

Real-world outcomes of collaborative surgery for gastrointestinal tumors by endoscopists and surgeons: a single-center retrospective analysis of 131 patients

Kazutoshi Higuchi^a, Osamu Goto^{a,b}, Nobuyuki Sakurazawa^c, Atsuko Sakanushi^d, Koji Sakamoto^d, Akira Matsushita^c, Nobutoshi Hagiwara^c, Akihisa Matsuda^c, Toshihiko Hoashi^e, Shun Nakagome^a, Tsugumi Habu^a, Yumiko Ishikawa^a, Eriko Koizumi^a, Jun Omori^a, Naohiko Akimoto^a, Ryuji Ohashi^f, Hidehisa Saeki^e, Kimihiro Okubo^d, Hiroshi Yoshida^c, Katsuhiko Iwakiri^a

Nippon Medical School, Graduate School of Medicine; Nippon Medical School Hospital, Tokyo, Japan

Abstract

Background Collaborative surgery by both endoscopists and surgeons is considered effective for providing less invasive local resection of gastrointestinal tumors, to offset the limitations of either pure endoscopic treatments or surgical intervention. The clinical outcomes of collaborative surgery were evaluated to investigate the feasibility and safety of this approach.

Methods In this single-center retrospective observational study, we collected data from consecutive patients who underwent collaborative surgery for lesions located from the laryngopharynx to the anus. The completeness of collaboration, technical success, procedure time, postoperative hospitalization period, and occurrence of adverse events were analyzed.

Results Collaboration surgery was performed for 134 lesions (33 laryngopharyngeal, 2 esophageal, 89 gastric, 8 duodenal and 2 recto-anal) in 131 patients. Collaboration completeness was achieved in 129 lesions (96%). *En bloc* resection and pathological R0 resection of lesions were achieved in 127 (95%) and 124 (93%) lesions, respectively. The mean procedure time was 188 min. The mean time of discharge was the 11th postoperative day. Five patients (4%) developed relevant postoperative adverse events.

Conclusions These results indicate that collaborative surgery by endoscopists and surgeons is feasible and safe, and may contribute to providing less invasive treatment than conventional surgery. Collaborative surgery is worth considering as a flexible and reliable surgical option, when cooperation may outperform either treatment alone.

Keywords Collaborative surgery, endoscopic full-thickness resection, endoscopic laryngopharyngeal surgery, endoscopic submucosal dissection, laparoscopic and endoscopic cooperative surgery

Ann Gastroenterol 2024; 37 (6): 699-707

Introduction

Endoscopic treatment using peroral/anal flexible endoscopy and dedicated through-the-scope electrocautery

Conflict of Interest: None

Correspondence to: Osamu Goto, MD, PhD, Department of Gastroenterology, Nippon Medical School, Graduate School of Medicine, 1-1-5 Sendagi, Bunkyo-ku, Tokyo, 113-8603 Japan, e-mail: o-goto@nms.ac.jp

Received 28 May 2024; accepted 13 August 2024; published online 23 October 2024

DOI: <https://doi.org/10.20524/aog.2024.0921>

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms

devices has been developed as a less invasive form of intraluminal surgery. In particular, endoscopic submucosal dissection (ESD), developed around 2000, drastically elevated the potentials of therapeutic endoscopy as an alternative to surgery [1-5]. Since gastric ESD was introduced, the targets of this technique have been expanded to the esophagus, colorectum and duodenum, overcoming the technical difficulties involved.

However, a limitation is observed in conventional ESD both vertically and horizontally: ESD is useful for superficial lesions; however, tumors located in deeper layers, including subepithelial tumors (SETs), are difficult to remove using this technique without intraoperative perforation, and secure endoscopic closure is not always guaranteed [6,7]. Furthermore, lesions that are too close to the mouth/anus are difficult to treat endoscopically, because of the endoscope's poor stability and maneuverability [8,9]. These lesions were conventionally treated by a surgical approach, which sometimes led to wider

resection and subsequently possible uncomfortable outcomes, including pain, loss of organ function, and a deterioration in the patient's quality of life.

Collaborative surgery by endoscopists and surgeons was developed to overcome these limitations of pure endoscopic treatments and surgical intervention. Laparoscopic and endoscopic cooperative surgery (LECS) is one of the representative collaborative approaches that aim to perform local resection of gastric SETs or duodenal neoplasms, which were difficult and risky to remove by pure endoscopic intervention [10-12]. Moreover, to obtain easy and reliable local resection, laryngopharyngeal cancer resection under external traction by rigid forceps was devised [13-15].

We aimed to apply this collaboration to various lesions in the gastrointestinal tract, considering the possible merits of this less invasive approach and its technical durability. To investigate the feasibility and safety of this approach, we here retrospectively evaluated the clinical outcomes of collaborative surgery by endoscopists and surgeons.

Patients and methods

Study design

This was a single-center retrospective observational study. Approval was obtained from the Institutional Review Board of our hospital (B-2023-822) and the study was carried out in accordance with the Declaration of Helsinki. Consent from each patient was obtained as an opt-out; therefore, written consent was waived.

