

Preprints are preliminary reports that have not undergone peer review. They should not be considered conclusive, used to inform clinical practice, or referenced by the media as validated information.

Effectiveness of Strategy-Focused Training in Colorectal Endoscopic Submucosal Dissection: A Retrospective Observational Study

Hideyuki Chiba h-chiba@omori.jrc.or.jp **Omori Red Cross Hospital** Ken Ohata NTT Medical Center Tokyo Keiichi Ashikari Ashikari Endoscopy Clinic Jun Tachikawa Hiratsuka City Hospital Naoya Okada Yokohama Rosai Hospital Akimichi Hayashi **Omori Red Cross Hospital** Yu Ebisawa **Omori Red Cross Hospital** Mikio Kobayashi **Omori Red Cross Hospital** Jun Arimoto **Omori Red Cross Hospital** Hiroki Kuwabara **Omori Red Cross Hospital** Michiko Nakaoka **Omori Red Cross Hospital**

Research Article

Keywords:

Posted Date: February 29th, 2024

DOI: https://doi.org/10.21203/rs.3.rs-3990882/v1

Additional Declarations: No competing interests reported.

Version of Record: A version of this preprint was published at Digestive Diseases and Sciences on April 25th, 2024. See the published version at https://doi.org/10.1007/s10620-024-08430-9.

Abstract

Background

Colorectal ESD, an advanced minimally invasive treatment, presents technical challenges, with globally varying training methods. We analyzed the learning curve of ESD training, emphasizing preoperative strategies, notably gravity traction, to guide ESD instructors and trainee programs.

Method

This retrospective study included 881 cases guided by an experienced supervisor. Six trainees received "strategy-focused" instruction. To evaluate the number of ESD experiences in steps, the following phases were classified based on ESD experiences of each trainees: Phase 0 (0–50 ESD), Phase 1 (51–100 ESD), Phase 2 (101–150 ESD), and Phase 3 (151–200 ESD). Lesion background, outcomes, and safety were compared across phases. Factors contributing to technical difficulty in early (Phase 0 and 1) and late phases (Phase 2 and 3) were identified, along with the utility of traction ESD with device assistance.

Result

Treatment outcomes were favorable, with 99.8% and 94.7% en bloc resection and curative resection rates, respectively. Approximately 90% self-completion rate could be achieved after experiencing about 50 cases (92.7% in Phase 1), signifying proficiency growth despite increased case difficulty. In early phases, factors such as right-sided colon, LST-NG morphology, and mild and severe fibrosis pose challenges. In late phases, mild and severe fibrosis remained significant. Traction-assisted ESD, utilized in 3% of cases, comprised planned (1.1%) and rescue (1.9%) methods. Planned traction aided specific lesions, while rescue traction was common in the right colon.

Conclusion

"Strategy-focused" ESD training consistently yields successful outcomes, effectively adapting to varying difficulty factors in different proficient stages.

Introduction

Colorectal endoscopic submucosal dissection (ESD) has progressed as a minimally invasive treatment for colorectal tumors due to improved endoscopic equipment and appropriate training methods. Recent reports also validated ESD in Western countries [1–3]. Colorectal ESD is widely acknowledged as technically challenging, primarily due to endoscopic maneuverability issues to the colon and higher complication rates related to the thin colonic wall.

Traditionally, the fundamental technique of ESD involves mucosal flap creation, advancing the scope behind the lesion, and guiding resection primarily via natural traction, predominantly gravity. The European Society of Gastrointestinal Endoscopy (ESGE) Technical Review outlines gravity-assisted ESD as a representative of traction techniques without device assistance in the technical aspects section [4]. Other similar methods such as tunneling, pocket creation method, and tissue traction are also described (ESD without devise assistance). Meanwhile, external or internal traction-devise assisted ESD (TA-ESD) techniques, such as ring-thread traction or clip and line etc., have shown favorable outcomes by facilitating easier resection [5-8]. Recently, TA-ESD are often compared to conventional ESD; however, the definition of conventional ESD remains unclear. Particularly, the preference for TA-ESD in all cases remains unclear. Upon initial training for colorectal ESD, familiarity with traction devices is often necessary when using TA-ESD. To provide effective traction, including traction direction and strength, it is very useful to have experience in daily ESD, wherein traction by natural gravity and optimal treatment strategy are considered while performing the procedure. TA-ESD may occasionally lead to unexpected directions or even interfere with the procedure. ESD is mainly performed without device assistance by simulating the treatment strategy simulated preoperatively and sometimes flexibly intraoperatively to preserve effective traction force until the end of treatment while giving awareness to tissue traction. To date, however, few comprehensive reports exist on the safety and validity of strategy-focused ESD training. Additionally, information on the necessary case volume is limited to allow sufficient proficiency and experience for a practitioner and consistently achieve stable results using this instructional approach.

This study aims to examine the validity and educational effectiveness of "strategy-focused" ESD training at our institution.

