Endoscopic submucosal dissection with a grasping-type scissors for early colorectal epithelial neoplasms: a large single-center experience

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Background and aims: The Clutch Cutter (CC) can grasp, pull, coagulate, and incise targeted tissue with the use of electrosurgical current. It was developed as a biopsy technique to reduce the technical difficulty of endoscopic submucosal dissection (ESD) with knives. The aim of this study was to evaluate the efficacy and safety of ESD using the CC (ESD-CC) for early colorectal epithelial neoplasms (ECENs).

Methods: In this prospective study, we enrolled 437 consecutive patients with a diagnosis of ECEN between January 2009 and January 2018. They all satisfied the Japanese colorectal cancer treatment guidelines for ESD; namely, confirmation by preliminary endoscopy, EUS, and endoscopic biopsy. The CC was used for all steps of ESD (mucosal incision, submucosal dissection, and hemostatic treatment); therapeutic efficacy and safety were assessed.

Results: The en bloc resection rate was 99.3% (434/437), and the R0 resection rate was 87.0% (380/437). The mean operating time was 88.3 minutes. Perforation occurred in 10 cases (2.3%) and was managed with conservative medical treatment. Post-ESD-CC bleeding occurred in 10 cases (2.3%) and was successfully treated by endoscopic hemostatic treatment.

Conclusions: ESD-CC is a technically efficient, safe, and easy method for resecting ECEN. (VideoGIE 2019;4:486-92.)

The main problem of endoscopic submucosal dissection (ESD) with a conventional knife is its technical difficulty. Consequently, it is associated with a high rate of adverse events, foremost of which are long procedure time and the need for advanced endoscopic techniques.[1] Conventional knives such as the IT knife (Olympus, Tokyo, Japan) and needle-knife gently push the knife into the tissue and cut it with electrosurgical current. These cutting methods, without the grasping function (for accurate targeting and hemostatic effect), and pulling the target tissue away from the muscularis propria layer, carry a risk of major adverse events such as perforation and bleeding.[2] To reduce the risk of adverse events related to ESD with a conventional knife, a grasping-type scissors (Clutch Cutter [CC]), which can accurately grasp, pull, coagulate, and/or incise the targeted tissue by using electrosurgical current, was developed.[2] In our previous pilot study for early colorectal neoplasms, we resected tumors safely and easily without unintentional incision by ESD using the CC (ESD-CC).[3] However, the outcomes in large numbers of patients with early colorectal epithelial neoplasm (ECEN) treated by this new method of ESD-CC have not been previously reported. In this study, we assessed the clinical outcomes of ESD-CC for ECEN in a large population.

METHODS

Patients and lesions

A total of 437 consecutive patients with ECENs who underwent ESD-CC at Aso Iizuka Hospital between January 2009 and January 2018 were enrolled in this prospective study. Inclusion criteria for colorectal ESD were intramucosal adenoma and adenocarcinoma or superficial submucosal adenocarcinoma (SM1: <1 mm from the muscularis mucosae), diagnosed by preoperative colonoscopy with biopsy and EUS. Tumors were macroscopically divided into protruding large tumor (type 0–I), and 4 subtypes of laterally spreading tumor according to Kudo's classification: granular and homogenous type, granular and nodular mixed type, nongranular and flat elevated type, and nongranular and pseudodepressed type.[4]

CC short type

The CC short type (DP2618DT-35; Fujifilm, Tokyo, Japan) (Fig. 1) can grasp and cut or coagulate a piece of tissue with electrosurgical current. It has a 0.4-mm-wide and 3.5-mm-long serrated cutting edge to facilitate grasping the tissue.[2] The outer side of the forceps is insulated so that electrosurgical current energy is

