturing from the serosal side of ESD site was performed for reinforcement. There were neither postoperative leakage nor other complications. Therefore, D-LECS can be performed safely and prevent perforation after ESD for SNADET. D-LECS could be selected as a treatment for SNADET which can be cured by ESD.

Introduction
Despite the fact that duodenal cancer is still very rare, recent improvements in endoscopy using high magnification for observing mucosal patterns and network vascular patterns have contributed to the early detection and accurate diagnosis of tumor invasion [1]. Because lymphadenectomy is not required for duodenal intramucosal carcinoma given the very low rate of lymph node metastasis [2,3], endoscopic treatment is recommended to avoid invasive procedures. Endoscopic submucosal dissection (ESD) is reported to have a higher en-bloc resection rate than endoscopic mucosal resection (EMR) [4,5]. However, when ESD is performed in the duodenum, there is a high risk of complications such as perforation and bleeding (6–50% and 0–7%, respectively) due to the thinness of the duodenal wall and technical difficulties in narrow duodenal lumen [6,7]. Further, duodenal delayed perforation was reported in some cases even after ESD without intraoperative perforation [6,8].

Recently, laparoscopic endoscopic cooperative surgery for duodenal tumors (D-LECS) has been developed as a new procedure which can prevent perforation by reinforcing the ESD site. However, details of the operative procedure and tips for performing D-LECS remain unclear. Herein, we report the procedural methods for performing D-LECS, which resulted in no postoperative perforation.
Patients and methods

Patients

Ten patients from September 2014 to November 2016 who had a duodenal tumor and were suitable for treatment by ESD were retrospectively enrolled in the study. All patients underwent diagnostic endoscopy with biopsy. Our therapeutic indications for D-LECS are shown in Table 1. EMR is applied to SNADET when it is smaller than 10 mm. All study participants provided informed consent, and the study design was approved by the ethics review board at Kobe University Hospital and conformed to the provisions of the 1995 Declaration of Helsinki.

Operative technique

Patient positioning

Under general anesthesia, the operation was started with the patient in the left lower half lateral decubitus position. When the surgeon performed the laparoscopic procedure, the operating table was rotated to the right side so that the patient was in a supine position. When the endoscopist performed the ESD, the operating table was rotated to the left side so the patient was in the left lateral decubitus position (Fig. 1a).

Laparoscopic Kocher maneuver

The operator stood on the patient’s left side. The trocars were placed as shown in Fig. 1b. The omentum was dissected from the right lateral side up to the front of the duodenum and the mesocolon was removed from the epigastric tissue. The procedure continued with dissection of the right hepatocolic ligament, with ultrasonic coagulating shears (SonoSurg, Olympus Medical System, Tokyo, Japan) being used to mobilize the right colic flexure. When the anterior wall of the duodenal second portion was well exposed, the laparoscopic Kocher maneuver was stopped to prevent difficulties with ESD due to loss of duodenal fixation on the retroperitoneum (Video 1). After the ESD, the surgeon moved to the right side of the patient and completed the Kocher maneuver beyond the vena cava until the ESD site was well exposed.

Endoscopic submucosal dissection

First, endoscopic markings were made on the mucosa surrounding the lesion after spraying indigo carmine using a forward-viewing endoscope (for example, GIF-Q260J; Olympus Medical System Co., Tokyo, Japan) and a Flush knife BT 1.5 mm (Fujifilm Medical Co., Tokyo, Japan). Sodium hyaluronate solution (0.4%) (MucoUp; Seikagaku Corp., Tokyo, Japan) was injected into the submucosal layer before the initial mucosal incision. After circumferential mucosal incision using a Flush knife BT 1.5 mm, a clip with thread was placed at the oral edge of the target lesion. Adequate traction was obtained by pulling the thread gently. Clip traction and frequent additional injections using the knife were effective and safe during submucosal dissection. A Flush knife BT was used with a short ST hood (DH-28GR; Fujifilm Medical Co., Tokyo, Japan) for dissection. In some cases, a Clutch Cutter (Fujifilm Medical Co., Tokyo, Japan) was also used in order to avoid perforation (Video 2).

