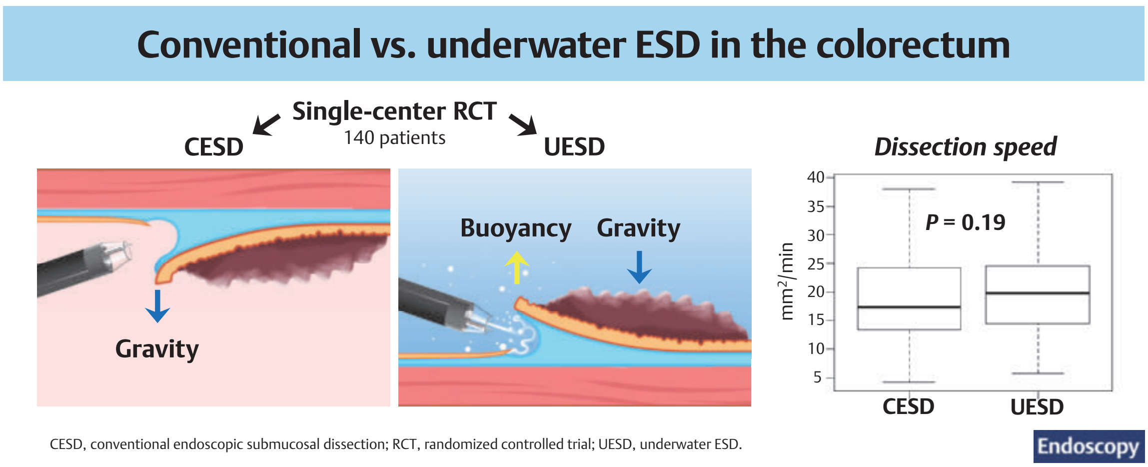
Prospective randomized trial comparing conventional and underwater endoscopic submucosal dissection for superficial colorectal neoplasms

OPEN ACCESS

GRAPHICAL ABSTRACT



CESD, conventional endoscopic submucosal dissection; RCT, randomized controlled trial; UESD, underwater ESD.

Authors
Mitsuru Nagata[1], Masayuki Namiki[2], Tomoaki Fujikawa[2], Hiromi Munakata[2]

Institutions
1 Endoscopy, Shonan Fujisawa Tokushukai Hospital, Fujisawa, Japan
2 Center for Digestive and Hepato-Biliary-Pancreatic Disease, Shonan Fujisawa Tokushukai Hospital, Fujisawa, Japan

received 13.6.2024
accepted after revision 17.10.2024
accepted manuscript online 18.10.2024
published online 2024

Bibliography
Endoscopy
DOI 10.1055/a-2445-4970
ISSN 0013-726X

Supplementary Material
Supplementary Material is available at https://doi.org/10.1055/a-2445-4970

Corresponding author
Mitsuru Nagata, MD, Department of Endoscopy, Shonan Fujisawa Tokushukai Hospital, 1-5-1, Tsujidokandai, Fujisawa, Kanagawa, 251-0041, Japan
mitsuru10jp@yahoo.co.jp

ABSTRACT

Background and study aims This study compared procedure-related outcomes of conventional and underwater endoscopic submucosal dissection (ESD) for superficial colorectal neoplasms (SCNs).

Patients and methods In this single-center, randomized controlled trial, patients with SCNs meeting the indications of the Japanese guidelines for ESD were randomly assigned to undergo conventional ESD (CESD) or underwater ESD (UESD) performed by an expert. The primary endpoint was dissection speed, defined as the specimen area per ESD time.

Results We analyzed the data of 69 and 70 CESD and UESD cases, respectively; however, no significant differences were found in median dissection speed (17.4 and 19.9 mm^2/min, respectively; $P = 0.19$). Multiple regression analysis revealed that the suitable positional relationship between the lesion and the direction of gravity (nongravity side for CESD and gravity side for UESD) was independently and positively associated with dissection speed ($P < 0.001$). En bloc resection was achieved without perforation in all cases. The incidence of post-ESD coagulation syndrome was not significantly different between the two groups (4.3% vs. 2.9%, respectively; $P = 0.68$).

Conclusions UESD did not expedite dissection speed in the overall patient population. CESD and UESD may be complementary in the colorectum depending on the positional relationship between the lesion and the direction of gravity.

