Journal of Gastrointestinal Surgery (2019) 23:2068–2074
https://doi.org/10.1007/s11605-019-04176-2

HOW I DO IT

Feasibility and Safety of a Novel Laparoscopic and Endoscopic Cooperative Surgery Technique for Superficial Duodenal Tumor Resection: How I Do It

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Received: 18 December 2018 / Accepted: 21 February 2019 / Published online: 11 March 2019

Abstract

Background Pancreatoduodenectomy is considered to be a very invasive treatment for early superficial duodenal tumors (SDTs), which have a lower risk of lymph node metastasis. Partial resection of the duodenum with endoscopic submucosal dissection for SDT resection is an attractive technique but it is associated with a high risk of complications. We describe our technique for SDT resection.

Method It includes the following elements: freeing the transverse mesocolon, exposing and mobilizing the second part of the duodenum and the head of the pancreas (Kocher maneuver), confirming the location of the ulcer bed for endoscopic submucosal dissection, and laparoscopic suturing by hand in the seromuscular layer of the duodenum. We performed this technique in 10 patients between March 2015 and March 2017.

Results The median tumor diameter and resected tissue diameter were 36 (20–54) and 41 (25–60) mm, respectively. Curative resection (R0) with negative margins was achieved for all patients. There were no conversions to open surgery in this series. No postoperative complications were above grade 2 in the Clavien-Dindo classification system. No recurrences were observed during the medium-term follow-up period.

Conclusion This technique is safe and feasible and can be an option for surgical SDT resection.

Keywords Duodenal tumor · Laparoscopic and endoscopic cooperative surgery · LECS

Introduction

Recently, duodenal tumors including adenoma, adenocarcinoma, and neuroendocrine tumors (NETs) are increasingly detected as early superficial duodenal tumors (SDTs) as a result of the development of endoscopic screening. However, standard treatment is not established because SDTs are rarely found in the gastrointestinal tract.[1] Pancreatoduodenectomy is considered the standard approach for SDT resection. It is undeniable that pancreatoduodenectomy is very invasive for SDTs, which are associated with a lower risk of lymph node metastasis.[2,3] Partial duodenal resection has also been attempted as an alternative treatment option for SDTs that do not require lymph node dissection. It is difficult to identify the location of the tumor from the serosal surface. Therefore, the incision in the duodenal wall might be excessive, possibly leading to duodenal leakage and stenosis after surgery.[4–7] There are a few reports of endoscopic submucosal dissection (ESD) and endoscopic mucosal resection (EMR) for SDTs.[8,9] However, they are not used as standard treatment because the anatomical features of the duodenum, such as the narrow lumen and thin walls, make endoscopic resection of

Presentation at a scientific meeting This article has never been presented at a scientific meeting.

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tumors very difficult. In fact, several recent reports have demonstrated that severe complications such as perforation and bleeding frequently occur during and after endoscopic treatment.[8–12]

Hiki et al. described laparoscopic and endoscopic cooperative surgery (LECS) for gastrointestinal stromal tumors. [13,14] This procedure enables precise assessment of tumor boundaries under endoscopic observation, thus facilitating adequate tumor resection. Laparoscopic suturing can minimize distortion of the shape of the gastrointestinal tract, which contributes to procedure safety and preservation of gastrointestinal function.[13,14] Some groups have described their experience with LECS or similar techniques for SDT resection.[15,16] However, these techniques involve full-thickness resection of the duodenal wall, which is associated with a risk of spreading tumor cells and digestive juices into the abdominal cavity. These techniques are considered to be ontologically incomplete and their long-term outcomes are unclear.

We have developed a novel technique for SDT resection that decreases the risk of tumor cell and digestive juice exposure to the abdominal cavity called non-exposed duodenum laparoscopic and endoscopic cooperative surgery (neo-DLECS). We describe our technique in detail and evaluate the feasibility and safety of neo-DLECS for SDT resection in this study.

