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DATABASE ANALYSIS

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A Retrospective Study of 290 Patients with Resectable Benign and Malignant Gastric Neoplasms to Compare Postoperative Outcomes of Endoscopic Resection with and without the Internal Traction Method Using a Spring-and-Loop with Clip (S-O Clip)

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Statistical Analysis C
Data Interpretation D
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Background: The spring-and-loop with clip (S-O clip) consists of a spring and a nylon loop located on one side of the claws of the clip, and is used in gastric endoscopic submucosal dissection (ESD) to allow countertraction. This retrospective study included 290 patients with early gastric neoplasms (eGNs) and aimed to compare postoperative outcomes of ESD with and without the use of the S-O clip.

Material/Methods: We retrospectively reviewed the data of 347 patients with eGN who underwent ESD, with or without an S-O clip, at our institution between April 1, 2017 and March 31, 2023. Overall, 290 patients were analyzed after excluding ineligible participants. The control group (n=149; adenoma: 1, carcinoma: 148) underwent ESD without an S-O clip between April 2017 and March 2020, while the S-O group (n=141; adenoma: 4, carcinoma: 137) used the clip between April 2020 and March 2023. Primary outcomes included procedure time, en bloc resection rate, and complete resection rate. Subgroup analysis for examined procedure time concerning endoscopist expertise, submucosal fibrosis, and neoplasm locations.

Results: The S-O group had a shorter procedure time (44.4±23.9 vs 61.1±40.9 min, P<0.001) and a higher complete resection rate (97.9% vs 92.6%, P<0.05) than the control group. Subgroup analysis revealed that the S-O clip significantly reduced procedure time for trainees compared to the control group (40.8±18.3 vs 61.1±35.6 min, P<0.05).

Conclusions: The scheduled use of S-O clips in gastric ESD is effective in improving procedural time and complete resection rates, benefiting endoscopists across all experience levels.

Keywords: **Endoscopy • Stomach Neoplasms • Traction**

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Introduction

In Japan, endoscopic submucosal dissection (ESD) is the standard treatment for early gastric neoplasms (eGN). It enables gastrointestinal endoscopists to achieve en bloc resection and has been adopted worldwide since Gotoda et al [1] reported the first 2 rectal cases using an insulation-tipped electrosurgical knife in 1999. ESD is a method whereby the mucosa surrounding the lesion is excised using a high-frequency diathermy device, followed by dissection of the submucosa beneath the lesion [2]. In the current domestic guidelines, principles for indications are limited to intramucosal malignancy where the probability of lymph node metastasis is low [3]. However, the indicative range of ESD has been at the center of controversy, as reported in a retrospective study based on a large series of cases for early gastric carcinoma, or international clinical practice guidelines [4-6]. Therefore, strategies to improve ESD techniques are still required. ESD is generally believed to be challenging and time-consuming and is associated with adverse events (AEs) such as gastric perforation and bleeding [7].

Methods involving the use of a traction device have been developed in recent decades to facilitate ESD. Although gravity, positional change in the patient, or a hood attached to the edge of the endoscope are sometimes effective as traction methods, they can be insufficient without additional methods. Traction methods enable endoscopists to identify the cutting line of lesions, which can shorten ESD procedure time and reduce AEs [8,9]. However, the direction of traction is limited, and the strength is sometimes undesirable.

A ready-made traction device, the Sakamoto-Osada clip, also known as the spring-and-loop with clip (S-O clip) (ZEON MEDICAL, Tokyo, Japan), has been developed for colonic ESD [8,9] (**Figure 1**). The S-O clip allows internal traction in any direction. Although the S-O clip is mainly used for colonic ESD in clinical practice, few reports have demonstrated its usefulness for gastric ESD [10-12]. Therefore, this retrospective study included 290 patients with eGN and aimed to compare postoperative outcomes of endoscopic resection with and without use of the S-O clip.

Material and Methods

Ethics Approval

All procedures were performed in accordance with the principles of the Declaration of Helsinki and the ethics guidelines of the institutional research committee. This study protocol was approved by the Institutional Review Board of Juntendo Urayasu Hospital (approval number: E23-0411). All patients provided written informed consent before undergoing ESD.