Data collection

We collected data of consecutive patients who underwent collaborative surgery between October 2017 and December 2023. In this study, collaborative surgery was defined as surgery for gastrointestinal tumor resection, aiming to use a flexible endoscope with surgical involvement. Target lesions were located mainly in the stomach, followed by the laryngopharynx and duodenum. Although rare, esophageal and recto-anal tumors were also included.

^aDepartment of Gastroenterology, Nippon Medical School, Graduate School of Medicine (Kazutoshi Higuchi, Osamu Goto, Shun Nakagome, Tsugumi Habu, Yumiko Ishikawa, Eriko Koizumi, Jun Omori, Naohiko Akimoto, Katsuhiko Iwakiri); ^bEndoscopy Center, Nippon Medical School Hospital (Osamu Goto); ^cDepartment of Gastrointestinal and Hepato-Biliary-Pancreatic Surgery, Nippon Medical School, Graduate School of Medicine (Nobuyuki Sakurazawa, Akira Matsushita, Nobutoshi Hagiwara, Akihisa Matsuda, Hiroshi Yoshida); ^dDepartment of Otorhinolaryngology, Nippon Medical School, Graduate School of Medicine (Atsuko Sakanushi, Koji Sakamoto, Kimihiro Okubo); ^eDepartment of Dermatology, Nippon Medical School, Graduate School of Medicine (Toshihiko Hoashi, Hidehisa Saeki); ^fDepartment of Integrated Diagnostic Pathology, Nippon Medical School, Graduate School of Medicine (Ryuji Ohashi), Tokyo, Japan

Procedures

Collaborative surgery was indicated by a suggestion from either flexible endoscopist- or surgeons-in-charge, considering that the cooperation might outperform single surgery by either of them, in terms of invasiveness, technical difficulty and safety. The final decision was made after agreement by both sides, and by each patient who was supposed to undergo the surgery. In this collaborative surgery, 3 endoscopists were involved as operators or supervisors. They were certified by the Japanese Gastrointestinal Endoscopy Society and had experience of more than 100 ESD cases. On the surgical side, 2 otolaryngologists, 6 gastrointestinal surgeons and 1 dermatologist participated in the respective procedures. They had also obtained certifications from societies of their specific fields and had more than 10 years of experience in surgery. Following hospital admission, the surgery was performed under general anesthesia.

For laryngopharyngeal lesions, squamous cell carcinoma was removed using the ESD technique performed by the endoscopist under laryngeal expansion, using a curved laryngoscope manipulated by the otolaryngologist [14,15]. In addition, to obtain sufficient endoscopic visualization and working space for resection, this technique was indicated for squamous cell carcinoma at the cervical esophagus [16]. Intraoperatively, transoral traction was occasionally provided using a rigid grasping forceps, depending on the situation.

For esophago-duodenal lesions, SET and cancer with contraindications for neither ESD nor standard surgery were assigned for local resection by flexible endoscopy and thoracoscopy/laparoscopy. For esophageal gastrointestinal stromal tumors (GISTs), we aimed to remove the lesions in a full-layered fashion by endoscopic full-thickness resection (EFTR) under thoracoscopic assistance. For gastric or duodenal lesions, we generally planned to perform LECS including LECS-related techniques, or EFTR under minimal laparoscopic assistance [10-12,17-21].

For recto-anal lesions, ESD or EFTR was performed on the basis of the lesions' depth of invasion, followed by surgical repair. For the anal lesions in particular, the dermatologist externally dissected the perianally expanded area following ESD from the rectal side by the endoscopist [22].

In all cases, detailed steps of the procedure can be changed depending on the situation, based on intraoperative discussion between the endoscopist- and surgeon-in-charge, the highest priority being the complete and safe removal of the lesion.

Outcomes measurements

In each organ, we evaluated the short-term surgical outcomes in terms of collaboration completeness, technical success, procedure time, postoperative hospitalization period, and occurrence of adverse events. Collaboration completeness was defined as the completion of local resection using both

endoscopic and surgical interventions. Technical success was assessed by an *en bloc* resection rate of lesions. A pathological R0 resection was used as criterion for histological success of the procedure. Procedure time was calculated as the duration from the initiation to the termination of the surgery. Adverse events were assessed using the Clavien-Dindo classification (CDC), and CDC grade IIIa or more was used to define relevant adverse events. In addition, we evaluated histology along with tumor size in the final diagnosis.

Statistical analysis

Owing to the nature of a single-arm non-comparative study, statistical analyses were not performed. Continuous variables were represented as means \pm standard deviations.

Results

Overall outcomes of gastrointestinal collaboration surgery

Gastrointestinal collaboration surgery was performed for 134 lesions in 131 patients (33 laryngopharyngeal, 2 esophageal, 89 gastric, 8 duodenal and 2 recto-anal lesions, in 30, 2, 89, 8 and 2 patients, respectively). The procedure was completed without severe intraoperative adverse events, and collaboration completeness was achieved in 129 lesions (96%). *En bloc* resection and pathological R0 resection of lesions were achieved in 127 (95%) and 124 (93%) lesions, respectively. The mean procedure time was 188 ± 93 min. The patients were discharged on mean postoperative day (POD) 11 ± 9 . Five patients (4%) developed CDC grade IIIa or more postoperative adverse events, including 1 patient who developed multiple events.