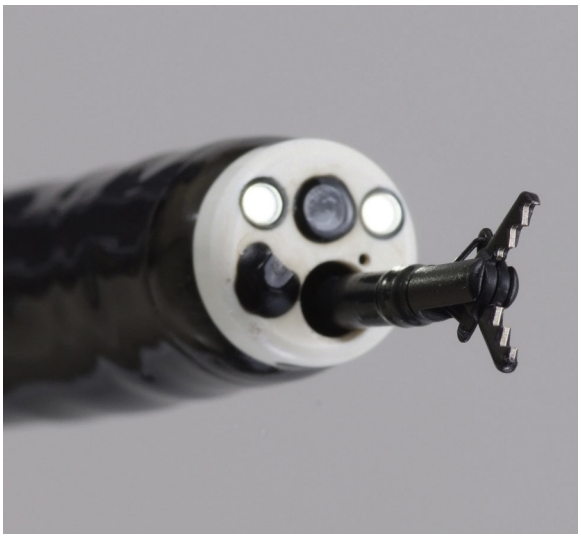

Figure 1. Distal tip of the short-type Clutch Cutter. The blade is 3.5 mm long. The serrated jaw provides accurate targeting (grasping). The outer side of the forceps is insulated so that electrosurgical current energy is concentrated at the blade to avoid burning the surrounding tissue. The forceps is rotatable to the desired orientation.

concentrated at the closed blade to avoid unintentional incision. This device is available for all steps of ESD. A high-frequency power supply (VIO300D; Erbe, Tübingen, Germany) was used. The endocut Q mode (effect 2, duration 3, interval 1) was used for cutting (mucosal incision and submucosal dissection), and the soft coagulation mode 100 W (effect 5) was used for precut-coagulation and hemostatic treatment.

ESD procedures

ESD-CC was carried out by use of a single-channel therapeutic endoscope with a single instrument channel and a water-jet system (EC-590MP; Fujifilm or PCF; Olympus) or double-balloon endoscope (EI-530B; Fujifilm) (Video 1, available online at www.VideoGIE.org). A long transparent hood (F-01; Top, Tokyo, Japan) or small-caliber-tip transparent hood (DH-15R; Fujifilm) was attached to the endoscopic tip to facilitate submucosal dissection by elevating the lesion. The reasons for using those hoods are (1) securing a field of view without air inflation, (2) ease of visualizing the target in front by suction without a retroflexion approach, (3) maintaining the optimum distance between the target and the tip of the endoscope, (4) obtaining a safe electric cut and coagulation space (intrahood ESD), and (5) obtaining up-and-down traction. The ESD-CC technique was performed as follows (Figs. 2, 3): 10% glycerin with 0.9% NaCl and 5% fructose (Glyceol; Chugai Pharmaceutical, Tokyo, Japan) or hyaluronic acid solution (MucoUp; Boston Scientific, Tokyo, Japan) mixed with a small volume of epinephrine and indigo carmine dye was injected into the submucosal