Laparoscopic suturing

The ESD site was easily identified from the serosal side due to white coloration caused by thermal denaturation (Fig. 2a). In addition, laparoscopic identification of the ESD site from the serosal side was possible in all patients by observing the trans-
mitted light of the endoscope (Fig. 2b). Two-layer suturing was carried out laparoscopically even when no perforation was suspected. Laparoscopic suturing of the duodenal wall was carried out with a manual intracorporeal knotted suture using a 3–0 vicryl suture (Ethicon GMBH, Norderstedt, Germany) in the full thickness layer. After the suturing, the endoscopic observation was performed to confirm the closure of ESD site (Fig. 2c). If inadequate, additional suturing with full-thickness layer was performed. Then, running suture using a 3–0 PDS™ (Ethicon) with Lapra-Ty™ (Ethicon) clips in the seromuscular layer was performed. After the suturing of the duodenal wall, the re-endoscopic observation was performed to confirm a patent lumen, any leakage and bleeding (Fig. 2d, Video 3).

Outcomes

Data on postoperative leakage rate within 1 month after surgery, laparotomy conversion rate, surgery-related death and any postoperative complications more than grade II according to the Clavien-Dindo classification of surgical complications [9] were collected to assess the safety of D-LECS.

Results

Patient characteristics and surgical outcomes are shown in Table 2. The median age was 63.5 years, and there were 7 male patients. All tumors were located in the second portion and 3 were located above ampulla and 7 were located below ampulla. Two patients were preoperatively diagnosed with cancer. The median laparoscopy procedure time was 120.5 min-
utes and the ESD procedure time was 99.5 minutes. Four patients had a perforation during ESD; however, no patients had postoperative leakage including delayed perforation. No patients had any other complications and there were no surgery-related deaths. The median size of resected specimen was 37 mm. The median times of starting food intake and discharge from hospital were the fourth and eleventh postoperative days, respectively. All dissected specimens were histologically found to be cancer with negative margins. All patients were able to maintain their food intake without any restriction.

Discussion
Simple laparoscopic resection may be a less invasive alternative for duodenal tumors. However, for SNADET, it is difficult to determine the resection line with adequate margin from the serosal surface of laparoscopic view even using endoscopic view. Laparoscopic excessive resection may cause deformity or/and stenosis and insufficient surgical margins may result in local recurrence. Adequate maneuver of the duodenum is necessary for suturing the duodenal ESD site; however, suturing from small wound including laparoscopic assisted surgery is difficult, especially for posterior side of duodenum. Considering invasiveness and maneuverability, reinforcement using technique of D-LECS is valid option for safe management after duodenal ESD.

However, there are some technical problems with D-LECS. First, suitable patient positioning differs between an endoscopic and a laparoscopic procedure. Generally, the supine position is suitable for laparoscopic procedures, whereas the left lateral decubitus position is suitable for endoscopic procedures. To overcome this problem, we started the operation in the left lower half lateral decubitus position. This position allows the patient to be moved into both the supine and left lateral decubitus positions that are suitable for laparoscopic and endoscopic procedures. Another technical problem is the endoscopic maneuverability, which is reduced due to loss of duodenal fixation on the retroperitoneum after the Kocher maneuver. However, the laparoscopic Kocher maneuver after ESD makes it difficult to recognize the proper layer due to leakage of CO2 during ESD. Therefore, to retain endoscopic maneuverability, the Kocher maneuver was stopped until exposure of the anterior wall of the second part of the duodenum. After completion of the ESD procedure, the Kocher maneuver was completed by exposing the posterior side of the second part of the duodenum, if necessary.