Introduction

Endoscopic submucosal dissection (ESD) is a minimally invasive procedure for resecting superficial colorectal neoplasms (SCNs), with conventional ESD (CESD) for SCNs performed with CO_2 insufflation [1]. CESD does however have disadvantages, such as visual field impairment due to halation and post-ESD coagulation syndrome (PECS) [2]. Moreover, if the lesion is on the gravity side, gravity obstructs the opening of the mucosal flap, and fluid collects around the lesion, impairing the visual field.

Underwater ESD (UESD) using saline is a newly developed method that offers a magnified visual field without halation, heat-sink effect, and buoyancy [3]. A retrospective study revealed that UESD improved the speed of submucosal dissection and decreased PECS compared with CESD in the resection of SCNs [4]. We hypothesized that UESD would expedite submucosal dissection compared with CESD. Therefore, we conducted a randomized controlled trial (RCT) comparing CESD and UESD among patients with SCNs, with dissection speed as the primary end point.

Methods

Study design and study population

This was a prospective, single-center (Shonan Fujisawa Tokushukai Hospital, Kanagawa, Japan), parallel two-arm (with 1:1 allocation ratio), open-label RCT. Computer-based block randomization was performed using a block size of four without stratification. This RCT was approved by the institutional review board on 20 August 2019.

Patients with SCNs, diagnosed during preoperative endoscopy as potentially mucosal or slightly submucosal invasive carcinoma, for which en bloc resection with snare endoscopic mucosal resection would be difficult to perform, were selected for eligibility for the study and to undergo ESD [5]. We included patients meeting the following criteria: age 20–94 years; no recurrent lesion after an endoscopic treatment; no complication of inflammatory bowel disease; lesion not extending to the appendix or ileum; and written informed consent provided by the patient. Patients meeting the following criteria were excluded: pregnant or potentially pregnant women; lactating women; previous enrollment in this study; and deemed ineligible for a specific reason.

End points

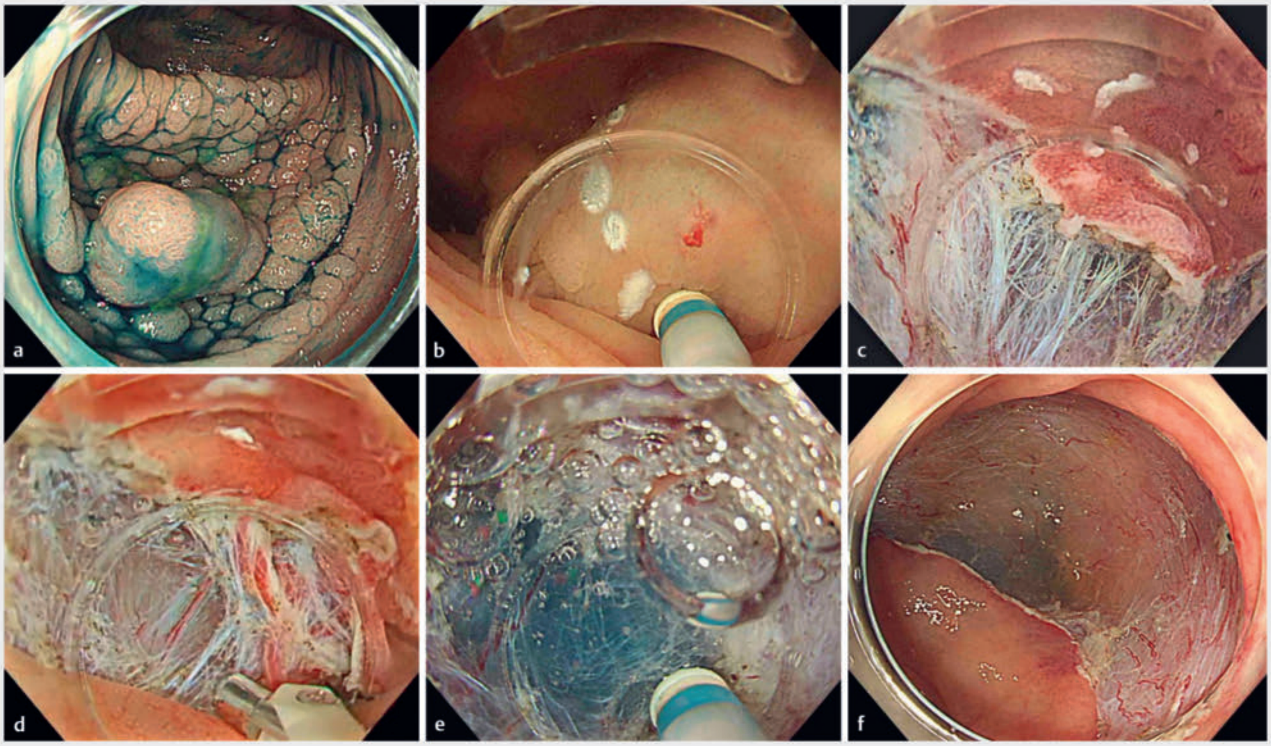
The primary end point was dissection speed. The predefined secondary end points were ESD time; en bloc resection; complete resection; post-ESD bleeding; perforation; PECS; mucosal flap creation time; quantity of saline; quantity of submucosal injection solution; frequency of hemostasis; recovery time after active bleeding; variations in white blood cell (WBC) count, C-reactive protein (CRP) level, and sodium level between the day of ESD and the day after; subgroup analysis for dissection speed and ESD time according to the positional relationship between the lesion and the direction of gravity (gravity side vs. nongravity side), submucosal fibrosis (absence vs. presence), and lesion location (rectum vs. left colon vs. right colon).