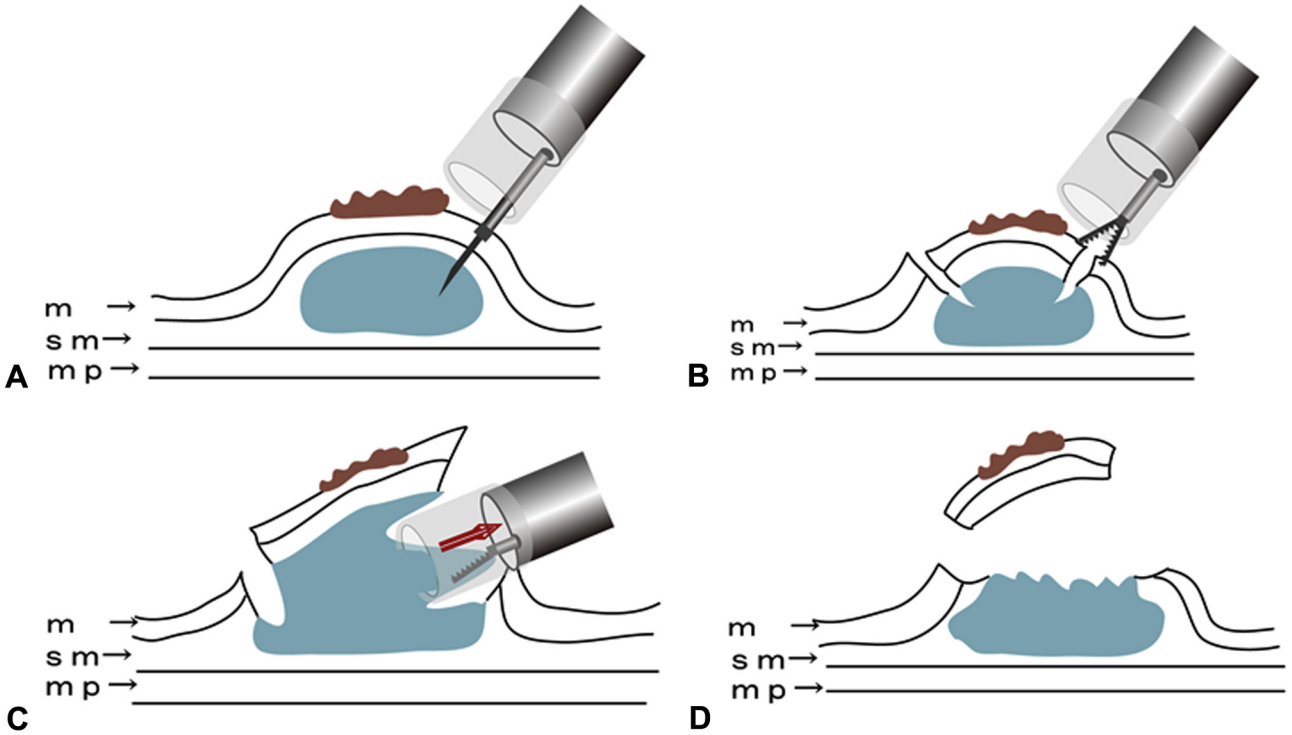

Figure 2. Basic technique of endoscopic submucosal dissection with the Clutch Cutter. **A**, Submucosal injection. **B**, Mucosal incision. **C**, Submucosal dissection. **D**, Resection of lesion in 1 piece. *Arrows* show the direction of pull. *m*, Mucosa; *sm*, submucosa; *mp*, muscularis propria.