Materials and Methods

Patients

From March 2015 to March 2017, 10 consecutive patients with SDTs underwent neo-DLECS at the Osaka International Cancer Institute. Clinicopathological data for these patients were prospectively collected and retrospectively analyzed. The study protocol was approved by the Human Ethics Review Committee of the Osaka International Cancer Institute (Protocol ID: 18033). All patients gave written informed consent prior to undergoing neo-DLECS. Data on age, gender, body mass index, histology, tumor location, tumor size, tumor depth, American Society of Anesthesiologists physical status classification, operative time, blood loss, resected tissue size, resection margin status, curative resection rate, R0 resection rate, intraoperative complications, postoperative complications with Clavien-Dindo classification grade ≥ 2, number of open conversions, number of days to starting an oral diet, and duration of postoperative hospital stay were prospectively collected and retrospectively analyzed. During postoperative surveillance, patients were examined by endoscopy at 3, 6, and 12 months and every year thereafter to assess for recurrence and strictures. Laboratory examinations, computed tomography, and ultrasound were performed alternately every 6 to 12 months.

Indications for Neo-DLECS

The indications for neo-DLECS to treat SDTs included tumors with a low risk of lymph node metastasis, expectation of cure with local resection, and approachable with endoscopic and laparoscopic techniques. The eligibility criteria were as follows: (1) SDT including adenoma, carcinoma, and neuroendocrine tumor grade 1 (NET G1)[17] without lymph node metastasis based on preoperative computed tomography and ultrasound imaging; (2) tumor depth confined to the mucosa and submucosa for adenoma and adenocarcinoma, with no exclusion criteria based on tumor size, and tumor size less than 10 mm and tumor depth confined to the mucosa for NET G1. (3) Tumor located more than 10 mm distal to the ampulla of Vater; (4) tumor comprising less than one-third of the duodenum lumen; and (5) tumor in the second part of the duodenum. These indications were determined based on the low rate of lymph node metastasis: 0.0% for mucosal carcinoma, 5.4% for submucosal carcinoma, and 3.5% for mucosal NET G1.[18]

Surgical Procedure

The patient was placed in the semi-Fowler and dorsosacral positions. Under general anesthesia, a 12-mm laparoscopy port was inserted through the umbilicus using the open method. After establishing pneumoperitoneum with carbon dioxide at a pressure of 10 mm H_2O, four additional trocars were inserted. From the left side of the patient, the greater omentum was divided at 3 cm from the right gastroepiploic vessels using laparoscopic coagulating shears (HARMONIC ACE +7; Ethicon Endo-Surgery, Cincinnati, OH, USA, or SonoSurg, Olympus, Tokyo, Japan) (Fig. 1a). The attachment of the transverse mesocolon was freed from the head of the pancreas and retroperitoneal tissues (Fig. 1b). Next, the second part of the duodenum and the head of the pancreas were exposed. During exfoliation, the accessory right colic vein was clipped and divided to avoid unnecessary bleeding (Fig. 1c). The duodenum and the head of the pancreas were mobilized from the retroperitoneum using the Kocher maneuver until confirm dorsal pancreas head and inferior vena cava (Fig. 1d).

Before the endoscopic procedure, the jejunum was clamped using laparoscopic removal forceps. The location of the tumor was confirmed using both endoscopy and laparoscopy. The periphery of the tumor was carefully marked using the endoscope. Using the ESD technique, a circumferential mucosal incision was made around the tumor with high-frequency knife forceps (Flush Knife; Fujifilm, Tokyo, Japan) or coagulation hemostatic forceps (Coagrasper; Olympus, Tokyo, Japan) after the injection of sodium hyaluronate (MucoUp; Seikagaku Corp., Tokyo, Japan). Standard ESD was performed for the SDT.