Definitions

Dissection speed was defined as the specimen area per ESD time; ESD time was the time from the first injection to the completion of submucosal dissection. The interval times were recorded by an independent observer and double-checked using video recordings. The number of interventions and times related to the end points were also measured using video recordings. The specimen area was calculated using the ellipse formula. Complete resection was defined as en bloc resection with pathologically negative lateral and vertical margins.

Perforation was diagnosed on endoscopy if a type IV or V injury according to the Sydney classification of deep mural injury [6] was observed, or radiographically if the presence of free air was observed. Post-ESD bleeding was defined as that requiring endoscopic intervention to achieve hemostasis. PECS was defined as local abdominal pain occurring around the ESD site within 4 days postoperatively without definite evidence of perforation [2].

The mucosal flap creation time was described as the time from the first mucosal incision on the side to create the mucosal flap to the time that the endoscope tip could completely enter the submucosal space. The frequency of hemostasis was the number of times hemostatic forceps were required. The recovery time after active bleeding indicated the interval from when hemostasis was initiated to the resumption of ESD (submucosal injection, mucosal incision, or submucosal dissection). The gravity direction was determined as the side where fluid accumulation occurred, with the positional relationship of the lesion being classified as either gravity side or nongravity side



▶ **Fig. 1** Endoscopic images of underwater endoscopic submucosal dissection (UESD) showing: **a** a laterally spreading tumor located in the cecum (granular type, 32 mm in diameter) sprayed with indigo carmine; **b** mucosal incision using a straight-needle-type electrosurgical knife being performed while confirming the marking dots around the lesion; **c** underwater conditions, which offer a magnified visual field without halation and a wider gap in the incised mucosa as it is opened by the water pressure despite the presence of submucosal fibrosis; **d** bipolar hemostatic forceps being applied, which can coagulate vessels even in saline immersion conditions; **e** visual field impairment that is caused by air bubbles generated by energizing the electrosurgical knife; **f** the defect with no evidence of perforation after en bloc resection of the lesion.

(intermediate and opposite to the gravity side). The degree of submucosal fibrosis was classified as: F0, absence; F1, mild; or F2, severe [7]. The degree of submucosal fatty tissue was classified as: grade 0, absence; grade 1, mild; or grade 2, severe [8]. The degree of endoscope maneuverability was categorized as good or poor.

Colorectal ESD perioperative settings

The patients were hospitalized on the day before ESD. Blood tests were performed on the day of the ESD and the day after. A chest radiograph was also performed on the day after ESD.