Method

This single-center, retrospective, observational study analyzed 1532 colorectal ESD cases performed between April 2012 and October 2023. ESD was initiated by the same supervising physician who had experienced about 500 ESD cases as of 2012 and performed by six trainee physicians with at least 50 cases of strategy-focused ESD training. ESD trainees included a total of 6 physicians with less than 30 ESD cases at their previous institution (JA, HK, and MN), including those without colorectal ESD experience (KA, JT, and NA). To evaluate the number of ESD experiences in steps, the following phases were classified based on the number of ESD experiences of each trainee in our institution: Phase 0 (0–50 ESD experiences), Phase 1 (51–100 ESD experiences), Phase 2 (101–150 ESD experiences), and Phase 3 (151– 200 ESD experiences) (Fig. 1).

The initial investigation compared lesion backgrounds, outcomes including en bloc resection and selfcompletion rates, and safety across each phase to determine the number of cases that the trainees underwent under the similar instruction needed for a stable ESD outcome. Second, cases with lower dissection speed were compared in the early phase (Phase 0,1: ESD < 100) and late phase (Phase 2,3: ESD 101–200) to identify their associated factors. Furthermore, cases with devise assistance in planned or rescue were examined. All ESDs were planned based on the Japanese guidelines for ESD and endoscopic mucosal resection of colorectal cancer [9]. Antithrombotic and anticoagulant agents were stopped prior the procedure in accordance with current guidelines [10]. If the tumor showed obvious expanded change with white light imaging, deep depressed surfaces, or was clearly Vi high or VN irregular with magnifying endoscopy, it was diagnosed as SM invasive carcinoma (SM2; >1000 μm) and was not an indication for ESD [11].

The technical prerequisite for training

The technical prerequisite for colorectal ESD training was an endoscopist who could accurately perform stable colonoscopy, colonic endoscopic mucosal resection, and magnified endoscopic observation using narrow band imaging and other techniques. About 30 cases of gastric ESD were experienced as a physician, while more than 20 cases of colorectal ESD were experienced as an assistant during the same period.

Colorectal ESD procedures (Fig. 2)

For all cases, ESD operators were chosen by the supervising physician according to the trainee's experience and performance. Training initially focused on rectal or ascending colon lesions with a tumor diameter of approximately 2 cm and good scope maneuverability, followed by gradually targeting more difficult lesions.

Colorectal ESD utilized a single-channel endoscope (PCF-Q260JI, GIF-Q260J, GIF-H290T; Olympus, Tokyo, Japan) with carbon dioxide insufflation. Intravenous sedation was administered using a combination of midazolam or flunitrazepam and pethidine according to each endoscopist's judgment. After injecting undiluted 0.4% sodium hyaluronate (Mucoup, Boston Scientific, Tokyo, Japan; ksmart, Olympus) and indigo carmine with diluted epinephrine, one or two ESD knives were primarily utilized for procedures. A Dual knife (KD-650L; Olympus, Tokyo, Japan), A TechKnife (Micro-Tech, Nanjing, China) was primarily utilized for mucosal incision and submucosal dissection. We used an ERBE electrosurgical unit, VIO300D or VIO3 (Erbe, Tübingen, Germany).

The ESD strategy for standard lesions was as follows: Initially, a mucosal flap was created from the proximal side using mainly cutting waves of sufficient size, allowing the scope to dive behind the lesion (effect 2, duration 2, interval 2). Afterwards, a sufficient endpoint was created distal to the lesion. The direction of fluid was taken as the direction of gravity, and incisional dissection was performed along that side. The submucosal layer on the gravity side was thoroughly dissected by re-entering behind the mucosal flap. Finally, the procedure was completed with the remaining gravity contralateral mucosal incision and dissection of the remaining submucosa. Prophylactic coagulation was not performed for remaining small vessels on the ulcer surface. The tunnel method was employed for large lesions larger than half circumference. The decision to perform TA-ESD depends on the physician's judgment; however, planned TA-ESD (pTA-ESD) is often done primarily for recurrent lesions after endoscopic treatment, diverticular extension lesions, and appendiceal orifice extension lesions, and sometimes rescue TA-ESD (rTA-ESD) is performed on short notice due to procedural difficulties.

For high-frequency device settings, EndoCutl was utilized for mucosal incisions. Submucosal dissection primarily employed Effect I mode, with swift or forced coagulation mode (Effect 2, 45W) occasionally applied for vascular-rich submucosal areas. Endoscopic hemostasis was achieved using the knife tip in coagulation mode, while resorting to hemostatic forceps if hemostasis could not be achieved with the knife alone.

During ESD by trainees, the procedure was switched to the supervising physician with the following conditions: (1) procedural difficulty (situations where the procedure did not proceed for a long time, uncontrolled intraoperative perforation, difficulty in controlling hemostasis), (2) instructive switching (when teaching a better or more appropriate procedure), and (3) for time management (when the procedure time was expected to exceed 2 hours).