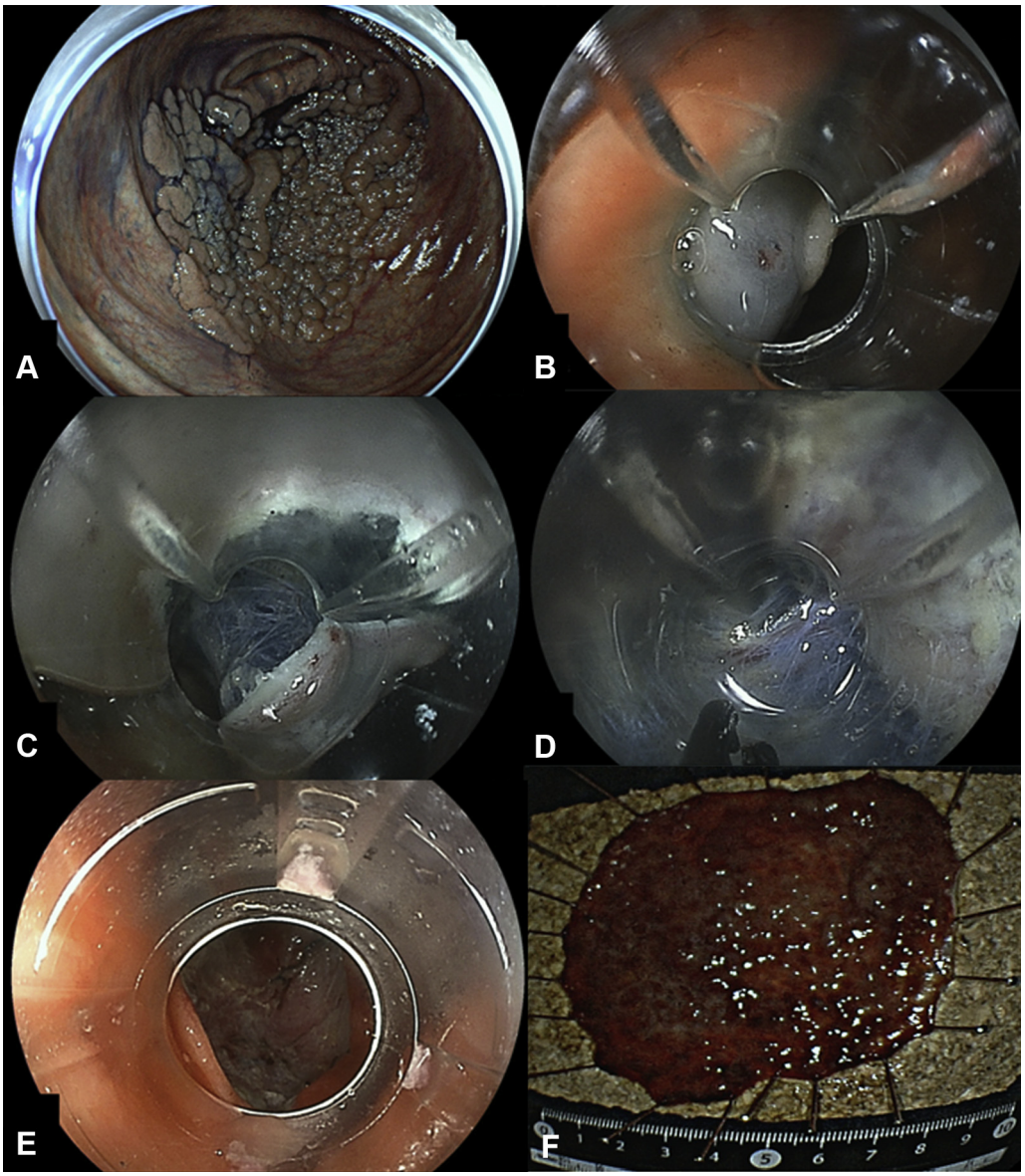

Figure 3. Endoscopic view of endoscopic submucosal dissection by use of the Clutch Cutter (CC) for granular and nodular mixed type laterally spreading tumor of the cecum. **A**, Chromoendoscopic view with indigo carmine revealing 50-mm tumor in the cecum. **B**, Lesion is lifted up by submucosal injection of hyaluronic acid solution. **C,** Mucosa is incised outside the tumor margin to separate the tumor from the surrounding nonneoplastic mucosa by use of the CC. **D**, Submucosal connective tissue immediately beneath the tumor is gradually dissected with the CC from the muscularis propria layer. **E**, Tumor is cut completely from the muscularis propria layer. **F**, Resected specimen showing en bloc resection of the tumor.

layer. Mucosal incision and submucosal dissection were performed to completely remove the lesion with the CC. The bleeding artery or vein was grasped, pulled/lifted, and coagulated with the CC by the use of electrosurgical current to stop the bleeding. Finally, the lesion was completely resected. All the cutting steps consisted of (1) grasping, (2) pulling or lifting up, (3) precut-coagulation with soft coagulation (if presence of a blood vessel was suspected), and (4) cutting with endocut Q.

Histopathologic evaluation

The excised specimens were sectioned perpendicularly at 2-mm intervals. Tumor size, depth of invasion, histologic type, lymphatic and vascular involvement, and tumor involvement in the horizontal and vertical margins were assessed. Histologic diagnoses were based on the Japanese Classification of Cancer of the Colon and Rectum.[5]

Assessment of therapeutic efficacy and adverse effects

The operating time was calculated as the time from the beginning of submucosal injection to the end of submucosal dissection. Resection was defined as en bloc when the lesion was resected in 1 piece and the resection margins were macroscopically tumor free. Resection was considered tumor free (R0) when the lateral and vertical margins

TABLE 1. Clinicopathologic characteristics (N = 437)