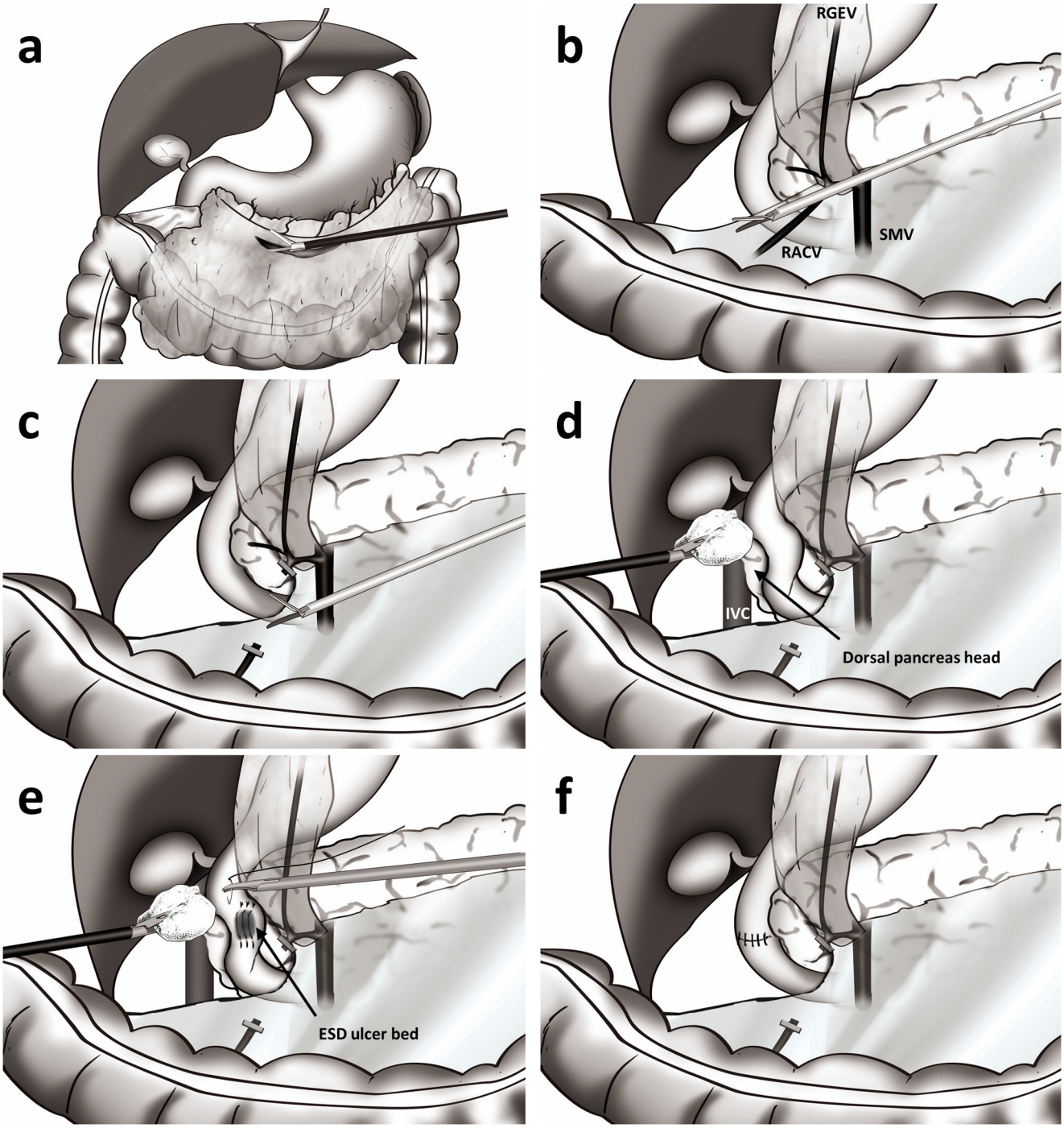

Fig. 1 Diagrammatic representation of non-exposed duodenum laparoscopic and endoscopic cooperative surgery. **a** Dividing the greater omentum. **b** Freeing the attachment of the transverse mesocolon from the head of the pancreas and retroperitoneal tissues. **c** Exposing the second part of the duodenum and the head of the pancreas. During exfoliation, clipping, and dividing the accessory right colic vein to avoid unnecessary bleeding. **d** Mobilizing the duodenum and the head of the pancreas from the retroperitoneum using the Kocher maneuver until confirm dorsal pancreas head and inferior vena cava. **e** Confirming the precise location of the ulcer bed after endoscopic submucosal dissection based on serosal color variations and thinning. Laparoscopic suturing by hand in the seromuscular layer perpendicular to the short axis of the duodenum. **f** Completing the procedure with neo-DLECS. Endoscopic confirmation of the absence of duodenal stenosis and air leak. RGEV, right gastroepiploic vein; RACV, right accessory colic vein; SMV, superior mesenteric vein; ESD, endoscopic submucosal dissection; IVC, inferior vena cava

Even after successful ESD, we reinforced the serosa of the ESD ulcer bed using a laparoscopic hand-sewing suturing technique in the seromuscular layer around the resected area. We confirmed the precise location of the ulcer bed based on

serosal color variations and thinning. The sutures were placed perpendicular to the short axis of the duodenum to avoid stenosis (Fig. 1e, f). If duodenal perforation was observed during ESD, the perforation was closed with hand-sewn serosal sutures. After completing the procedure, the endoscope was inserted and passed over the resected area to confirm that there was no stenosis or leakage.