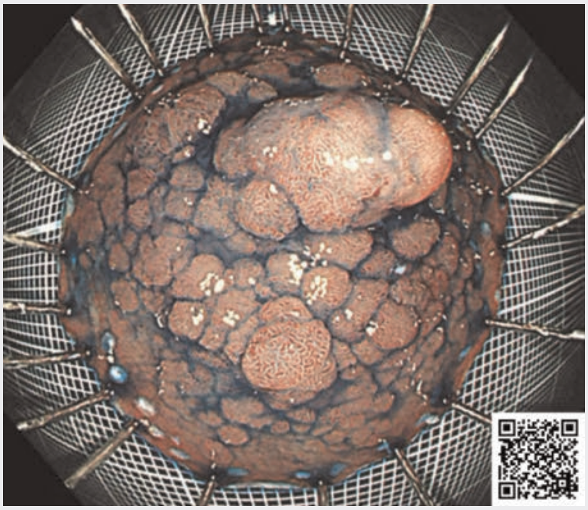
All ESD procedures were performed by a single endoscopist (M.N.) who had an accumulated experience of >900 ESD procedures, including >50 UESD procedures for SCNs, at the beginning of the trial. A therapeutic endoscope (PCF-H290ZI or GIF-Q260J; Olympus, Tokyo, Japan) with a tapered hood (DH-28GR or DH-29CR; Fujifilm, Tokyo, Japan) and a straight-needle electrosurgical knife (DualKnife, KD-650L; Olympus) was used for ESD. Monopolar (Coagrasper, FD-411QR; Olympus) and bipolar hemostatic forceps (Tighturn, RH8C40; Zeon Medical, Tokyo, Japan) were used for CESD and UESD, respectively. A VIO300 D (ERBE Elektromedizin GmbH, Tübingen, Germany) was used as the electrosurgical generator. Hyaluronic acid (0.4%; MucoUp; Boston Scientific, Marlborough, Massachusetts, USA) was used for submucosal injection.

In both intervention groups, the operator was allowed to change the default ESD method or electrosurgical knife only when this was required to prioritize patient safety when experiencing technical difficulties, such as submucosal fibrosis, poor endoscope maneuverability, difficulty in securing the visual field, and perforation. Traction devices were not used.

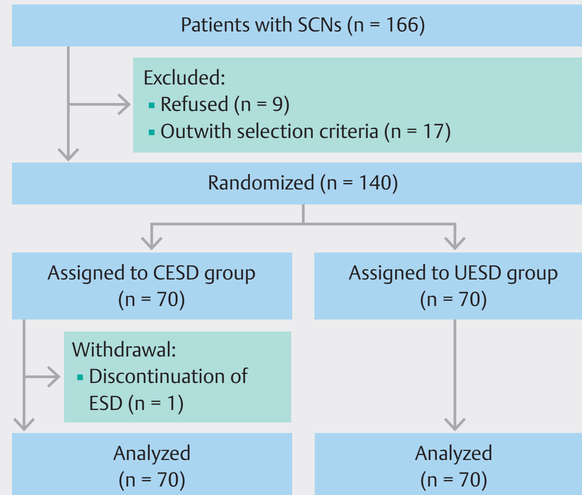
ESD procedure

The UESD procedure was performed as previously reported (▶ **Fig. 1**; ▶ **Video 1**) [3], with saline used to create the underwater conditions. Whenever possible, the patient's posture was adjusted to set the lesion on the gravity side. Submucosal dissection was performed in underwater conditions, and submucosal injection and mucosal incision were performed under gas (CO_2) or underwater conditions. If the visual field was lost because of bleeding, underwater conditions were switched to gas conditions. Hemostasis was then performed using hemostatic forceps or a knife while pressing the bleeding point using the hood tip. When hemostasis was achieved, saline replacement was performed.

In CESD, all procedures not specific to CESD were conducted as described in the UESD procedure. Whenever possible, the



▶ **Video 1** Underwater endoscopic submucosal dissection (UESD) is performed for a laterally spreading tumor (granular type, 32 mm in diameter) located at the cecum.
Online content viewable at:
https://doi.org/10.1055/a-2445-4970



▶ **Fig. 2** Flowchart of patient enrollment and group allocation. SCN, superficial colorectal neoplasm; ESD, endoscopic submucosal dissection; CESD, conventional ESD; UESD, underwater ESD.

patient's posture was adjusted to place the lesion on the side opposite to the direction of gravity.

Statistical analysis

In our pilot study, the mean dissection speed of the UESD group was 2.9 mm^2/min faster than that of the CESD group, with a common SD of 5.8mm^2/min. To ensure a power of 80% with a 5% two-sided error, we required 126 participants. Therefore, the final sample was 140 participants to allow for a dropout rate of approximately 10%.