Video 1 The omentum was dissected and the mesocolon was removed from the epigastric tissue. Right hepatocolic ligament was dissected to mobilize the right colic flexure. Kocher maneuver was stopped after exposing the anterior and right sides of the duodenal second portion.

Video 2 Endoscopic markings followed by circumferential mucosal incision was performed. Then a clip with thread was placed at the oral edge of the lesion for an adequate counter traction. Clip traction and additional injections using the knife were effective during dissection.

Video 3 Kocher maneuver was performed until the endoscopic submucosal dissection (ESD) site was well exposed. The ESD site was identified by the transmitted light of the endoscope and then two-layer suturing of the duodenal wall was carried out.
In our early experience, 50% of cases had a perforation after treating SANDETS with ESD alone (data not shown), while no patients had perforation when treated with D-LECS. Therefore, ensuring confirmation and reinforcement of thin duodenal wall after ESD is essential for the laparoscopic procedure during D-LECS. The transmitted light from the endoscope is useful for laparoscopic detection of the thin duodenal wall after ESD. Furthermore, confirmed closure of ESD site after suturing is necessary for secure prevention of delayed perforation. We believe that rough closure of the ESD site by suturing the full-thickness layer prior to suturing the seromuscular layer is useful for secure reinforcement of the whole ESD site. Further, reinforcement by

### Table 2 Patient characteristics and operative outcomes

| D-LECS (n = 10) |
|-----------------|
| **Patient characteristics** |
| Age, median (range) | 63.5 (47 – 73) |
| Sex, male/female | 7/3 |
| Tumor location |
| first/second portion | 0/10 |
| above/below ampulla | 3/7 |
| Tumor size, mm, median (range) | 20 (12 – 40) |
| **Preoperative diagnosis (adenoma/cancer)** | 8/2 |
| **Operative outcomes** |
| Conversion to open surgery | 0 |
| Total operation time, median (range), min | 208 (134 – 291) |
| Laparoscopy procedure time, median (range), min<sup>1</sup> | 120.5 (99 – 167) |
| ESD procedure time, median (range), min<sup>1</sup> | 99.5 (22 – 124) |
| **Size of resected specimen** |
| Major axis, mm, median (range) | 37 (25 – 55) |
| Minor axis, mm, median (range) | 25 (21 – 42) |
| **Size of resected tumor** |
| Major axis, mm, median (range) | 23 (12 – 33) |
| Minor axis, mm, median (range) | 14 (7 – 26) |
| **Resection margin** |
| Vertical margin (negative) | 10 |
| Horizontal margin (negative) | 10 |
| **Complications** |
| Perforation | 4 |
| - Intraoperative perforation | 4 |
| - Delayed perforation | 0 |
| Leakages | 0 |
| - Operation related death | 0 |
| - Any other complications | 0 |
| **Postoperative diagnosis (adenoma/cancer)** | 0/10 |
| **Fasting day, median (range)** | 4 (3 – 6) |
| **Postoperative stay, median (range)** | 11 (9 – 14) |

<sup>D-LECS, duodenum laparoscopy endoscopy cooperative surgery; ESD, endoscopic submucosal dissection</sup>

<sup>1</sup> Loss of data for 2 cases.
suturing the full-thickness layer may contribute to prevention of postoperative bleeding.

**Conclusion**

Despite including a small number of patients due to the low incidence of duodenal tumors, our report is important as it demonstrates a surgical technique for avoiding perforation after duodenal ESD. All patients in the current study had no complications and were able to maintain their food intake. We were able to achieve en-bloc resection by ESD in cases in which the ESD site was near the Vater’s ampulla and large circumferential lesions; however, further study is needed to determine the technical limitations of D-LECS. Because all of the duodenal tumors were intramucosal carcinoma, strict follow-up and examination of long-term outcomes are necessary.

**Competing interests**

Dr. Toyonaga invented the Flush Knife-BT in conjunction with Fujifilm and received royalties from its sale.

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