Results

Patient Characteristics

Table 1 shows patients' demographic and clinicopathological features. Ten patients with SDT underwent neo-DLECS. The median age was 62.5 (56–74) years. There were eight males and two females. The median body mass index was 22.6 (19.8–26.9) kg/m^2. Pathological diagnosis was adenocarcinoma for six patients, adenoma for three patients, and NET G1 for one patient. All tumors were located in the second part of the duodenum. The median tumor size was 36 (20–54) mm; all tumors were 20 mm or larger. Tumor depth was mucosal for nine patients and submucosal for one patient.

Table 1 Demographic and clinicopathological characteristics ($n = 10$)

Characteristic	
Age (years)	62.5 (56–74)
Gender	
Male	8
Female	2
Body mass index (kg/m^2)	22.6 (19.8–26.9)
Histology	
Adenocarcinoma	6
Adenoma	3
Neuroendocrine tumor	1
Tumor location	
Second part of the duodenum	10
Tumor size (mm)	36 (20–54)
Tumor depth	
Mucosal	9
Submucosal	1
ASA classification*	
1	0
2	9
3	1

Values are presented as medians (range) and *n*

*ASA, American Society of Anesthesiologists physical status classification

Surgical Outcomes

Figure 2 shows representative intraoperative views of the neo-DLECS procedure for SDT resection. Surgical outcomes are summarized in Table 2. The median operative time was 227.5 (180–390) min. The median blood loss was 0 (0–175) ml. The median size of resected tissue specimens was 41 (25–60) mm. Curative resection (R0) with negative margins was achieved for all cases. Intraoperative perforation occurred in two patients during ESD. All perforations were closed using hand-sewn sutures. No postoperative complications including intraoperative bleeding and postoperative leakage, bleeding, or stenosis above grade 2 in the Clavien-Dindo classification system[19] were observed in this series. The median number of days to starting an oral diet and median duration of postoperative hospital stay were 4 (2–7) and 9 (5–12) days, respectively. The median follow-up was 15.0 (12.0–38.0) months. There were no recurrences or strictures observed in any patients.

Discussion

In this retrospective analysis, we demonstrated that neo-DLECS is feasible and safe for SDT resection. Duodenal tumors are rare; the incidence of primary duodenum neoplasia based on autopsy studies is approximately 0.5%.[20,21] Duodenal cancer accounts for approximately 0.5% of all gastrointestinal tract cancers.[1] Therefore, there are no treatment guidelines for SDTs due to the low number of cases and insufficient evidence. Pancreatoduodenectomy is often selected for duodenum neoplasia. However, it is very invasive for SDTs, which have a lower risk of lymph node metastasis. Therefore, partial duodenal resection may be a more appropriate procedure for SDTs. It is difficult to identify the location of tumors from the serosal surface during laparoscopy. Therefore, the duodenal wall might be resected excessively, possibly leading to duodenal leakage and stenosis after surgery. The least invasive procedures for SDTs are EMR and ESD. However, EMR has a low en bloc resection rate of 62–82%, a low curative resection rate of 30–59%, and a high local recurrence rate of 5.8–8.3%.[22–24] These results suggest that EMR leads to ontologically unacceptable outcomes. ESD has more favorable outcomes. The en bloc resection rate is 86–100%, the curative resection rate is 78–90% and the local recurrence rate is 0.0%.[22–25] However, ESD has a higher complication rate than EMR. For example, with ESD, the intraoperative perforation rate is 6.6–35.7%, the delayed perforation rate is 0–35.7%, the bleeding rate is 0–18.4%, and the emergency surgery rate is 3.3–14.3%.[22–26] In this series, neo-DLECS allowed for en bloc curative resection (R0) of SDTs with negative margins in all patients. There were no complications such as intraoperative bleeding and postoperative