We performed an intention-to-treat (ITT) analysis, except for a patient for whom the ESD procedure was discontinued. Multiple regression analysis was performed to identify the factors that affected dissection speed. The exploratory variables included: submucosal fibrosis and endoscope maneuverability, which have been identified as factors contributing to the difficulty of colorectal ESD [9]; the ESD method; suitable positional relationship between the lesion and the direction of gravity (nongravity side for CESD and gravity side for UESD); lesion location; and submucosal fatty tissue.

All statistical analyses were performed using R version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria). Categorical variables were analyzed using Fisher's exact test and are presented as numbers and percentages. Continuous variables are expressed as median (interquartile range), and differences between the groups were analyzed using the Mann–Whitney *U* test. All tests were two-sided, and differences between variables were considered statistically significant at $P<0.05$.

Results

Overall outcomes

▶ **Fig. 2** presents the flowchart for patient enrollment. Between 26 November 2019 and 11 October 2023, 140 patients were enrolled in the study and randomly assigned to the CESD or UESD groups. In the CESD group, one patient was excluded from the analysis as ESD was discontinued because of a muscle-retracting sign [10]. The baseline characteristics were well balanced between the two groups (▶ **Table 1**).

Three cases were temporarily converted to UESD in the CESD group, whereas four were temporarily converted to CESD in the UESD group. Procedure-related outcomes are shown in ▶ **Table 2**. The median dissection speed for the CESD and UESD groups were 17.4 and 19.9mm^2/min, respectively ($P=0.19$). No significant differences were found in complete resection, post-ESD bleeding, perforation, PECS, mucosal flap creation time, and endoscope maneuverability between the two groups. There were trends toward a higher frequency of hemostasis and longer recovery time after bleeding in the UESD group. The median variation in WBC count between the day of ESD and the following day was significantly lower in the UESD group than in the CESD group.

We also performed a per-protocol analysis for procedure-related outcomes in patients who received the allocated treatment, and the results were similar to those of the ITT analysis (**Table 1s**, see online-only Supplementary material).

Subgroup analysis

Tables 2s and **3s** present the results of the subgroup analysis. The UESD group demonstrated significantly faster dissection speed for gravity-side lesions, whereas the CESD group demonstrated significantly faster dissection speed for nongravity-side

▶ **Table 1** Baseline characteristics of the patients who were analyzed in the conventional (CESD) and underwater endoscopic submucosal dissection (UESD) groups.

	CESD n = 69	**UESD n = 70**
Age, median (IQR), years	71 (63–78)	71 (61–79)
Sex, female, n (%)	31 (44.9)	38 (54.3)
Tumor size, median (IQR), mm	26 (23–31)	25 (20–30)
Lesion location, n (%)		
▪ Rectum	11 (15.9)	8 (11.4)
▪ Left colon	12 (17.4)	15 (21.4)
▪ Right colon	46 (66.7)	47 (67.1)
Morphology, n (%)		
▪ Flat and/or depressed[1]	39 (56.5)	34 (48.6)
▪ Elevated[2]	30 (43.5)	36 (51.4)

IQR, interquartile range.
[1] Laterally spreading tumors (nongranular type) are included in this category.
[2] Laterally spreading tumors (granular type) and 0-I are included in this category.

lesions. For rectal lesions, the UESD group had a significantly faster dissection speed than the CESD group.

Multivariate analysis

Table 4s shows the results of multiple regression analysis (*F* statistic; P<0.001; adjusted R^2 = 0.41; all variance inflation factors were <1.3). Endoscope maneuverability, the lesion being in a suitable position with respect to gravity, and submucosal fibrosis were independently associated with dissection speed.