Patient Enrollment by Our Procedural Policy

A total of 347 patients with eGN underwent gastric ESD at Juntendo Urayasu Hospital (Chiba, Japan) between April 1,

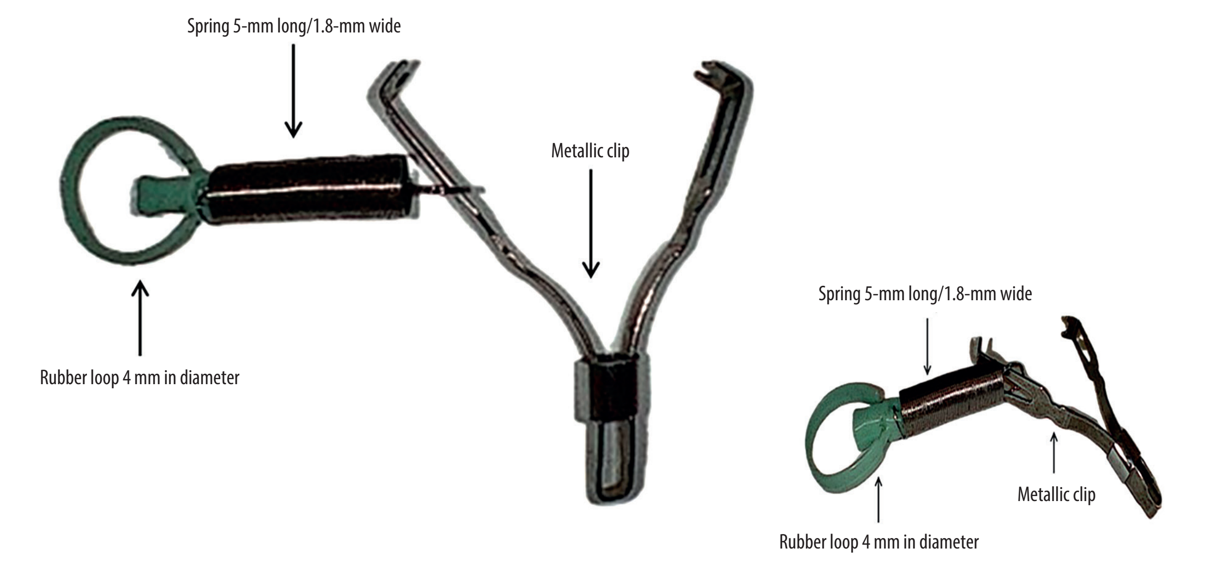

Figure 1. The S-O clip. This device consists of a metallic clip and a 5-mm long spring with a rubber loop, which is anchored to one side of the clip. Attaching the clip to the edge of the specimen, followed by attaching another clip in a contralateral direction, provides traction at any location without switching to a multi-bending scope (GIF-2TQ260M, Olympus Optical, Japan). *The image editing software used was the Adobe Photoshop software (Adobe Inc., version 25.0).*