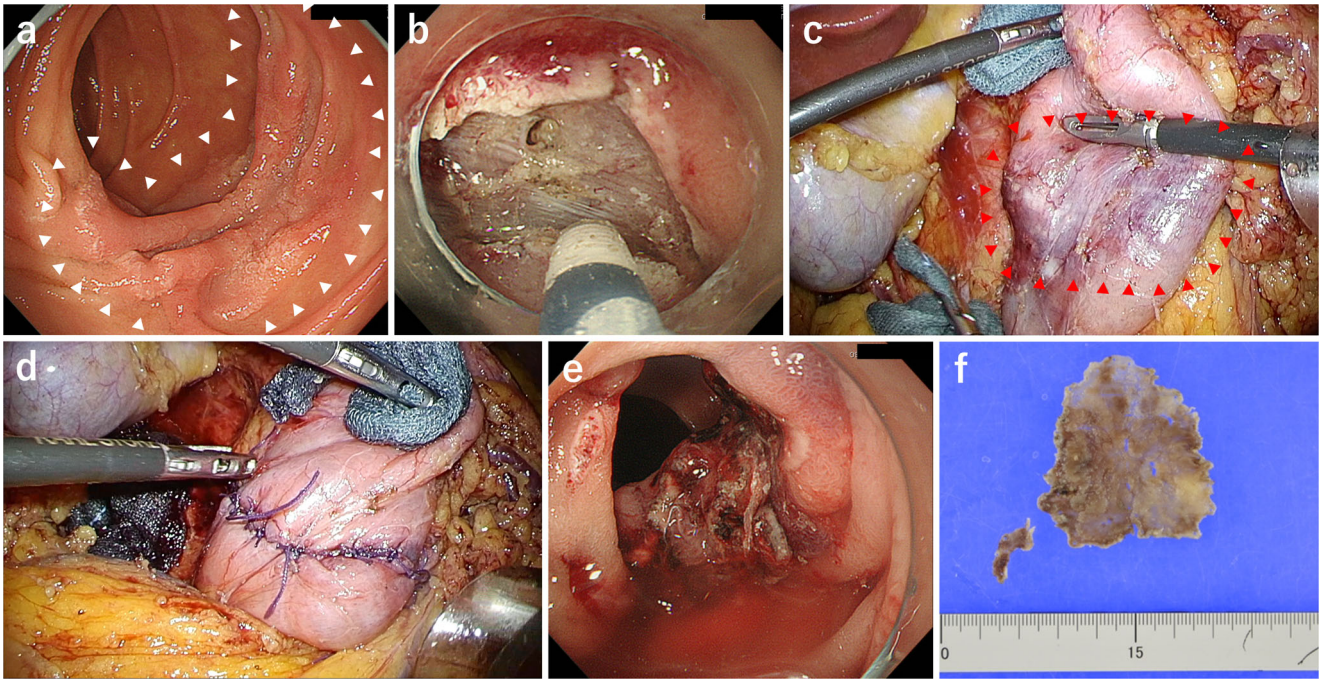

Fig. 2 A representative case of non-exposed duodenum laparoscopic and endoscopic cooperative surgery. **a** Endoscopic view of a duodenal carcinoma. White triangles show tumor boundaries. The tumor occupied approximately one-third of the lumen. **b** The ulcer bed after endoscopic submucosal dissection. **c** Laparoscopic view of the serosa. The precise location of the ulcer bed was confirmed based on serosal color variations and thinning (red triangles). **d** Reinforcing the serosa of the ulcer bed after endoscopic submucosal dissection using laparoscopic hand-sewn sutures in the seromuscular layer placed perpendicular to the short axis of the duodenum. **e** Confirming the absence of duodenal stenosis and air leak using endoscopy after the procedure. **f** Specimen of duodenal tissue

leakage, bleeding, or stenosis. These favorable results were considered to be the result of the advantages of both laparoscopic surgery and ESD. ESD can assess tumor boundaries precisely, thus allowing for resection with minimal tumor boundaries. Laparoscopic suturing can minimize distortion of the duodenum, which decreases the risk of perforation. Perforation during ESD was observed in two (20.0%) patients, which is comparable to the frequency in previous reports.[22–26] Almost all of our cases consisted of pinhole perforations that can be repaired under endoscopy. These perforations were considered to be due to adapting neo-DLECS for relatively large SDTs. Leakage after surgery was not observed after closing the perforations and reinforcing the serosa. These results showed that SDT resection with ESD alone is associated with a high risk of perforation; it needs to be supported by laparoscopy.