Discussion

The hypothesis that UESD expedites submucosal dissection compared with CESD could not be demonstrated in this study. This result could be attributed to two possible reasons. First, in the UESD group, the recovery time after active bleeding tended to be longer with a higher frequency of hemostasis. Second, air bubbles generated by mainly submucosal dissection during UESD impaired the visual field, particularly when they accumulated in the hood. Once air bubbles were trapped inside the hood, operators had to remove them to secure the visual field; however, this step was occasionally challenging and time-consuming. Because the coagulation mode (e. g. Swift coagulation) generates more air bubbles than the cut mode (e. g. Endocut I), there can be a hesitation to apply coagulation mode for submucosal dissection, resulting in insufficient coagulation of vessels. Such an event would increase the frequency of hemostasis in the UESD group. Nevertheless, the increase in dissection speed (2.5 mm^2/min), even with these issues, may be clinically relevant, and further advancements in underwater devices or techniques could enhance dissection speed. Novel solutions for air bubble removal have recently been reported [11, 12, 13, 14] and the use of gel immersion may also facilitate the management of bleeding [15]; however, these solutions need to be validated in further studies.

The results of subgroup and multiple regression analyses imply the possible complementarity of the two techniques depending on the positional relationship between the lesion and the direction of gravity. On the gravity side, UESD may be more advantageous than CESD as complete submergence is easily achieved. Furthermore, buoyancy favorably opens the mucosal flap and provides natural traction on the dissection plane. Conversely, gravity will droop the mucosal flap and cause visual field impairment owing to fluid collection when performing CESD. On the nongravity side, CESD may be more advantageous than UESD as it prevents visual field impairment due to fluid collection. Furthermore, gravity can help open the mucosal flap and provide natural traction, especially when the lesion is on the side opposite the direction of gravity. Performing UESD causes air bubbles to accumulate and form air pockets around the lesion, causing difficulty in maintaining the underwater conditions. Moreover, buoyancy working against gravity will hinder the opening of the mucosal flap.

Although the gravity direction can be adjusted by changing the patient's posture, this step can alter endoscope maneuverability or the approach angle to the lesion, occasionally causing difficulties. Consequently, selecting the most suitable posture for the patient based on the positional relationship between the lesion and the direction of gravity is difficult. Indeed, 23% of patients in the CESD group underwent ESD on the gravity side, and 20% in the UESD group underwent ESD on the nongravity side. In clinical practice, endoscopists can use either UESD or CESD depending on the situation. Therefore, UESD can be performed as a rescue therapy for CESD [16].

Faster dissection speed was observed in the UESD group for rectal lesions; however, this result may be unimportant because the endoscope maneuverability or the approach angle to the lesion is less affected within the rectum by changing the patient's posture.

Factors that make CESD challenging include not only lesions on the gravity side but also submucosal fibrosis and poor endoscope maneuverability [9]. UESD may facilitate safe and effective submucosal dissection even where there is severe submucosal fibrosis [17] and a degassed colorectal lumen is expected to improve endoscope maneuverability; however, UESD was not associated with faster dissection speed for lesions with submucosal fibrosis and did not demonstrate an improvement in endoscope maneuverability. Combining UESD and traction devices [18] or the pocket-creation method (PCM) [19] may however be effective because traction devices help open the narrow submucosal space, and the PCM can improve endoscope maneuverability. Internal traction devices that do not require reinsertion are easy to apply in the colorectum, and those made of mild elastic material (e. g. double clip and rubber band [20]) may provide sufficient traction force in the collapsed colorectal lumen in UESD.

► **Table 2** Comparison of procedure-related outcomes between the conventional (CESD) and underwater endoscopic submucosal dissection (UESD) groups.