Making the preoperative ESD strategy (Strategy-focused ESD)

The trainee developed a preoperative ESD strategy and discussed it with the supervising physician. This strategy covered not only the endoscopic device, injection needle, and solution, but also the most challenging lesion locations, initial mucosal incision sites, and which incision should be made last, considering the direction of gravity. Additionally, the overall strategy was described as specific as possible (scope manipulation, controlled amount of local injection or air in the lumen, device placement, concrete cutting technique, etc.), as well as the predicted procedure time, which the supervising physician revised as needed (Fig. 3). Regarding video recording during ESD from October 2018, both endoscopic videos and actual endoscopic procedures were recorded to facilitate better understanding of the endoscopic hand and scope operation. After synchronizing with the endoscopic video, a two-screen video of the case was generated, including the voice of the supervising physician providing advice and the sounds of the incision and coagulation of the high-frequency device. Reviewing this video post-ESD helped the trainee identify strengths and areas for improvement (video). Recently, our online platform has been developed for learning by using two and three screens of actual ESD videos, which can also be one of the learning by watching them before and after ESD (Ohata Endosalon https://www.jamtea.org/endosalon/).

Data analysis and evaluations

The primary outcome was the self completion rate between phases, with comparisons made regarding lesion difficulty and treatment outcome. Dissection speed (DS) was calculated by dividing the area of the resected specimen into the procedure time (cm²/min). The area of the resected specimen was considered to be oval in shape. Hence, it was calculated as follows: $3.14 \times 0.25 \times long$ axis × minor axis. DS < 9 was defined as difficult-to-treat cases, with multivariate analysis comparing factors associated with early-stage (Phase 0,1: ESD < 100) and late-stage (Phase 2,3: ESD101-200) ESD. Second, regarding TA-ESD, two categories were investigated: planned traction-assisted ESD (pTA-ESD) and rescue traction-assisted ESD (rTA-ESD).

Histopathological Assessment

En bloc resection was defined as removing a tumor whole in a single piece. Patients were considered to have undergone "curative resection" when meeting all the following criteria based on the Japanese Classification for Cancer of the Colon and Rectum: lateral and vertical margins were free of tumor, well- or moderately differentiated or papillary carcinoma, no vascular invasion, submucosal invasion depth < 1,000 mm, and grade 1 budding [9].

Definitions

The degree of submucosal fibrosis was classified into three types (F0–2) (F0: no fibrosis, which manifested as a blue transparent layer; F1: mild fibrosis, which appeared as a white web-like structure in the blue submucosal layer; F2: whitish submucosa or severe fibrosis, which appeared as a white muscular like structure without a blue transparent layer in the submucosal layer) [12]. Delayed bleeding was defined as the presentation of bloody stools within 14 days post-ESD, followed by an emergency colonoscopy. Intraoperative perforation was defined as the occurrence of an immediately recognizable hole in the bowel wall. Delayed perforation was defined as colon perforation occurring after the scope had been withdrawn following ESD completion without intraprocedural perforation [10]. Post-ESD coagulation syndrome (PECS) was defined as a presence of pain and fever due to inflammation of the peritoneum, which occasionally occurs after electrocoagulation despite the absence of subsequent perforation [14].

Statistical Analysis

For comparing categorial variables, a two-sided χ^2 - or Fisher's exact test was performed. Continuous variables (patient characteristics) were assumed to have a normal distribution according to the central limit theorem, and an ANOVA was utilized to compare the four phases. Meanwhile, other continuous variables (procedural, and lesion characteristics) were compared using the Kruskal-Wallis test. Factors significant in univariate analysis were entered into the multivariate logistic regression analysis model. The odds ratio (OR) and 95% confidence interval (CI) were calculated for each variable. All analyses were conducted using SPSS 23 for Windows, with *P*-values \leq 0.05 considered statistically significant.

Ethics

The study was conducted in accordance with the principles in the Declaration of Helsinki. Informed consent was obtained from all patients prior the procedures. This was also approved by the institutional review board of our hospital(No.23–38).

Results

A total of 881 cases were included, including 6 trainees with 300 lesions in Phase 0 (0-50 ESD), 6 trainees with 286 lesions in Phase 1 (51-100 ESD), 4 trainees with 195 lesions in Phase 2 (101-150 ESD), and 2 trainees with 100 lesions in Phase 3 (150-200 ESD). Each physician were trained in the following time periods: 86 cases in 3 years and 2 months for KA (about 29 cases/year), 100 cases in 3 years and 6 months for JT (about 29 cases/year), 145 cases in 3 years and 8 months for NO (about 39 cases/year), 1 case in 5 years for JA (about 30 cases/year), 150 cases in 6 years and 3 months for HK (about 32 cases/year), and 5 years 200 cases in 3 months for MN (about 38 cases/year).

Patient background is summarized in Table 1. The location, macroscopic type, and difficult situation (postbiopsy, post-endoscopic treatment, diverticulum-related lesions, and appendiceal orifice-related lesions) were similar for each phase. Overall, the outcome of treatment was favorable, with 99.8% (879/881) of cases resected en bloc and 94.7% (834/881) of cases curatively resected (Table 2). Tumor diameter was similar for all phases; however, lesions >5 cm were most common in Phase 1. Treatment time and dissection speed increased with increasing phase.