Sex, male/female	250/187
Mean age, years ± SD (range)	69.3 ± 9.4 (39–93)
Histologic type of lesion (%)	
Differentiated type adenocarcinoma	188 (43)
Adenoma	249 (57)
Depth of invasion (%)	
Mucosa	384 (88)
Superficial submucosa (SM1)	31 (7)
Deep submucosa (SM2<)	22 (5)
Morphologic type (%)	
0–I	65 (15)
LST-GH	107 (25)
LST-GM	105 (24)
LST-NG-F	97 (22)
LST-NG-PD	63 (14)
Size of lesion, mm (%)	
0–20	175 (40)
21–40	205 (47)
≥41	57 (13)
Location of lesion (%)	
Rectum	114 (26)
Sigmoid colon	100 (23)
Descending colon	25 (6)
Transverse colon	55 (12)
Ascending colon	92 (21)
Cecum	51 (12)

SD, Standard deviation; *LST,* laterally spreading tumor; *GH*, granular and homogenous type; *GM,* granular and nodular mixed type; *NG-F,* nongranular and flat elevated type; *NG-PD,* nongranular and pseudo-depressed type.

of a specimen were both negative for tumor cells, independently of its histologic features.

Intra-ESD perforation was diagnosed endoscopically. Post-ESD perforation was diagnosed by abdominal pain and/or the presence of free air on plain radiography and/or CT after ESD. Perforations detected during ESD were immediately closed with a clip, and the patient was given antibiotics. Post-ESD bleeding was defined as clinical evidence of bleeding after ESD that required endoscopic hemostasis. After ESD, all patients stayed in the hospital and were prohibited from eating until 2 days after ESD. At that time, they were permitted soft food orally and were discharged 7 days after the procedure.

For evaluating the learning curve of ESD-CC, 437 cases were grouped chronologically into 8 periods: 1, cases 1 to 50; 2, cases 51 to 100; 3, cases 101 to 150; 4, cases 151 to 200; 5, cases 201 to 250; 6, cases 251 to 300; 7, cases 301 to 350; and 8, cases 351 to 437.

Statistical analysis

The χ^2 test, Fisher exact test, trend test, and Kruskal-Wallis test were used for statistical analyses as appropriate with the statistical software package (SAS version 9.2 and JMP version 8.0.1, SAS Institute Inc, Cary, NC, USA). A *P* value of less than .05 was considered to be significant.

TABLE 2. Technical results of ESD with use of the Clutch Cutter (N = 437)

Mean ± SD size of the lesion, mm (range)	26.5 ± 13.0 (6–95)
Mean ± SD size of resected specimen, mm (range)	36.7 ± 13.5 (10–103)
En bloc resection rate (%)	434/437 (99.3)
R0 resection rate (%)	380/437 (87.0)
Mean operating time, minutes (range)	88.3 ± 66.3 (11–549)
Complication rate (%)	20/437 (4.6)
Perforation rate (%)	10/437 (2.3)
Intra-ESD perforation rate (%)	8/437 (1.8)
Post-ESD perforation rate (%)	2/437 (0.5)
Bleeding rate (%)	10/437 (2.3)
Intra-ESD uncontrollable bleeding rate (%)	0/437 (0)
Post-ESD bleeding rate (%)	10/437 (2.3)

ESD, Endoscopic submucosal dissection; *SD,* standard deviation.

Ethical approval

This study was carried out at Aso Iizuka Hospital and was approved by its ethics committee (registration No 12120). Written, informed consent was obtained from all the patients in accordance with the Declaration of Helsinki.

RESULTS

The patients' clinicopathologic characteristics are shown in Table 1. The technical outcomes are summarized in Table 2. The grasping and pulling or lifting up steps before the targeted tissue was cut provided accurate cutting of the target area and allowed the use of sufficient precut coagulation. The en bloc resection rate was 99.3%, and the R0 resection rate was 87.0%. Twenty-seven cases showed R1 resection. The number of cases of lateral-margin positive, vertical-margin positive, and both lateral- and vertical-margin positive were 22, 3, and 2, respectively. The mean operating time was 88.3 minutes. Perforation occurred in 10 cases (2.3%) and was managed with endoscopic clipping and conservative medical treatment. Post-ESD-CC bleeding occurred in 10 cases (2.3%) and was successfully treated by endoscopic hemostatic treatment. Technical parameters according to clinicopathologic factors are shown in Table 3. The learning curve showed the changes in proficiency over time (Fig. 4, Table 4). There was a statistically significant proficiency in operating time only, not in the R0 resection rate and perforation rate.