	CESD n = 69	UESD n = 70	*P* value
Dissection speed, median (IQR), mm^2/min	17.4 (13.3–24.2)	19.9 (14.4–24.6)	0.19
ESD time, median (IQR), minutes	55.5 (33.9–75.4)	48.3 (33.8–66.3)	0.38
Mucosal flap creation time, median (IQR), minutes	4.2 (1.8–8.3)	3.5 (2.1–6.5)	0.29
Positional relationship, n (%)			**<0.001**
▪ Gravity side	16 (23.2)	56 (80.0)	
▪ Nongravity side	53 (76.8)	14 (20.0)	
Saline used, median (IQR), mL	100 (50–210)	900 (613–1590)	**<0.001**
Submucosal injection solution used, median (IQR), mL	45 (30–59)	33 (25–50)	0.06
Hemostasis requirements[1]			0.25
▪ 0	47 (68.1)	40 (57.1)	
▪ 1	17 (24.6)	16 (22.9)	
▪ 2	4 (5.8)	10 (14.3)	
▪ 3	0 (0.0)	2 (2.9)	
▪ 4	1 (1.4)	2 (2.9)	
Recovery time, median (IQR), minutes[2]	2.5 (1.9–4.1)	3.3 (2.3–4.0)	0.17
Poor endoscope maneuverability, n (%)	36 (52.2)	39 (55.7)	0.74
Submucosal fibrosis, n (%)			>0.99
▪ F0	43 (62.3)	44 (62.9)	
▪ F1	21 (30.4)	22 (31.4)	
▪ F2	5 (7.2)	4 (5.7)	
Submucosal fatty tissue, n (%)			0.78
▪ Grade 0	38 (55.1)	42 (60.0)	
▪ Grade 1	15 (21.7)	12 (17.1)	
▪ Grade 2	16 (23.2)	16 (22.9)	
Use of second knife, n (%)	0 (0)	1 (1.4)	>0.99
Conversion to the other method, n (%)	3 (4.3)	4 (5.7)	>0.99
Specimen size, median (IQR), mm	35 (31–44)	37 (32–41)	0.66
Pathology, n (%)			**0.04**
▪ Adenoma or SSL	34 (49.3)	39 (55.7)	
▪ Intramucosal carcinoma	21 (30.4)	27 (38.6)	
▪ Carcinoma with submucosal invasion	14 (20.3)	4 (5.7)	
En bloc resection, n (%)	69 (100)	70 (100)	NA
Complete resection, n (%)	67 (97.1)	70 (100)	0.25
Adverse events, n (%)			
▪ Post-ESD bleeding	2 (2.9)	0 (0)	0.25
▪ Perforation	0 (0)	0 (0)	NA
▪ PECS	3 (4.3)	2 (2.9)	0.68

▶ Table 2 (Continuation)

	CESD n = 69	UESD n = 70	*P* value
Changes in results, median (IQR)[3]			
▪ WBC, per µL	25 (15–41)	21 (8–27)	**0.03**
▪ CRP, mg/dL	0.2 (0.1–0.6)	0.2 (0.1–0.4)	0.71
▪ Sodium, mEq/L	0 (−1 to 0)	−1 (−1 to 1)	0.67

IQR, interquartile range; NA, not applicable; SSL, sessile serrated lesion; PECS, post-ESD coagulation syndrome; CRP, C-reactive protein; WBC, white blood cell count.
[1] Number of times hemostatic forceps applied.
[2] After active bleeding (per instance).
[3] Between the day of ESD and the following day.

Prevention methods for PECS have not yet been established, although the heat-sink effect of UESD may prevent PECS by reducing thermal damage [4]. In this study, the variation in WBC between the day of ESD and the following day was significantly lower in the UESD group, which may be reflective of the heat-sink effect; however, no significant difference was found in the incidence of PECS between the CESD and UESD groups. Possible reasons for this finding are the trend toward a higher frequency of hemostasis in the UESD group and the insufficient sample size.

This study has several limitations. First, our study used a single operator who performed all ESD procedures and focused mainly on the dissection speed; however, complete resection without adverse events (successful ESD) could be a more significant factor. Therefore, a multicenter RCT is warranted, and the composite end point of dissection speed and successful ESD should be considered. Second, the statistical nonsignificance of the primary end point may be owing to a lack of statistical power as the sample size originally intended for a parametric test was assessed using a nonparametric test. Therefore, increasing the sample size might have addressed this issue.

In conclusion, our findings suggest that UESD does not expedite dissection speed in the overall patient population. CESD and UESD may be complementary in the colorectum depending on the positional relationship between the lesion and the direction of gravity.

Conflict of Interest

The authors declare that they have no conflict of interest.

Clinical Trial

Trial Registration: UMIN Japan (http://www.umin.ac.jp/english/) | Registration number (trial ID): UMIN000038529 | Type of study: Prospective, Randomized, Single-Center Study

References

[1] Saito Y, Uraoka T, Matsuda T et al. A pilot study to assess the safety and efficacy of carbon dioxide insufflation during colorectal endoscopic submucosal dissection with the patient under conscious sedation. Gastrointest Endosc 2007; 65: 537–542 doi:10.1016/j.gie.2006.11.002

[2] 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 doi:10.1055/s-0044-101451

[3] Nagata M. Usefulness of underwater endoscopic submucosal dissection in saline solution with a monopolar knife for colorectal tumors (with videos). Gastrointest Endosc 2018; 87: 1345–1353 doi:10.1016/j.gie.2017.11.032