The self-completion rate improved with each phase. Notably, the self-completion rate was 92.7% in Phase 1, without cases of ESD interruption. No significant difference was found in the rate of en bloc resection and curative resection between phases. Regarding adverse events, 2 cases (2%) of perforation were observed in Phase 3, which was more common than in other phases.

Difficult cases were defined as DS<9 (cm²/min), and their associated factors were examined in the early phase (Phase 0,1: ESD<100) and late phase (Phase 2,3: ESD101-200). Results revealed that in early phase, right-sided colon (OR 3.383, 95% CI: 1.113-10.283, p=0.032), LST-NG (OR 2. 222, 95% CI 1.019-4.845, p=0.045), mild fibrosis (F1) (OR 2.521, 95% CI: 1.364-4.661, p=0.003), severe fibrosis (F2) (OR 13.237, 95% CI: 5.203-33.674, p<0.0001), and in the late stage, mild fibrosis (F1) (OR 4.182, 95%CI: 1.398-12.511, p=0.01), severe fibrosis (F2) (OR 25.096, 95% CI: 7.437-84.685, p<0.0001) were identified (Table 3).

TA-ESD was performed in 26 cases (3.0%) overall, with an increasing trend with increasing phase (Table 2). Ten cases (38.5%) were planned TA-ESD, and 16 cases (61.5%) were rescue TA-ESD (Table 4). pTA-ESD was performed in 3 cases of diverticular extension, 3 cases of supranastomotic lesions, 2 cases of large and stalked lesions, 1 case of appendiceal extension lesion, and 1 case of recurrent lesion after endoscopic treatment. Meanwhile, rTA-ESD was performed in 11 of 16 cases in the later stages (Phase 2 and 3), 12 cases in the right colon, especially in the cecum (all cases with appendiceal extension), 9 cases with fibrosis (F1: 3 cases, F2: 6 cases), and both operation time and DS took longer than in other cases, with one case of intraoperative perforation (Table 4).

Discussion

The study evaluated the outcomes of six trainees trained in strategy-focused colorectal ESD and the training's validity. By systematically performing a preoperative strategy simulations considering the physician's experience and treatment difficulty levels, trainees achieved favorable ESD outcomes, with 99.8% and 94.7% of cases resected en bloc and curatively, respectively. Moreover, 97% of cases could be safely resected in a short time without device assistance. This strategy-focused training method resulted in a self-completion rate of about 90% in more than 50 cases, remaining high even in challenging cases. Under this strategy-focused training method, the planned traction method with device assistance proved useful for more difficult cases.

Colorectal ESD is challenging due to the thin colon wall and poor operability. While various training methods for colorectal ESD have been reported in the past, they vary depending on the country and institution [4, 13,15]. Especially in Asia, many institutions start colorectal ESD after prior experience with

gastric and esophageal ESD, and certain proficiency is achieved with approximately 30 to 80 cases [15, 16]. However, training for colorectal ESD was deemed difficult in Europe and the United States due to limited experience with gastric cancer ESD and the lack of supervising physicians. Zhang et al. also reported that 280 ESD cases were necessitated to achieve colorectal ESD proficiency (en bloc resection >90%, R0 resection >80%, and resection speed >9 cm²/h) [13]. A national survey from Italy reported that perforation rates in the colon and rectum were significantly lower with experience of >150 compared to 80-150 cases [17]. The primary goal of any training method is to develop skills for safely and reliably completing ESD, even for challenging lesions. At our institution, a single experienced supervisor trained physicians using the similar teaching method (strategy-focused ESD), achieving a high self-completion rate of about 90% in more than 50 cases, with a DS of 14.9 cm^2 /min and a curative resection rate of 94.3%. In subsequent phases, as more difficult cases were selected, the self-completion rate improved, and speed increased to a DS of 19.6 cm²/min, a trend that continued to improve with each phase. Preoperative simulation and strategy creation tailored to intraoperative situations are crucial. Furthermore, the angle manipulation of the scope and endoscope is essential to ensure successful ESD completion, and we believe that simultaneous video recording on two screens (video of the inside and outside of the endoscope) is a useful educational tool. While its usefulness cannot be evaluated since it has not been compared with other training methods of ESD, this educational method is very effective given an overall median procedure time by the trainees of 30 minutes, a very high en bloc resection rate (99.7%), and relatively low complication frequency.

In the present study, treatment difficulty was classified into early and late stages, anticipating variation based on operator experience. Factors identified in the early stage included right-sided colon, LST-NG, and mild/severe fibrosis, while in the late stage, only fibrosis was significant, with no notable differences in location or morphology type. Poor operability, common in the right-sided colon, poses a challenge in colorectal ESD, with Boda et al. recommending gaining scope operability experience in the first 20 cases [18]. Familiarity with operability and experience likely decreases treatment difficulty by location, possibly due to increased fibrosis in LST-NG, as previously reported. [19]. Preoperative simulation of the lesion, including its characteristics and maneuverability, contributed to this learning curve.