TABLE 3. Technical parameters for ESD with the Clutch Cutter according to clinicopathologic factors (N = 437)

Characteristic	R0 resection rate (%)	Mean operating time ± SD, min (range)	Perforation rate (%)	Post-ESD bleeding rate (%)
Tumor size, mm				
0–20	157/175 (89.7)	66.5 ± 46.3 (11–311)	5/175 (3)	5/175 (3)
21–40	175/205 (85.4)	87.8 ± 54.2 (20–337)	2/205 (1)	3/205 (1)
≥41	48/57 (84.2)	157.0 ± 102.8 (34–549)	3/57 (5)	2/57 (4)
P value	NS (0.35)	< 0.001	NS (0.102)	NS (0.45)
Histologic type				
Adenoma	209/249 (83.9)	90.5 ± 65.8 (11–405)	7/249 (3)	4/249 (2)
Adenocarcinoma	171/188 (90.9)	85.5 ± 67.0 (14–549)	3/188 (2)	6/188 (3)
P value	< 0.05 (0.032)	NS (0.54)	NS (0.53)	NS (0.34)
Morphologic type				
0–I	55/65 (84.6)	56.1 ± 38.6 11–228)	0/65 (0)	2/65 (3)
LST-GH	93/107 (86.9)	97.1 ± 80.5 (19–388)	1/107 (1)	1/107 (1)
LST-GM	91/105 (86.7)	91.4 ± 66.6 (20–480)	2/105 (2)	1/105 (1)
LST-NG-F	83/97 (85.6)	96.1 ± 68.0 (24–337)	6/97 (6)	4/97 (4)
LST-NG-PD	58/63 (92.1)	89.7 ± 48.5 (27–270)	1/63 (2)	2/63 (3)
P value	NS (0.74)	< 0001	NS (0.102)	NS (0.44)
Location				
Rectum	99/114 (86.8)	81.4 ± 72.1 (11–549)	0/114 (0)	4/114 (3)
Sigmoid colon	88/100 (88.0)	74.6 ± 56.1 (11–317)	1/100 (1.0)	4/100 (4)
Descending colon	22/25 (88.0)	119.2 ± 75.9 (26–282)	2/25 (8.0)	0/25 (0)
Transverse colon	50/55 (90.9)	101.1 ± 66.8 (21–337)	2/55 (4.0)	0/55 (0)
Ascending colon	74/92 (80.4)	90.3 ± 65.7 (26–405)	4/92 (4.3)	2/92 (2)
Cecum	47/51 (92.2)	98.4 ± 60.4 (31–388)	1/51 (1.9)	0/51 (0)
P value	NS (0.41)	< 0001	< 0.05 (0.038)	NS (0.55)

Statistical significance was analyzed by the χ^2 test or Kruskal-Wallis test.
ESD, Endoscopic submucosal dissection; *SD,* standard deviation; NS, not significant; *LST,* laterally spreading tumor; *GH,* granular and homogenous type; *GM,* granular and nodular mixed type; *NG-F,* nongranular and flat elevated type; *NG-PD,* nongranular and pseudo-depressed type.