Laryngopharyngeal lesions

The clinicopathological characteristics and outcomes of the laryngopharyngeal collaborative surgery are presented in Table 1. ESD under laryngeal expansion was performed for 33 lesions in 30 patients (Fig. 1). Twenty-six patients were male (87%), and 85% of lesions were in the hypopharynx. Collaboration completeness was achieved in all cases (100%), and *en bloc* resection was achieved in 26 lesions (79%) in a mean procedure time of 105 min. The mean tumor size was 20 mm, and pathological R0 resection was noted in 25 lesions (76%). Transoral traction was provided in 21 lesions (64%). In 1 patient, who had a previous history of chemoradiation therapy for laryngeal cancer and underwent multiple ESD for oro- and hypopharyngeal lesions in a single session, dysphasia occurred because of post-ESD pharyngeal deformity, and percutaneous gastrostomy was finally required for nutrition.

Table 1 Characteristics and outcomes of collaborative laryngopharyngeal surgery

Patients	n=30
Age (years), mean \pm SD	69 \pm 9
Male, n (%)	26 \pm 87
Lesions	n=33
Location	
Oropharynx, n (%)	5 (15)
Hypopharynx, n (%)	28 (85)
Gross type	
Protruded/Flat-elevated, n (%)	12 (36)
Flat-depressed, n (%)	21 (64)
Outcomes: Time and postoperative courses	n=30
Procedure time (min), mean \pm SD*	105 \pm 61
Discharge (POD), mean \pm SD	12 \pm 10
Adverse events [†]	
Postoperative bleeding, n (%)	0 (0)
Dysphasia, n (%)	1 (3)
Outcomes: Resection and histology	n=33
Collaboration completeness, n (%)	33 (100)
<i>En bloc</i> resection, n (%)	26 (79)
Transoral traction provided, n (%)	21 (64)
Tumor size (mm), mean \pm SD	20 \pm 10
R0 resection, n (%)	25 (76)
Histology	
Squamous cell carcinoma, n (%)	29 (88)
Tis-T1, n (%)	26 (79)
Lymphovascular infiltration, n (%)	1 (3)

[†]Clavien-Dindo classification grade IIIa or more

*Two lesions are treated in a single session in 3 patients
SD, standard deviation; POD, postoperative day

Esophageal lesions

Esophageal collaborative surgery was performed in 2 patients: ESD for 53-mm cervical esophageal cancer and EFTR for 10-mm GIST in the middle thoracic esophagus (Table 2). In the patient who underwent ESD, the oral margin of the lesions was located at the upper esophageal sphincter. By expanding the laryngeal space using a curved laryngoscope, sufficient endoscopic visualization was obtained, and the lesion was successfully removed in an *en bloc* fashion. Local injection followed by oral steroid administration was effective in preventing postoperative stricture. In the patient who underwent EFTR, thoroscopic preparation was initially performed by separating the middle esophagus from the descending aorta. Subsequently, the lesion was endoscopically removed in a full-thickness fashion and retrieved transorally. The full-layered defect was closed by endoscopic hand-suturing for the inner circular muscle layer and mucosal clipping, followed by thoroscopic hand-suturing for the outer longitudinal muscle layer. Pathological R0 resection was achieved in both cases.

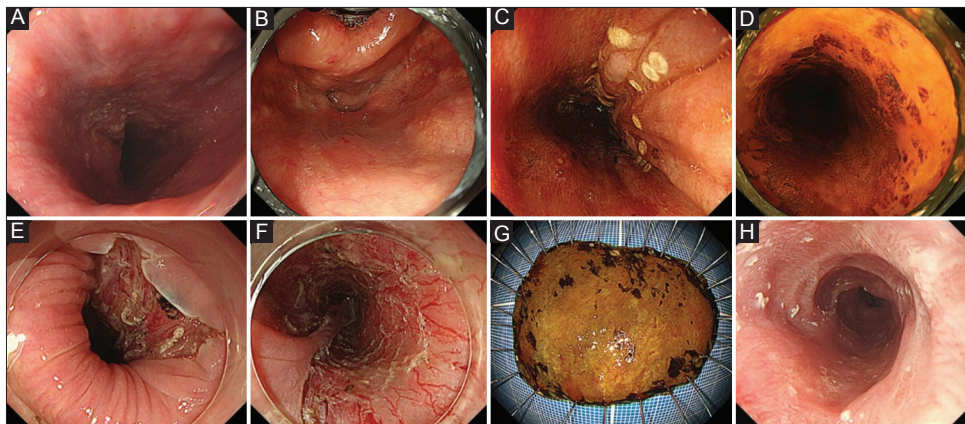


Figure 1 Endoscopic submucosal dissection with pharyngeal expansion for cervical esophageal cancer. (A) The cervical esophageal cancer extends to the upper esophageal sphincter. The endoscope is unstable, and the endoscopic view is not clearly obtained because of the existence of the sphincter. (B) Pharyngeal expansion using a curved laryngoscope has maintained cervical esophageal broadening. (C) The oral margins of the lesion could be well-visualized and markings around the tumor are easily placed. (D) The lesion is expanded to three fourths of the circumference. (E) A mucosal incision is created at a sufficient distance from the oral edge of the tumor. (F) The resection area extends semi-circumferentially. Local injection and oral administration of steroids are provided. (G) The lesion is removed in an *en bloc* fashion with negative tumor margins. (H) No symptomatic stricture has developed 2 months later