ESD with device assistance occurred less frequently, with 26 cases (3.0%) categorized as planned traction and rescue traction for difficult cases. Planned traction was used for lesions extending into diverticula or appendiceal orifices where preoperative gravity traction was not expected [20,21]. Meanwhile, rescue traction was utilized when gravity traction was less effective, and a consistent endoscopic view could not be obtained. Since it is crucial to imagine the ideal traction direction and traction force prior the procedure, it is assumed that these factors are always imagined during the usual ESD to ensure a smooth rescue traction.

This study has several limitations. This study was conducted in Japan and involved one supervising physician teaching six physicians using the similar training method. Hence, a validation study is warranted to identify whether this training method is appropriate for facilities lacking a supervising physician and whether it is equally effective for physicians starting their training with colorectal ESD. Furthermore, it remains unclear if physicians completing this training can consistently perform the procedure at other

facilities. However, in more than 50 cases of colorectal ESD, a self-completion rate of about 90% was obtained, including difficult lesions, and it is expected that physicians will step up to become proficient in colorectal ESD.

In conclusion, this study evaluated the effectiveness of "strategy-focused" training, emphasizing preoperative strategy development and natural traction. After conducting 881 cases by six trainee physicians, results showed a progressive improvement in self-completion rates, lesion outcomes, and safety across training phases. The strategy-focused approach achieved a 95% self-completion rate in the later phase without device assistance. The study suggests that this training method is effective in enhancing ESD skills, emphasizing preoperative simulation and strategy development for successful and safe outcomes.

Declarations

Author Contribution

HC, KA, JT, KO, JA, HK, and MN performed the colorectal ESD. HC recruited the study participants. HC, KA, JT, KO, JA, HK, MN, AH, YE, and MK collected the clinical data of the study participants. Analysis and interpretation of the data was conducted by HC and KO. All the authors have read the final manuscript and approve of its submission for publication.

References

- Ohata K, Kobayashi N, Sakai E et al. Long-term Outcomes After Endoscopic Submucosal Dissection for Large Colorectal Epithelial Neoplasms: A Prospective, Multicenter, Cohort Trial From Japan. Gastroenterology 2022; 163: 1423-1434
- Pimentel-Nunes P, Pioche M, Albéniz E, et al. Curriculum for endoscopic submucosal dissection training in Europe: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement.Endoscopy 2019; 51: 980-992
- 3. Draganov PV, Aihara H, Karasik MS et al. Endoscopic Submucosal Dissection in North America: A Large Prospective Multicenter Study. Gastroenterology 2021; 160: 2317-2327
- Libânio D, Pimentel-Nunes P, Bastiaansen B et al. Endoscopic submucosal dissection techniques and technology: European Society of Gastrointestinal Endoscopy (ESGE) Technical Review. Endoscopy 2023; 55: 361-389
- 5. Mori H, Kobara H, Nishiyama N, et al. Novel effective and repeatedly available ring-thread counter traction for safer colorectal endoscopic submucosal dissection. Surg Endosc 2017; 31: 3040-3047
- 6. Yamasaki Y, Takeuchi Y, Uedo N et al. Traction-assisted colonic endoscopic submucosal dissection using clip and line: a feasibility study. Endosc Int Open 2016; 4: E51–E55
- 7. Takezawa T, Hayashi Y, Shinozaki S, et al. The pocket-creation method facilitates colonic endoscopic submucosal dissection (with video).Gastrointest Endosc 2019; 89: 1045-1053

- 8. Suzuki Y, Ohata K, Sakai E et al. Palisade technique as an effective endoscopic submucosal dissection tool for large colorectal tumors. Endosc Int Open 2021; 9: E210-E215
- 9. Hashiguchi Y, Muro K, Saito S, et al. Japanese Society for Cancer of the Colon and Rectum (JSCCR) Guidelines 2019 for the treatment of colorectal cancer. Int J Clin Oncol 2020; 25: 1–42
- Tanaka S, Kashida H, Saito Y, et al. Japan Gastroenterological Endoscopy Society guidelines for colorectal endoscopic submucosal dissection/endoscopic mucosal resection. Dig Endosc 2020; 32: 219–23
- 11. Matsuda T, Fujii T, Saito Y, et al. Efficacy of the invasive/non-invasive pattern by magnifying chromoendoscopy to estimate the depth of invasion of early colorectal neoplasms. Am J Gastroenterol 2008; 103: 2700-6
- 12. Matsumoto A, Tanaka S, Oba S, et al. Outcome of endoscopic submucosal dissection for colorectal tumors accompanied by fibrosis. Scand J Gastroenterol. 2010; 45: 1329-1337
- Zhang X, Ly EK, Nithyanand S, et al Learning Curve for Endoscopic Submucosal Dissection With an Untutored, Prevalence-Based Approach in the United States. Clin Gastroenterol Hepatol 2020; 18: 580-588
- Arimoto J, Higurashi T, Kato S, et al. Risk factors for post-colorectal endoscopic submucosal dissection (ESD) coagulation syndrome: a multicenter, prospective, observational study. Endosc Int Open 2018; 6: E342-E349
- 15. Ohata K, Ito T, Chiba H, et al. Effective training system in colorectal endoscopic submucosal dissection. Digestive Endoscopy 2012; 24: 84–89
- 16. K. Hotta, T. Oyama, T. Shinohara, et al. Learning curve for endoscopic submucosal dissection of large colorectal tumors Digestive Endoscopy 2010; 22: 302-306
- 17. Maselli R, Iacopini F, Azzolini F, et al. Endoscopic submucosal dissection: Italian national survey on current practices, training and outcomes.Dig Liver Dis 2020; 52: 64-71
- 18. Boda K, Oka S, Tanaka S, et al. Real-world learning curve analysis of colorectal endoscopic submucosal dissection: a large multicenter study. Surg Endosc 2020; 34: 3344-3351
- 19. Chiba H, Tachikawa J, Arimoto J, et al. Predictive Factors of Mild and Severe Fibrosis in Colorectal Endoscopic Submucosal Dissection. Dig Dis Sci 2020; 65: 232-242
- 20. Muramoto T, Ohata K, Sakai E, et al. Endoscopic submucosal dissection for colorectal neoplasms in proximity or extending to a diverticulum. Surg Endosc 2021; 35: 3479-3487
- 21. Tashima T, Ohata K, Nonaka K, et al. Endoscopic submucosal dissection for laterally spreading tumors involving the appendiceal orifice.Surg Endosc 2017; 31: 5444-5450