[4] Koyama Y, Fukuzawa M, Aikawa H et al. Underwater endoscopic submucosal dissection for colorectal tumors decreases the incidence of post-electrocoagulation syndrome. J Gastroenterol Hepatol 2023; 38: 1566–1575 doi:10.1111/jgh.16259

[5] Tanaka S, Kashida H, Saito Y et al. JGES guidelines for colorectal endoscopic submucosal dissection/endoscopic mucosal resection. Dig Endosc 2015; 27: 417–434 doi:10.1111/den.12456

[6] Burgess NG, Bassan MS, McLeod D et al. Deep mural injury and perforation after colonic endoscopic mucosal resection: a new classification and analysis of risk factors. Gut 2017; 66: 1779–1789 doi:10.1136/gutjnl-2015-309848

[7] 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 doi:10.3109/00365521.2010.495416

[8] Yoshida N, Naito Y, Hirose R et al. Risk of lens cloudiness during colorectal endoscopic submucosal dissection and ability of a novel lens cleaner to maintain and restore endoscopic view. Dig Endosc 2015; 27: 609–617 doi:10.1111/den.12442

[9] Kamigaichi Y, Oka S, Tanaka S et al. Factors for conversion risk of colorectal endoscopic submucosal dissection: a multicenter study. Surg Endosc 2022; 36: 5698–5709 doi:10.1007/s00464-022-09250-6

[10] Toyonaga T, Tanaka S, Man IM et al. Clinical significance of the muscle-retracting sign during colorectal endoscopic submucosal dissection. Endosc Int Open 2015; 3: E246–E251 doi:10.1055/s-0034-1391665

[11] Nagata M. Tapered hood with wide holes in its sides for efficient air bubble removal during underwater endoscopic submucosal dissection. Dig Endosc 2022; 34: 654 doi:10.1111/den.14232

[12] Nagata M. Continuous low water pressure dissection technique minimizing air bubbles during underwater endoscopic submucosal dissection. Endoscopy 2024; 56: E699–E700 doi:10.1055/a-2368-9612

[13] Nomura T, Sugimoto S, Hayashi Y et al. Colorectal endoscopic submucosal dissection using a gas-free saline-immersion dissection technique. Endoscopy 2023; 55: E1039–E1040 doi:10.1055/a-2155-6107

[14] Sasaki M, Masunaga T, Miyazaki K et al. Automatic water irrigation synchronized with the electrosurgical unit: Bubble-free underwater endoscopic submucosal dissection. Endoscopy 2024; 56: E468–E469 doi:10.1055/a-2316-9305

[15] Tashima T, Nakano Y, Jinushi R et al. Gel immersion endoscopic submucosal dissection for an anorectal tumor with hemorrhoids close to the dentate line. Endoscopy 2022; 54: E298–E299 doi:10.1055/a-1519-6939

[16] Cecinato P, Lucarini M, Campanale C et al. Underwater endoscopic submucosal dissection and hybrid endoscopic submucosal dissection as rescue therapy in difficult colorectal cases. Endosc Int Open 2022; 10: E1225–E1232 doi:10.1055/a-1882-4306

[17] Ozeki Y, Hirasawa K, Ikeda R et al. Safety and efficacy of water pressure endoscopic submucosal dissection for colorectal tumors with submucosal fibrosis (with video). Gastrointest Endosc 2021; 94: 607–617.e602 doi:10.1016/j.gie.2021.03.026

[18] Mavrogenis G, Mavrogenis I, Anastasiadis S et al. Underwater endoscopic submucosal dissection in saline solution with rubber-band countertraction for a cecal polyp extending into a diverticulum. Ann Gastroenterol 2019; 32: 527

[19] Despott EJ, Hirayama Y, Lazaridis N et al. Saline immersion therapeutic endoscopy facilitated pocket-creation method for endoscopic submucosal dissection (with video). Gastrointest Endosc 2019; 89: 652–653 doi:10.1016/j.gie.2018.10.005

[20] Jacques J, Charissoux A, Bordillon P et al. High proficiency of colonic endoscopic submucosal dissection in Europe thanks to countertraction strategy using a double clip and rubber band. Endosc Int Open 2019; 7: E1166–E1174 doi:10.1055/a-0965-8531