Gastric lesions

The background characteristics and outcomes of the 89 gastric lesions are summarized in Table 3. Eighty-one lesions were SETs (91%) and 47 lesions were located in the upper third of the stomach (53%). In 2 SETs located at the fundus, LECS was switched to open proximal gastrectomy because of technical difficulty. In another 2 cases, endoscopic intervention was skipped, and the lesions were removed solely by the laparoscopic approach. Conversely, as the lesion was removed by ESD in 1 case, LECS was not performed. Therefore, the collaboration completeness was 94% (84 lesions). In 5 of these 84 cases, a small abdominal incision was provided intraoperatively. Subsequently, in 79 cases (89%), LECS or EFTR under minimal laparoscopic assistance was completed as scheduled. In all cases (100%), the lesions (mean size, 28 mm) were safely removed in an *en bloc* fashion, with a mean procedure time of 201 min; the patients were discharged on mean POD 10. Pathological R0 resection was achieved in 88 lesions (99%). Endoscopic *en bloc* resection was achieved in 1 case who underwent EFTR; however, pathological horizontal margins of a very low-risk GIST were found to be tumor positive. Reoperation by conventional LECS for removing the surgical scar created by the previous procedure was performed 2 months after the initial surgery, and no residual tumor was detected in the resected specimen. In 2 patients, the following CDC grade IIIa adverse events occurred: postoperative stenosis requiring endoscopic balloon dilatation in 1; and postoperative bleeding from the anastomotic site requiring endoscopic hemostasis, followed by anastomotic leak in another patient.

Duodenal lesions

Eight duodenal lesions including 6 epithelial tumors and 2 SETs underwent duodenal LECS (Table 2). In principle,

ESD followed by laparoscopic sero-muscular suturing for postoperative perforation prevention was considered in superficial epithelial tumors (Fig. 2), while endoscopic and laparoscopic full-thickness resection with laparoscopic full-layered closure was indicated in advanced cancers or SETs. All procedures were completed without intraoperative adverse events, with a mean procedure time of 305 min; pathological R0 resection was achieved in all lesions. The mean postoperative hospitalization duration was 15 days. In 1 patient with a 50-mm epithelial lesion at the superior duodenal angle, delayed bleeding and anastomotic leak occurred on POD 28, which required endoscopic hemostasis and clipping. In another case with a neuroendocrine tumor, in which enucleation of a metastasized lymph node at the pancreatic head was performed simultaneously, a pancreatic fistula was detected on POD 2, and transabdominal puncture was required for the abdominal abscess on POD 16. Both cases had favorable clinical courses and were discharged without further surgical intervention.

Recto-anal lesions

Two patients (13-mm recurrent GIST following incomplete endoscopic resection and anal canal cancer with pagetoid spread) underwent collaboration surgery with a colorectal surgeon and a dermatologist, respectively (Table 2). In the case with recurrent GIST, the lesion was endoscopically removed in a full-thickness fashion, followed by transanal suturing of the full-thickness defect. The procedure time was 221 min. Although endoscopic *en bloc* resection was achieved, the anal margins were histologically tumor positive. No recurrence occurred during the 60-month observation period. In the case with anal canal cancer with diffuse type components, circumferential rectal ESD was initially performed, followed by perianal subcutaneous dissection from the outside and skin defect repair by gluteal fold flaps. The procedure was successfully completed

Table 2 Characteristics and outcomes of collaborative esophageal, duodenal, and recto-anal surgery

No.	Organ	Age (years)	Sex	Disease*	Location†	Tumor size (mm)	Resection‡	Closure
1	Esophagus	68	Female	GIST	Mt	10	EFTR	Endoscopic and thoroscopic suturing
2	Esophagus	68	Male	Epithelial neoplasm	Ce	53	ESD under laryngeal expansion	Not performed
3	Duodenum	79	Male	Epithelial neoplasm	SDA	50	LEFTR	Open suturing
4	Duodenum	55	Female	Epithelial neoplasm	2 nd portion	72	ESD	Laparoscopic suturing
5	Duodenum	59	Female	SET	3 rd portion	18	LEFTR	Laparoscopic suturing
6	Duodenum	68	Male	Epithelial neoplasm	Bulb	47	ESD	Laparoscopic suturing, endoscopic clipping
7	Duodenum	75	Female	Epithelial neoplasm	SDA	26	LEFTR	Laparoscopic suturing
8	Duodenum	76	Female	Epithelial neoplasm	2 nd portion	15	ESD	Laparoscopic suturing, endoscopic clipping
9	Duodenum	50	Female	SET	2nd portion	7	EFTR	Laparoscopic suturing, endoscopic clipping
10	Duodenum	83	Male	Epithelial neoplasm	Bulb	18	LEFTR	Laparoscopic suturing
11	Rectum	62	Male	GIST	Rb	13	EFTR	Transanal suturing
12	Anus	69	Female	Epithelial neoplasm	Anus	95	ESD+ subcutaneous dissection	Gluteal fold flap
Procedure completeness	Procedure time (min)	Histology*	En bloc resection	R0 resection	Postoperative hospitalization (days)	Adverse events [□]		
Completed	236	GIST	Yes	Yes	13	No		
Completed	181	Squamous cell carcinoma	Yes	Yes	4	No		
Small abdominal incision required	405	Adenocarcinoma	Yes	Yes	41	Delayed bleeding, anastomotic leak		
Completed	368	Adenoma	Yes	Yes	8	No		
Completed	302	GIST	Yes	Yes	9	No		
Completed	310	Neoplasms of uncertain malignant potential	Yes	Yes	8	No		
Completed	263	Adenocarcinoma	Yes	Yes	7	No		