Tables

Table 1 The Characteristics of the patients

	Phase 0	Phase 1	Phase 2	Phase 3	P value
Case, n	300	286	195	100	
Sex (male), n (%)	153 (51)	157 (54.9)	109 (55.9)	45 (45)	0.398
Age, mean ± SD	68.8 ± 12.6	67.1± 12.1	65.5 ± 12.9	63.5 ± 14.2	0.003
Location*, n (%)					0.584
Right colon	186 (62)	187 (65.4)	137 (70.3)	64 (64)	
Left colon	66 (22)	63(22.0)	35 (17.9)	20 (20)	
Rectum	48 (16)	36 (12.6)	23 (11.8)	16 (16)	
Morphology, n (%)					0.171
0-1	42 (14	49 (17.18	40 (20.5	18 (18)	
LST-G	67 (22.3	53 (18.5	25 (12.8🛛	18 (18)	
LST-NG	191 (63.7)	184 (64.3)	130 (66.7)	64 (64)	
Difficult situation, n (%)	25 (8.3)	23 (8.0)	11 (5.6)	9 (9)	0.527
Post ER	1	5	5	1	
Pre-biopsy	9	4	0	1	
Diverticulum**	7	4	4	2	
Appendiceal orifice***	8	10	2	5	

*The right colon refers to the transverse colon-cecum, and the left colon to the sigmoid colon-descending colon.

** The diverticulum refers to the lesion spreading to the diverticulum.

*** The appendiceal orifice refers to the lesion spreading to the appendiceal orifice.

LST-G; laterally spreading tumor- granular type, LST-NG: laterally spreading tumor- nongranular type, ER; endoscopic resection.

Table 2 The treatment outcome per phase in six trainees ESD training

	Phase 0	Phase 1	Phase 2	Phase 3	Р
ESD experience	0-50	51-100	101-150	151-200	value
Case, n	300	286	195	100	
Size (mm), median (IQR)	20.0	21.5	20.0	20.0	0.97
	(18.0 - 28.0)	(18.0 - 30.0)	(16.0 - 26.0)	(18.0 - 26.5)	
Time (min), median (IQR)	36	29	25.0	24.5	<0.001
	(23 - 55)	(19- 46)	(17.0 - 41.0)	(16.0 - 37.8)	
Dissection speed (cm ² /min),	14.9	19.6	20.8	23.7	<0.001
median (IQR)	(10.6 - 21.4)	(13.7 - 27.7)	(14.1 - 30.2)	(17.5 - 33.0)	
Devise traction, n (%)	1 (0.3)	6 (2.1)	11 (5.6)	8 (8)	<0.001
Rescue traction, n (%)	0	5 (1.7)	8 (4.1)	4 (4.0)	0.279
Tunnel method, n (%)	3 (1)	11 (3.8)	13 (6.7)	4 (4)	0.009
Fibrosis, n (%)	44 (14.7)	65 (22.7)	26 (26)	25 (25)	0.005
F1 (mild)	30 (10)	55 (19.2)	15 (7.7)	19 (19)	
F2 (severe)	14 (4.7)	10 (3.5)	11 (7.6)	6 (6)	0.637
Self-completion, n (%)	254 (84.7)	265 (92.7)	180 (92.3)	95 (95)	0.001
Interruption, n (%)	0	0	0	0	-
Histology, n (%)					0.371
Adenoma	161 (53.7)	140 (49.0)	109 (55.9)	50 (50)	
Tis	115 (38.3)	123 (43.0)	70 (35.9)	40 (40)	
T1a	7 (2.3)	12 (4.2)	4 (2.1)	2 (2)	
T1b or deeper	16 (5.3)	8 (2.8)	8 (4.1)	7 (7)	
Others	1 (0.3)	3 (1.0)	4 (2.1)	1 (1)	
En bloc resection, n (%)	300 (100)	285 (99.7)	194 (99.5)	100 (100)	0.614
Curative resection,	283 (94.3)	275 (96.2)	184 (94.4)	92 (92)	0.43
n (%)					
Adverse events, n (%)	12 (4)	14 (4.9)	8 (4.1)	7 (7)	0.637
post bleeding	6 (2)	5 (1.7)	4 (2.1)	1 (1)	0.919

perforation	0 (0)	0 (0)	1 (0.5)	2 (2)	0.016
delayed perforation	1 (0.3)	0 (0)	1 (0.5)	0 (0)	0.63
PECS	5 (1.7)	9 (3.1)	2 (1.0)	4 (4)	0.241