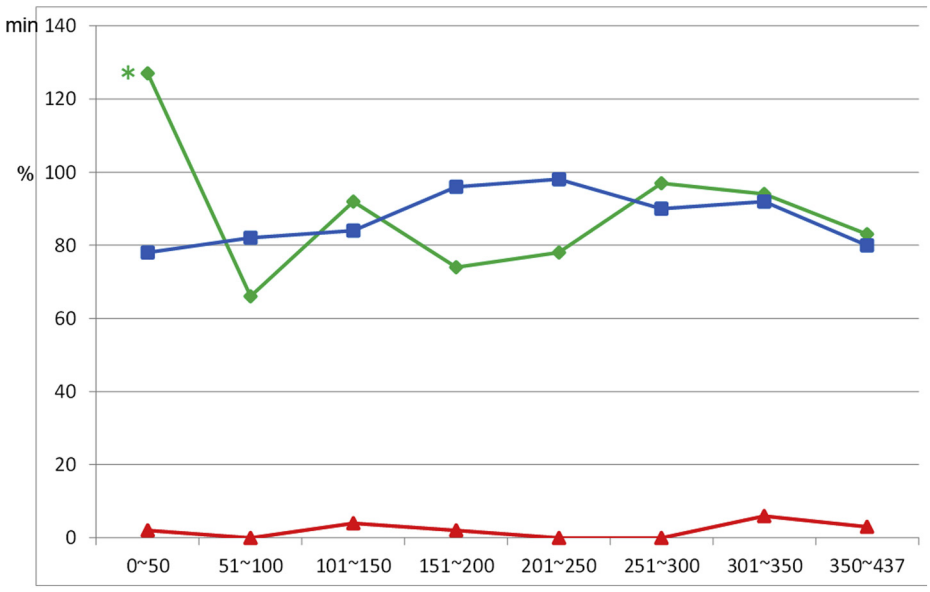

Figure 4. Learning curve of endoscopic submucosal dissection with Clutch Cutter for early colorectal epithelial neoplasms. ◆ Operating time (*P = .0004). ■ R0 resection rate (P = .428). ▲ Perforation rate (P = .284). Statistical significance was analyzed by the Kruskal-Wallis test or the trend test.

TABLE 4. Baseline demographic data of each period

Period	1	2	3	4	5	6	7	8	*P* value
Endoscopists									
Expert, n	4	4	4	5	5	5	3	3	
Nonexpert, n	2	5	5	7	11	12	8	9	.728
Tumor size, mm									
≤20	22	13	19	15	23	22	20	41	
>20	28	37	31	35	27	28	30	36	.211
Tumor histology									
Adenoma	35	13	33	32	30	25	32	49	
Adenocarcinoma	15	37	17	18	20	25	28	38	< .001
Tumor location									
Rectum	16	19	11	11	11	11	12	23	
Sigmoid colon	9	12	11	9	14	15	12	18	
Descending colon	5	2	5	3	0	2	2	6	
Transverse colon	3	4	10	4	4	9	10	11	
Ascending colon	12	7	7	15	13	10	8	20	
Cecum	5	6	6	8	8	3	6	9	.534

Statistical significance was analyzed by the Fisher exact test.

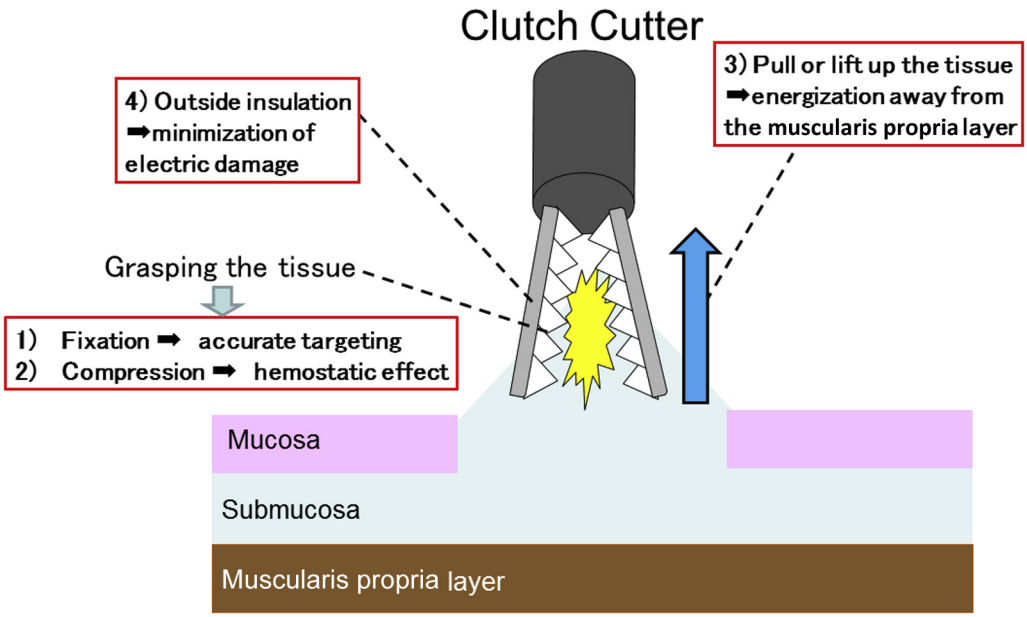

Figure 5. Safety mechanisms of the Clutch Cutter.