(Contd...)

Table 2 (Continued)

Procedure completeness	Procedure time (min)	Histology*	En bloc resection	R0 resection	Postoperative hospitalization (days)	Adverse events [□]
Completed	313	Adenoma	Yes	Yes	9 [†]	No
Completed	270 [§]	Neuroendocrine tumor	Yes	Yes	28	Pancreatic fistula, intraabdominal abscess
Completed	212	Adenocarcinoma	Yes	Yes	10	No
Completed	221	GIST	Yes	No	9	No
Completed	517	Adenocarcinoma with pagetoid spread	Yes	Yes	26	No

[†]Mt, middle thoracic esophagus; SDA, superior duodenal angle; Rb, lower rectum

[§]EFTR, endoscopic full-thickness resection; LEFTR, laparoscopy-assisted endoscopic full-thickness resection; ESD, endoscopic submucosal dissection

^{||}17b lymph node dissection is included

^{||}Positive horizontal margins

[†]Rehospitalization is required owing to postoperative stenosis

[□]Clavien-Dindo classification grade IIIa or more

*GIST, gastrointestinal stromal tumor; SET, subepithelial tumor

Table 3 Characteristics and outcomes of collaborative gastric surgery

Patients	n=89
Age (years), mean±SD	67±14
Male, n (%)	50 (56)
Lesions	n=89
Location	
Upper third, n (%)	47 (53)
Middle third, n (%)	36 (40)
Lower third, n (%)	6 (7)
Circumference	
Lesser curvature, n (%)	21 (24)
Posterior wall, n (%)	23 (26)
Greater curvature, n (%)	20 (22)
Anterior wall, n (%)	25 (28)
Diagnosis	
Subepithelial tumor, n (%)	81 (91)
Cancer, n (%)	8 (9)
Outcomes: Time and postoperative courses	n=89
Procedure time (min), mean±SD*	201±80
Discharge (POD), mean±SD	10±8
Adverse events [†]	
Postoperative bleeding, n (%)	1 (1)
Anastomotic leak, n (%)	1 (1)
Stenosis, n (%)	1 (1)
Outcomes: Resection and histology	n=89
Resection type	
LECS, n (%)	57 (64)
EFTR, n (%)	22 (25)
LECS with abdominal incision, n (%)	5 (6)
Open proximal gastrectomy, n (%)	2 (2)
Laparoscopic local resection, n (%)	2 (2)
ESD, n (%)	1 (1)
Collaboration completeness, n (%)	84 (94)
En bloc resection, n (%)	89 (100)
Tumor size (mm), mean±SD	28±11
R0 resection, n (%)	88 (99)
Histology	
GIST, n (%)	62 (70)
Cancer, n (%)	8 (9)
Leiomyoma, n (%)	8 (9)
Schwannoma, n (%)	5 (6)
Others, n (%)	6 (7)

*Additional time for other surgeries is included in 3 patients

[†]Clavien-Dindo classification grade IIIa or more

SD, standard deviation; POD, postoperative day; GIST, gastrointestinal stromal tumor; LECS, laparoscopic and endoscopic cooperative surgery; EFTR, endoscopic full-thickness resection; ESD, endoscopic submucosal dissection

in 517 min. The pathological diagnosis was a 95-mm signet cell adenocarcinoma of the anal canal with pagetoid spread, and R0 resection was achieved. Four months later, endoscopic dilatation was performed for the subclinical anal stricture, and defecation was controlled by continuous laxative administration.