ESD; endoscopic submucosal dissection, PECS; post-ESD coagulation syndrome

Table 3 Risk Factors for difficult cases* in each Phase

Early Phase	Univariate,	P value	Multivariate,	P value
(Phase 0 and 1)	OR (95%CI)		OR (95%CI)	
Location **				
Rectum	1		1	
Left colon	3.486 (1.142 - 10.644)	0.028	3.116 (0.966 - 10.048)	0.057
Right colon	3.608(1.271 - 10.238)	0.016	3.383 (1.113 - 10.283)	0.032
Shape				
LST-G	1		1	
LST-NG	2.12(1.014 - 4.430)	0.046	2.222 (1.019 - 4.845)	0.045
Protruded	2.667 (1.119 - 6.352)	0.027	2.267 (0.854 - 6.019)	0.1
Fibrosis				
F1 (mild)	2.396 (1.315 - 4.364)	0.004	2.521 (1.364 - 4.661)	0.003
F2 (severe)	12.483 (5.258 - 29.636)	<0.001	13.237 (5.203 - 33.674)	<0.001

Late Phase	Univariate,	P value	Multivariate,	P value
(Phase 2 and 3)	OR (95%CI)		OR (95%CI)	
Location**				
Rectum	1		1	
Left colon	2.043 (0.506 - 8.251)	0.316	2.083 (0.4141 - 10.468)	0.373
Right colon	1.180 (0.330 – 4.217)	0.799	1.420 (0.310 – 6.494)	0.651
Shape				
LST-NG	2.13 (0.838 - 5.413)	0.112	3.05 (0.983 - 9.462)	0.053
Protruded	1.074 (0.416 – 2.771)	0.883		
Fibrosis				
F1 (mild)	3.52 (1.252 - 9.897)	0.017	4.182 (1.398 - 12.511)	0.01
F2 (severe)	18.482 (6.186 - 55.223)	<0.001	25.096 (7.437 - 84.685)	<0.001

*Difficult cases were defined as dissection speed <9 (cm^2/min).

**The right colon refers to the transverse colon-cecum, and the left colon to the sigmoid colon-descending colon.

LST-G; laterally spreading tumor- granular type, LST-NG: laterally spreading tumor- nongranular type, ER; endoscopic resection.

Table 4 Sixteen cases treated by ESD with rescue traction method

No	Phase	Size (mm)	Shape	Site	Difficult situation	Fibrosis	Time (min)	DT	En bloc	Adverse events
1	1	33	G	Т	-	F1	70	16.1	Yes	-
2	1	24	NG	Ce	AO	F2	96	9.2	Yes	-
3	1	21	I	Т	-	F2	132	3.5	Yes	-
4	1	35	I	S	-	F2	190	5.2	Yes	-
5	1	25	NG	Ce	AO	F1	58	12.3	Yes	-
6	2	20	I	Т	-	-	26	18.9	Yes	-
7	2	20	NG	Т	-	F2	110	2.9	No	-
8	2	45	NG	D	-	F2	120	6.5	Yes	-
9	2	25	NG	D	-	F2	120	6.5	Yes	-
10	2	25	NG	Т	-	F1	123	4.8	Yes	-
11	2	15	NG	D	-	-	10	23.6	Yes	-
12	2	20	NG	А	-	-	46	9.8	Yes	-
13	3	20	I	Т	-	-	12	47.1	Yes	-
14	3	18	I	Ce	AO	_	80	2.9	Yes	-
15	3	28	NG	Ce	AO	-	80	7.1	Yes	Perforation
16	3	20	NG	Ce	AO	-	35	12.9	Yes	-
	median	22.5					80	8.2		

ESD; endoscopic submucosal dissection, G; laterally spreading tumor-granular type, NG: laterally spreading tumor- nongranular type, I: protruded type, Ce; cecum, A; ascending colon, T; transverse colon, D; descending colon, S: sigmoid colon, AO: appendiceal orifice, F1: mild fibrosis, F2; severe fibrosis, DT; dissection time (cm²/min)

