Editorial

Minimally invasive endoscopic surgery for complex colorectal lesions: progress from standard treatments to full thickness resections

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With the widespread implementation of the screening colonoscopy, opportunities to encounter early-stage colorectal cancer and/or precancerous lesion have increased. A complex colorectal lesion is defined as benign appearing colorectal lesion that is deemed unresectable by conventional endoscopic resection, such as polypectomy or endoscopic mucosal resection (EMR). These complex colorectal lesions have traditionally undergone colectomy, despite the lesion being histologically benign. However, with the current development and improvement of endoscopic resection techniques, these lesions can now be removed by advanced endoscopic surgery. One of the major advanced endoscopic surgeries is endoscopic submucosal dissection (ESD). ESD was first reported by Ono *et al.* and Gotoda *et al.* in 1998 using the IT knife for removal of an early gastric and rectal cancer (1,2). ESD utilizes circumferential mucosal cutting and submucosal dissection by using an electronic knife which is different from conventional EMR. Though ESD was first used in the stomach, it is now being applied in other areas including the esophagus and colorectum (3). ESD allows for a very high probability of *en-bloc* resection, leads to accurate pathological evaluation and results in a low risk of recurrence (4). Many safety devices have been developed, however, ESD still remains technically difficult in some cases and results in long procedure times and a relatively high perforation rate (5). The majority of centers performing frequent ESD and publishing findings are in Asia, thus treatment outcomes and complication rates in Western countries remain unclear.

In January 2018, this journal published a paper entitled "Experience in colon sparing surgery in North America: advanced endoscopic approaches for complex colorectal lesions" by Gorgun *et al.* (6). The authors reviewed their treatment outcomes for 110 patients undergoing advanced endoscopic surgeries, including ESD and combined endoscopic-laparoscopic surgery (CLES). After histopathology review, 10 (9.1%) of the 110 patients had invasive cancer that ultimately required surgery. Pre-operative detailed endoscopic diagnosis is important before advanced endoscopic surgery to appropriately utilize surgical resection. ESD and CLES is indicated for superficial colorectal tumors without lymph node metastasis. If the tumor appears to have features suggesting invasive cancer, a colectomy with *en-bloc* removal of regional lymph nodes is recommended due to the possibility of lymph node metastasis (7). Besides the usual technical difficulties of ESD, the T stage endoscopic diagnosis is another necessary hurdle that must be correctly assessed to perform ESD and CLES. High definition endoscopy with an optical magnifying function has been used for the T stage diagnosis in Japan and some classifications available for discriminating invasive cancer, such as pit pattern classification and the Japan Narrow Band Imaging Expert Team (JNET) classification system (8,9). In laterally spreading tumors (LSTs), included in the category of complex colorectal lesions, the presence of a large nodule (≥10 mm), a circumscribed deep depression and an invasive pit pattern were independent predictors of invasive cancer in a study

of 822 LSTs (10). Notably, the pit pattern diagnosis is the most reliable method to judge the invasive depth of the tumor. However, lesions showing a protruded morphology (type 0–I in the Paris classification) sometimes appear non-invasive, even when they deeply invade. This is because the intramucosal tumor component covers the lesion and masks the surface of the invasive component. Furthermore, an invasive pit pattern suggesting deep submucosal invasion was more often associated with non-granular type LSTs (52%) than granular type LSTs (71%) (10). In another large-scale study, the sensitivity of pit pattern diagnosis for identifying deep invasion of flat and depressed lesion (97.5%) was superior to that of polypoid lesions (75.8%) (8). In these polypoid lesions, it can be difficult to predict the tumor depth of invasion by only observing the surface of the lesion. Therefore, in an attempt to reduce the number of surgeries performed for non-invasive lesions, it is considered acceptable to perform diagnostic endoscopic resection.

It is noteworthy to mention the high success rate of *en-bloc* resection at 88.2% (97/110) using advanced endoscopic surgery. This resulted in a 29% reduction in surgery for unresectable benign polyps over a 3-year period. After the introduction of colorectal ESD, two additional studies reported a decrease in colectomies with lymph node dissection in Japan (11,12). When comparing the *en-bloc* resection rate of colorectal ESD with that of laparoscopic colectomy (LAC) in Japan, the rate of successful R0 *en-bloc* resection became equivalent. (13) Furthermore, the hospital stay was reduced by half, the complication rate was lower, overall healthcare cost was reduced, and the quality of life was improved in the patients undergoing ESDs compared to LACs (13-15). The safety profile and possibility of curative treatment with ESD provides an advantage for the treatment of superficial colorectal tumors. However, the colorectal ESD has a relatively slow learning curve. An estimated 20 to 40 cases of ESD are required to achieve self-sufficiency in both Asian and Western countries (16-18). In addition, prior experience with gastric ESD and expert supervision can expedite competency of colorectal ESD during training. Currently in the US, the availability of ESD expertise and the number of early gastric cancer ESD cases are limited (19).