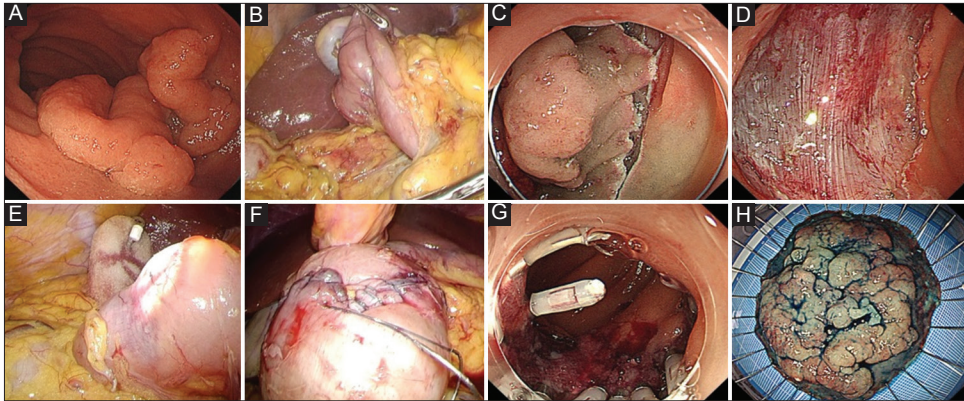


Figure 2 Duodenal laparoscopic and endoscopic cooperative surgery. (A) A 70-mm epithelial tumor is located in the second portion of the duodenum. (B) By Kocher mobilization, the duodenum is laparoscopically rotated. (C) Endoscopic submucosal dissection is performed. (D) The tumor is successfully removed in an *en bloc* fashion without perforation. (E) Laparoscopically, a mucosal defect is detected through the thin sero-muscular layer. (F) To avoid possible postoperative perforation and stricture, laparoscopic sero-muscular suturing is performed in a short-axis direction. (G) Mucosal clipping is additionally performed to reinforce sero-muscular suturing. (H) The pathological diagnosis is duodenal adenoma. Negative tumor margins are obtained both laterally and horizontally

Discussion

This is the first report on the clinical outcomes of collaborative surgery in various gastrointestinal organs at a single institution with a large number of patients. We have demonstrated that collaborative surgery by endoscopists and surgeons was feasible and safe, and may contribute to providing less invasive treatment. All 134 procedures were safely completed in approximately 3 h, and the planned surgery was completed in 96% of the lesions. The *en bloc* resection rate and pathological R0 resection were 95% and 93%, respectively, indicating that the cure rate also seemed favorable. Relevant adverse event occurrence was considered acceptable (4%). The results indicated that the collaborative surgery was worth considering as a flexible and reliable surgical option.

For superficial laryngopharyngeal cancers, ESD would be the most suitable method, because it allows accurate demarcation and precise resection, owing to the magnified visualization in the narrow working space. This advantage is expanded by elevation of the larynx using a dedicated laryngoscope [14], although the usefulness of this technique is difficult to estimate, as there are only a few examples of laryngopharyngeal ESD without laryngeal expansion [8]. Otolaryngologists who are accustomed to managing the pharyngeal space should be able to perform this procedure more effectively. Compared with ESD performed by an endoscopist alone, or conventional peroral laryngopharyngeal surgery, this collaborative procedure with otolaryngologists has the following advantages: first, traction can be applied orally with rigid grasping forceps to facilitate lesion removal; second, possible postoperative adverse events, such as laryngeal edema, can be addressed by experts who are familiar with the laryngopharyngeal region (e.g., emergency tracheostomy); third, lesions close to the upper esophageal sphincter, which are difficult to treat with peroral rigid devices, can be safely approached using a flexible endoscope with a transparent hood attached to the tip. Consequently, hypopharyngeal to

cervical esophageal cancers would be appropriate candidates for this collaborative surgery. The relatively low R0 rate (76%), although favorable considering previous reports (59% [23] to 78.5% [15]), may be because of the difficulty in demarcating the lesions. In patients with laryngopharyngeal tumors, small precancerous lesions expressed as multiple Lugol-voiding lesions are noted, while the tumor margins may appear unclear, particularly at the oropharynx. Furthermore, to prevent postoperative deformity and stricture, a wider resection should be avoided. Here, laryngeal expansion is considered mandatory for obtaining an ideal surgical circumstance. This concept will also be applicable to ESD for cervical esophageal cancers.

In lesions in the deeper layer, including SETs and advanced cancers, rigid and flexible endoscopic collaboration is reasonable for a safe and reliable procedure, as suggested when the LECS concept was introduced. Viewing from the outside of the organ using only rigid endoscopes, such as laparoscopes or thoroscopes, does not allow accurate recognition of the extent of epithelial neoplasms or intraluminally-growing type SETs, resulting in excessive resection to achieve a secure resection. Using flexible endoscopy during the collaborative procedure, the resection area can be determined under direct visualization. As a result, the resection area can be minimized and organ function is preserved as much as possible. Full-thickness defect closure or mucosal defect reinforcement can be safely performed by conventional surgical approaches. Although pure endoscopic procedures, including gastric EFTR and duodenal ESD, are considered ideal for minimally invasive surgery [6,7,24], this advantage may be outweighed by various disadvantages, including possible postoperative adverse events, technical difficulty and poor generalizability. Particularly in technically challenging cases for the pure endoscopic procedure, or indeterminate cases for the resection method, the collaborative approach should be safe and can be flexibly adaptable to intraoperative conditions. Unlike previous reports on conventional gastric LECS, in which the completeness of the procedure was almost 100% [10-12], we changed a surgical

style intraoperatively in 6% of gastric cases, by upgrading the bidirectional resection to pure ESD without laparoscopic resection in 1 case, or conversely downgrading the procedure to pure laparoscopic or open surgery in 4 cases. The procedure might have been an overtreatment, or discontinued, if either a laparoscopic or endoscopic approach was applied to these cases. Therefore, when we encounter lesions where it is difficult to determine the resection style preoperatively, the collaborative approach should be reasonable, ideally allowing completion of the treatment in a single session; this approach will be further enhanced by emerging robotic surgery [25]. In current circumstances, we consider that the indication of thoracoscopic/laparoscopic and endoscopic collaborative surgery would be favorable for duodenal epithelial lesions that have a potential risk of fatal adverse events by pure endoscopic procedure, or intraluminally-growing type SETs that are difficult to demarcate from outside the tract.