Figures

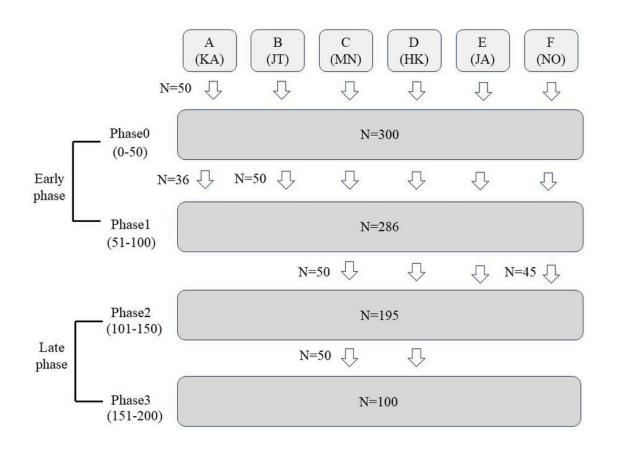


Figure 1

Study flow

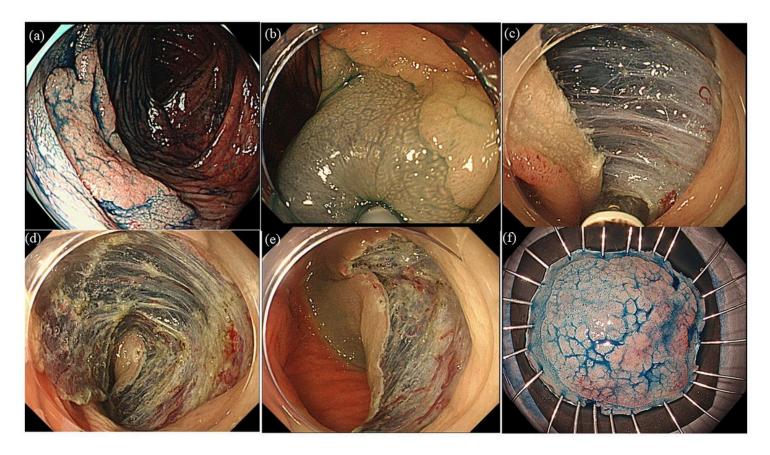


Figure 2

Endoscopic submucosal dissection of 40mm 0-IIa lesion treated by trainee

(a) 40mm, laterally spreading tumor-non granular type lesion

(b) An initial incision was started from the oral side because the approach to the oral side of the lesion was predicted to be more difficult.

(c) Next, a mucosal flap was created from the anal side.

(d) Efficient dissection was proceeded with the use of gravity traction (the uncut mucosa remains at 2 o'clock, indicating that tissue traction is being applied).

(e) Ulcer surface immediately after ESD. The resection was completed without adverse events within 45 minutes.

(f) The histopathology revealed an intramucosal carcinoma with negative margins.

ESD experience	78 cases		
Age, Sex	70 y.o., female	Strategy	A 40 mm large LST-NG lesion of mid-T that straddles the low colonic fold. The transverse colon is strongly curved and the scope can be easily slipped out. Left side,
Location	Transverse		stable visibility with the scope in a pushing position. At the time of examination, the lesion is oriented at 7 o'clock and the direction of gravity is in front of the lesion in the
Size	40mm		left side position. As time passes, the lesion may rotate to 11 o'clock. The right hand is often unable to release the scope, and it may be necessary to deflate the lumen. The first
Shape	LST-G-FE		step is to create a mucosal flap on the anal side. Local injection is performed on the ana side. The angle of the needle tip should be slightly angled to stand on the mucosal
Scope	PCF-Q260JI with single-ballon overtube		surface, and the depth of the local injection needle should be adjusted so that the local injection fluid enters well into a good submucosal layer. Because the lesion is large, the
Equipment	23G 4mm injection needle		needle tip is inserted as deep as necessary so that the local injection fluid can enter under the lesion (without spreading unnecessarily around the lesion). Bring the lesion as far as
Device	Tech knife 1.5mm		possible toward 6 o'clock and rotate the scope from left to right (counterclockwise) + angle manipulation to make the incision. Ideally, the tip of the sheath should hold the mucosa and be slightly dissected at the initial incision. The device is held out long
Reflextion points	After positioning the scope at a stable site, begin treatment. Do not start without careful consideration.		enough to form a flap. Then, the right front is dissected from the inside to the outside, exposing the fibers of the submucosal edge firmly, and the edge is now dissected from
Difficult situation	Because of the middle transverse colon, it is easy to pull out the scope and the lesion is relatively large. It		the outside to the inside.Once the scope is stable and can go under the mucosal flap, the endpoint incision of the lesion is placed. Going under the mucosal flap again, continue
Start point	If the approach to the oral side is easy, a mucosal flap is made on the anal side, but if the approach to the oral side is difficult, begin by making an end point on the oral side.		dissection from the edge, and once the lesion is fully dissected, make a final mucosal incision on the left side of the lesion to make a full circumferential incision. The remaining small amount of submucosa can be smoothly removed using the force of gravity, and the en bloc resection is completed.
Which areas of tissue traction should be left in place?	(Checking gravity) Leave the mucosa on the left side of the lesion.		
Traction device	not planned	Operating time (expected)	60min

Figure 3

The strategy note

Before ESD, the trainee simulates the target lesion in as much detail as possible and describes the simulation. The content is revised by the supervising physician before the procedure and modified as appropriate.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

• video.mp4