DISCUSSION

ESD with a knife is more technically demanding than EMR with a snare, and it carries a substantial risk of perforation and bleeding.[1] ESD-CC has 4 safety mechanisms (Fig. 5): (1) fixation by grasping (grasping the target tissue brings accurate targeting); (2) compression by grasping (high hemostatic capability); (3) pulling or lifting up (energization away from the muscularis propria layer reduces risk of perforation); and (4) outside insulation (minimization of outside electric damage).[2] In this study, we were able to stop intraoperative bleeding quickly and easily using the CC without changing the hemostatic forceps (Video 1). Therefore, it is possible to perform all steps of ESD with the CC only (1-device ESD method).

The overall en bloc and R0 resection rates of ESD-CC were high (>85%). Furthermore, the R0 resection rate by ESD-CC was high (>80%) irrespective of the differences in tumor size, morphologic type, and location.

Perforation is a major adverse event when knives are used; the reported frequency is 5.2%.[1,6] The perforation rate of ESD-CC was 2.3% in the present study. To prevent perforation, it is necessary to avoid unintentional electric sparking to the muscularis propria layer. The safety mechanisms of CC, such as the fixation and pulling effect and the outside insulation, are effective in preventing perforation. In our ESD-CC study, we observed perforation in 10 patients (2.3%), mainly caused by misidentification of the muscularis propria layer as fibrotic tissue. These patients were successfully treated by immediate closure of the perforation by endoscopic clipping and medical treatment without surgical intervention. The perforation rate of tumors in the ascending, transverse, or descending colon was high (4%–8%). In such difficult locations, special attention must be paid to perform ESD, and it is desirable to use a special strategy such as the pocket creation method.[7]

Bleeding is the remaining major adverse event of ESD. The prevention and immediate hemostasis of any intra-ESD bleeding is vital because bleeding can impair the endoscopic view, resulting in increased operating time and ESD-related perforation.[2] The CC has accurate and effective hemostatic mechanisms, as just described. Therefore, we were able to perform effective precut coagulation and stop unintentional bleeding immediately using the CC without changing the hemostatic forceps. There were no significant differences in the post-ESD bleeding rate of ESD-CC in relation to tumor size, histologic type, morphologic type, and location.

Previous studies showed the learning curve of ESD when knife devices were used, resulting in decreased operating time and perforation rate, and increased rate of R0 resection over time.[8] However, ESD-CC is a simple technique like a standard bite biopsy. Therefore, we obtained flat learning curves with a high R0 resection rate and low perforation rate from the introduction period of ESD-CC, because of the ease of learning, although we had little experience of conventional knife ESD (<30 cases in gastric ESD). Operating time was shortened after our experience with over 50 patients, and we maintained the flat learning curve. Thus, ESD-CC is a safe and effective way for facilities to introduce ESD for the first time.

Conventional ESD needs several specific knives or hemostatic forceps for each step.[1,2,6] In contrast, ESD-CC can be performed by a single device, the CC.[2,3] In this study, we used only the CC device in all steps of ESD. The ESD-CC reduces the number of devices and the cost of ESD.

In conclusion, the results of our single-center, large series study suggest that ESD-CC is an excellent endoscopic treatment of ECENs because it is a single-device method, effective, safe, and technically simple to perform.

DISCLOSURE

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Abbreviations: CC, clutch cutter; ESD, endoscopic submucosal dissection; ESD-CC, endoscopic submucosal dissection using clutch cutter; ECEN, early colorectal epithelial neoplasm.

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