Furthermore, considering organ function preservation, minimally invasive local resection is acceptable in recto-anal lesions. Rectal EFTR for GIST is a desirable approach; however, full-thickness defect closure will be beneficial, as the surgeon performed transanal hand suturing in this study. Endoscopic suturing techniques were recently developed [26,27]; therefore, pure endoscopic treatment should be established in the near future [28]. Generally, anal cancers should be treated by dermatologists. However, in anal canal tumors with pagetoid spread, an external approach to the extended part on the rectal side is sometimes difficult. Here, owing to the fine endoscopic visualization and precise resection of the lesion, an endoscopic approach would be reasonable; however, clear demarcation of the tumor may remain challenging [22]. Bilateral submucosal dissection from both the oral and lateral sides of the lesion will be useful for obtaining complete removal of broadly spread superficial anal neoplasms. Accordingly, lesions that spread widely across both rectal and anal areas should be an optimal indication for this approach.

The cost-effectiveness of this collaborative surgery is a relevant issue to be discussed. In Japan, although the clinical impact of this approach is generally recognized, and a certain amount of evidence has been accumulated, guaranteed surgery in terms of medical expense remains limited to gastric or duodenal lesions; this situation may hamper further expansion of this technique. In this collaborative surgery, personnel and device costs for the endoscopic procedure are required in addition to those of conventional surgery, which should be reimbursed on the basis of clinical efficacy. Further accumulation and permeation of positive evidence from collaborative surgery in each organ would be a mandatory part of a continuous future agenda to obtain appropriate recognition in terms of medical insurance.

This study had several limitations. First, it was a single-center retrospective analysis without a control arm; however, considering the rarity of the target diseases, the number of cases in 1 institution does not appear small. Second, the indications for this approach were not strictly determined, and the target lesions were selected on the basis of a preoperative agreement reached by endoscopists and surgeons. Third, no assessment of prognosis was performed, owing to the short

observational period following the procedure. To demonstrate the feasibility and efficacy of this approach, a well-designed multicenter prospective study with a long observational period will be required.

In conclusion, we showed that collaborative surgery by flexible endoscopists and surgeons in various gastrointestinal organs was feasible and safe at a single institution. This approach may contribute to providing patients with a less invasive treatment when unidirectional intervention by either endoscopy or surgery might be considered as excessive or insufficient treatment. To establish this concept, further accumulation of cases and pieces of evidence by well-designed studies is needed.

Acknowledgment

We sincerely thank endoscopic technicians in the Endoscopy Center, Nippon Medical School Hospital for assisting with the collaborative surgery

Summary Box

What is already known:

- Local resection of gastrointestinal tumors contributes to preserving organ function
- Collaborative surgery with flexible endoscopists and surgeons has been introduced as a less invasive treatment technique
- Published data have appeared for each organ, mainly for laryngopharyngeal and gastric lesions, but there are few reports on collaborative surgery involving multiple organs at a single institution

What the new findings are:

- In this retrospective study of consecutively collected patients, we investigated the feasibility and safety of collaborative surgery for various gastrointestinal organs, including rare cases
- Favorable short-term outcomes were obtained from resection by flexible endoscopists and surgeons
- Collaborative surgery is worth considering as a useful option when cooperation might outperform a unidirectional approach by either endoscopists or surgeons

References

1. Ono H, Yao K, Fujishiro M, et al. Guidelines for endoscopic submucosal dissection and endoscopic mucosal resection for early gastric cancer. *Dig Endosc* 2016;**28**:3-15.