In recent years, attention has turned towards full-thickness resection which has further advanced ESD. The authors used a CELS technique in 28 cases (25.6%). In CELS, used in 28 cases (25.6%) in the author's study, ESD was applied after lesion identification with colonoscopy using the standard method of submucosal injection and mucosal cutting. Then, laparoscopy was applied to invaginate the colonic wall underlying the lesions to improve visualization of the cutting line and to optimize snaring. Furthermore, when a perforation occurred, the repair was immediately performed by laparoscopy. If ESD was not technically feasible despite laparoscopic assistance, the authors converted to a laparoscopic wedge resection of the involved bowel segment using a linear stapler without anastomosis. A further advantage of this technique is immediate analysis of the wedge resection with frozen section to aid in the decision regarding a colectomy.

CELS, also known as laparoscopic endoscopic cooperative surgery (LECS), is a full-thickness resection that allows for minimal resection using a combination of laparoscope and endoscope. In 2008, Hiki *et al.* first reported seven patients with successful resections of gastrointestinal stromal tumors, which led to a breakthrough in laparoscopic wedge resection (20). The perforation risk during surgery could lead to potential tumor seeding into the peritoneal cavity, therefore, LECS is mainly indicated for gastric submucosal tumor at the present time. Recently, the LECS technique has been modified to include a non-exposed endoscopic wall-inversion method which is a good alternative option for difficult ESD case (21). On the contrary, colonic function is generally preserved after standard partial colectomy, however, this is not the case with wedge resection. Thus, the indication of LECS should be technically difficult ESD cases such as tumor with fibrosis [LST-nongranular (LST-NG) or pseudo-depressed type], near or within a diverticulum, or at a difficult location (cecum or flexure). In this scenario, we have to be cautious as another laparoscopic surgery would be required if the resected specimen contains submucosal deep invasive cancer. The possibility of a second LECS is a concern as this is less desirable due to increased technical difficulty due to adhesions formed during the first laparoscopy. Robotic technology may also prove to be advantageous in reducing difficultly in colorectal ESD (22). The Master and Slave Transluminal Endoscopic Robot (MASTER) combined robotic technology and endoscopy, has the potential to reduce procedural ESD time (23).

There have been several novel techniques recently developed to improve ESD. The appearance of dedicated endoscopic full-thickness resection (EFTR) devices such as the Padlock clip and over-the-scope clip (OTSC) have made it possible to perform EFTR without laparoscopic assistance using the "close then cut" technique (24). This

method reduces the possibility of tumor cell seeding into the peritoneal cavity. In addition to these dedicated EFTR devices, endoscopic full layer suturing devices such as "OverStitch" EFTR are indicated not only for subepithelial lesions (SELs) but also gastrointestinal epithelial lesions. There are several limitations and concerns with the EFTR procedure including the requirement for general anesthesia, the risk of incomplete resection and iatrogenic peritoneal tumor cell seeding. Therefore, the indication of EFTR for cancerous lesion remains controversial (24).

As these techniques are novel, the acquisition of outcome data has become a priority. From the outcome data available, only two adenomatous recurrences were reported in each ESD and CELS groups during a median follow-up period of 16 months. Adverse events were reported with an incidence of 11.8% (13/110) after advanced endoscopic surgery for complex colorectal disease. Of the 13 adverse events, 7 (4 delayed bleedings and 3 perforations) were related to ESD and the remaining 6 were related to the surgery (3 surgical site infections and 3 postoperative ileus). Recent studies about long-term outcomes of colorectal ESD from Japanese institutions revealed favorite outcomes. Yamada *et al.* reported a 5-year overall survival rate of 95.9% (95% CI, 94–98%) after following 423 lesions. The 5-year overall cumulative endoscopic recurrence rates and cancerous recurrence rates in eligible patients for endoscopic follow-up were 2.4% (95% CI, 0.8–4.1%) and 0.6% (95% CI, 0–1.4%) (4). Shigita *et al.* studied outcomes of 224 lesions and reported that 5-year overall survival rate and local recurrence rate in patients with *en-bloc* resection during median follow-up period of 6.6 years were 94.6% and 0.6%, respectively (25). ESD seems to have solid long-term clinical outcomes when compared to conventional EMR and has a lower adverse event rate than surgery. With regards to CELS, long term data is not currently available, however, ongoing studies are accumulating outcome data including complication and recurrence rates.

Ultimately, advanced endoscopic surgery can be performed safely and effectively. The study by Gorgun *et al.* reframes our treatment strategy for complex colorectal lesions. There is no standard indication for CELS, but proposed candidates should be submucosal tumors and technically difficult colorectal ESD lesions. When a lesion does not meet the threshold for ESD, it should be removed by conventional EMR. The data discussed and reviewed in this article has the bias of being acquired by experienced endoscopists. ESD can be very challenging due poor scope maneuverability and possible thinness of the wall during the colorectal ESD. Piecemeal resection during challenging cases may result in a higher likelihood of recurrence and should be of concern to the doctor and patient. Additional data is required to establish an endoscopic treatment strategy to optimize patient outcomes and reduce recurrence and complication rates with advanced endoscopic surgery.

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