Table 2 Surgical outcomes

Operative time (min)	227.5 (180–390)
Blood loss (ml)	0 (0–175)
Resected tissue size (mm)	41 (25–60)
Resection margin	
Vertical margin negative (%)	100.0
Horizontal margin negative (%)	100.0
Curative resection rate (%)	100.0
R0 resection rate (%)	100.0
Intraoperative complications	
Perforation during ESD*	2
Bleeding	0
Postoperative complication**	0
Leakage	0
Bleeding	0
Stenosis	0
Open conversion	0
Starting an oral diet (days)	4 (2–7)
Postoperative hospital stay (days)	9 (5–12)

*ESD, endoscopic submucosal dissection

**Clavien-Dindo classification grade ≥ 2

Otowa and Ichikawa reported a procedure similar to our neo-DLECS procedure. Their procedure was associated with a few postoperative complications such as leakage and pancreatic fistula.[16,27] In their procedure, the ESD ulcer bed was confirmed using light transmitted from the endoscope's lumen. In neo-DLECS, which was not associated with any complications, the ESD ulcer bed was confirmed based on serosal color variations and thinning. Confirming the margins of the ulcer bed using transmitted light may be insufficient due to blurring around the edges. Therefore, to identify the margins of the ulcer bed, confirming both serosal changes with laparoscopy and transmitted light from the endoscope's lumen

may be more definite. In addition, regarding the purpose of suturing the duodenum, only the duodenum was mobilized from the retroperitoneum using the Kocher maneuver in their procedure. However, in our procedure, both the duodenum and the head of the pancreas were mobilized until confirm dorsal pancreas head and inferior vena cava. This process facilitated obtaining a good visual field for suturing the duodenum more safely. Our procedure might also be beneficial for tumors of a larger size or located in the posterior wall. Duodenum dysfunction, such as stasis, is associated with destruction of the surrounding duodenum tissue, which was not observed in this series. Moreover, there have been small case reports where the indications for treatment included tumor size less than 10 mm; such tumors can be safely resected using EMR.[28,29] In this series, all patients had tumor greater than 20 mm in size. Neo-DLECS might be suitable for relatively large tumors that commonly require ESD.

Endoscopy-assisted laparoscopic full-thickness resection is another technique for SDTs that has been reported to have favorable short-term outcomes.[15,16] However, these techniques are associated with a risk of spreading tumor cells and digestive juices into the abdominal cavity because they involve full-thickness resection of the duodenum. These techniques are considered to be ontologically incomplete.

In this study, tumors were located in the second part of the duodenum in all patients. If there was tumor in the first part, it was resected with laparoscopic distal gastrectomy, which is an established technique. If neo-DLECS was performed for the first part of the duodenum, postoperative quality of life might be maintained by avoiding distal gastrectomy. We have not encountered tumors located in the third part of the duodenum. Ichikawa et al. reported that LECS could be performed with good visualization of the third part of the duodenum by resecting the hepatocolic ligament and mobilizing the right colic flexure from the retroperitoneum.[16]

This study has several limitations. First, this study included a small number of cases analyzed retrospectively at a single institution. Therefore, the sample size may not be sufficient to accurately evaluate short-term outcomes. The ideal study design would consist of multiple surgical teams and prospective analysis. Second, oncological safety has not been determined yet. In particular, perforation during ESD might involve the risk of intra-abdominal dissemination of tumor cells. There were no recurrences during the follow-up period; however, that is just a medium-term outcome. Thus, long-term outcomes should be evaluated.

Conclusion

In this series, R0 resection was achieved with neo-DLECS in all patients and the serosa of the ESD ulcer bed was reinforced under good visualization. There were no complications or recurrences. Neo-DLECS is safe and feasible and can be an option for surgical SDT resection.

Authors' Contributions Yoshitomo Yanagimoto designed the study and wrote the initial draft of the manuscript. Takeshi Omori contributed to the analysis of data and interpretation of results and assisted in the preparation of the manuscript. All other authors contributed to data collection and interpretation of results and critically reviewed the manuscript. All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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