2. Ishihara R, Arima M, Iizuka T, et al; Japan Gastroenterological Endoscopy Society Guidelines Committee of ESD/EMR for Esophageal Cancer. Endoscopic submucosal dissection/endoscopic mucosal resection guidelines for esophageal cancer. *Dig Endosc* 2020;**32**:452-493.
3. Tanaka S, Kashida H, Saito Y, et al. JGES guidelines for colorectal endoscopic submucosal dissection/endoscopic mucosal resection. *Dig Endosc* 2015;**27**:417-434.
4. Pimentel-Nunes P, Libanio D, Bastiaansen BAJ, et al. Endoscopic submucosal dissection for superficial gastrointestinal lesions: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2022. *Endoscopy* 2022;**54**:591-622.
5. Al-Haddad MA, Elhanafi SE, Forbes N, et al. American Society for Gastrointestinal Endoscopy guideline on endoscopic submucosal dissection for the management of early esophageal and gastric cancers: methodology and review of evidence. *Gastrointest Endosc* 2023;**98**:285-305.
6. Zhou PH, Yao LQ, Qin XY, et al. Endoscopic full-thickness resection without laparoscopic assistance for gastric submucosal tumors originated from the muscularis propria. *Surg Endosc* 2011;**25**:2926-2931.
7. Shichijo S, Uedo N, Yanagimoto Y, et al. Endoscopic full-thickness resection of gastric gastrointestinal stromal tumor: a Japanese case series. *Ann Gastroenterol* 2019;**32**:593-599.
8. Shimizu Y, Yamamoto J, Kato M, et al. Endoscopic submucosal dissection for treatment of early stage hypopharyngeal carcinoma. *Gastrointest Endosc* 2006;**64**:255-259.
9. Hon SS, Ng SS, Chiu PW, et al. Endoscopic submucosal dissection versus local excision for early rectal neoplasms: a comparative study. *Surg Endosc* 2011;**25**:3923-3927.
10. Hiki N, Yamamoto Y, Fukunaga T, et al. Laparoscopic and endoscopic cooperative surgery for gastrointestinal stromal tumor dissection. *Surg Endosc* 2008;**22**:1729-1735.
11. Inoue H, Ikeda H, Hosoya T, et al. Endoscopic mucosal resection, endoscopic submucosal dissection, and beyond: full-layer resection for gastric cancer with nonexposure technique (CLEAN-NET). *Surg Oncol Clin N Am* 2012;**21**:129-140.
12. Goto O, Koizumi E, Higuchi K, et al. Cutting-edge technologies for gastrointestinal therapeutic endoscopy. *J Nippon Med Sch* 2021;**88**:17-24.
13. Tateya I, Muto M, Morita S, et al. Endoscopic laryngo-pharyngeal surgery for superficial laryngo-pharyngeal cancer. *Surg Endosc* 2016;**30**:323-329.
14. Iizuka T, Kikuchi D, Hoteya S, Yahagi N, Takeda H. Endoscopic submucosal dissection for treatment of mesopharyngeal and hypopharyngeal carcinomas. *Endoscopy* 2009;**41**:113-117.
15. Ogasawara N, Kikuchi D, Tanaka M, et al. Long-term outcome of cervical lymph node metastasis in superficial pharyngeal squamous cell carcinoma after endoscopic submucosal dissection. *Gastrointest Endosc* 2023;**98**:524-533.
16. Furue Y, Katada C, Kano K, Yoshida T, Yamashita T. Endoscopic submucosal dissection of cervical esophageal cancer with hypopharyngeal invasion using a curved laryngoscope. *VideoGIE* 2021;**6**:533-535.
17. Matsuda T, Nunobe S, Kosuga T, et al; Society for the Study of Laparoscopy and Endoscopy Cooperative Surgery. Laparoscopic and luminal endoscopic cooperative surgery can be a standard treatment for submucosal tumors of the stomach: a retrospective multicenter study. *Endoscopy* 2017;**49**:476-483.
18. Onimaru M, Inoue H, Ikeda H, et al. Combination of laparoscopic and endoscopic approaches for neoplasia with non-exposure technique (CLEAN-NET) for gastric submucosal tumors: updated advantages and limitations. *Ann Transl Med* 2019;**7**:582.
19. Aoyama J, Goto O, Kawakubo H, et al. Clinical outcomes of non-exposed endoscopic wall-inversion surgery for gastric submucosal tumors: long-term follow-up and functional results. *Gastric Cancer* 2020;**23**:154-159.
20. Nunobe S, Ri M, Yamazaki K, et al. Safety and feasibility of laparoscopic and endoscopic cooperative surgery for duodenal neoplasm: a retrospective multicenter study. *Endoscopy* 2021;**53**:1065-1068.
21. Sawada A, Hirasawa K, Sato C, et al. Endoscopic resection with one-port placement: A newly developed technique for the safe management of advanced endoscopic resection for gastric gastrointestinal stromal tumors. *Digestion* 2023;**104**:460-467.
22. Furuta K, Kimoto Y, Kano Y, et al. A case of anal canal carcinoma with pagetoid spread that was curatively resected by multiple endoscopic and surgical treatments. *DEN Open* 2024;**4**:e340.
23. Sakaguchi Y, Saito Y, Ando M, et al. Risk factors for incomplete resection with pharyngeal endoscopic submucosal dissection and long-term prognosis after resection. *Surg Endosc* 2023;**37**:3593-3601.
24. Kato M, Takeuchi Y, Hoteya S, et al. Outcomes of endoscopic resection for superficial duodenal tumors: 10 years' experience in 18 Japanese high volume centers. *Endoscopy* 2022;**54**:663-670.
25. Mimamimura K, Hara K, Matsumoto S, et al. Current status of robotic gastrointestinal surgery. *J Nippon Med Sch* 2023;**90**:308-315.
26. Goto O, Oyama T, Ono H, et al. Endoscopic hand-suturing is feasible, safe, and may reduce bleeding risk after gastric endoscopic submucosal dissection: a multicenter pilot study (with video). *Gastrointest Endosc* 2020;**91**:1195-1202.
27. Abe S, Saito Y, Tanaka Y, et al. A novel endoscopic hand-suturing technique for defect closure after colorectal endoscopic submucosal dissection: a pilot study. *Endoscopy* 2020;**52**:780-785.
28. Goto O, Kaise M, Iwakiri K. Endoscopic full-thickness resection with endoscopic hand suturing for rectal neoplasm involved in an anastomotic line. *Dig Endosc* 2022;**34**:e36-e37.