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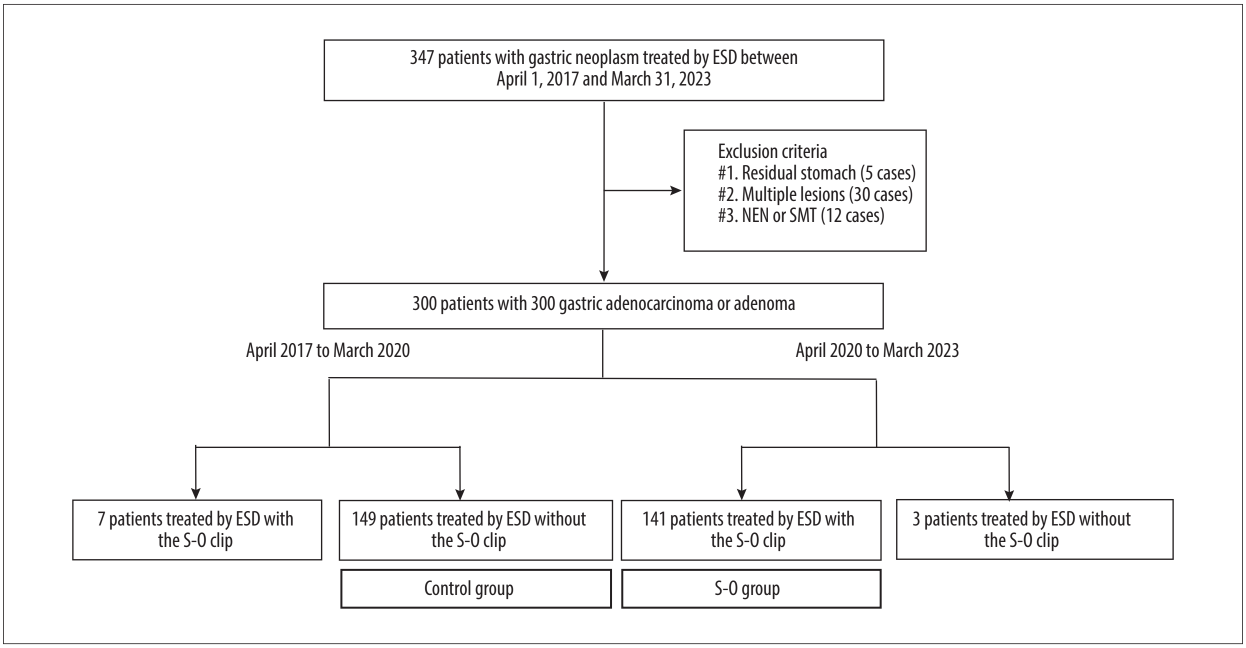

Figure 2. Flow diagram of the study design. ESD – endoscopic submucosal dissection; NEN – neuroendocrine neoplasm; SMT – submucosal tumor.

2017, and March 31, 2023. The indications for gastric ESD in each case were decided by a conference in our Department of Gastroenterology and were based on the current domestic guidelines [3]. General status, respiratory conditions, and ability to maintain body stillness during the endoscopic procedure were considered for ESD. We limited the cases to only adenocarcinoma or adenoma to avoid a bias related to different types of tumors. Therefore, we excluded ESD cases of residual stomach (n=5), multiple lesions (n=30), and neuroendocrine neoplasm or submucosal tumor (n=12). Our department did not use the S-O clip until March 2020; however, we determined whether the S-O clip could be routinely used for gastric ESD since April 2020. We also excluded 7 cases with exceptional use of the S-O clip from 156 cases of ESD performed between April 2017 and March 2020 and 3 without the use of the S-O clip from 144 cases of ESD performed between April 2020 and March 2023 (**Figure 2**).

Definition of the Comparative Groups

We classified 290 patients into the following 2 groups: 149 control cases where ESD was performed without the use of an S-O clip between April 2017 and March 2020, and 141 cases where ESD was performed with the use of an S-O clip between April 2020 and March 2023 (**Figure 2**).

Definitions of Endoscopists

An expert operator was defined as an endoscopist who had performed >40 cases of ESD, whereas a trainee was defined as an endoscopist who had conducted <40 cases of ESD according to a previous report that defined achieving proficiency in gastric ESD [13]. Three trainees and 4 experts were included as operators in the control group, and 4 trainees and 2 experts were included in the S-O group.

Endoscopic Procedures

The procedures were performed by endoscopists with experience of >1000 upper endoscopies. During each procedural session, vital signs, such as consciousness, blood pressure, heart rate, oxygen saturation, and blood temperature, were continuously monitored in all patients. They were placed in the lateral position and administered a topical pharyngeal spray containing 10% lidocaine. According to the latest Japanese guidelines for sedation in gastroenterological endoscopy [14], these patients were sedated using intravenous agents, including 0.5 mg/kg of propofol with 35 mg of pethidine hydrochloride as an initial dosage. Propofol was continuously administered at a rate of 2-3 mg/kg/h. To control the sedation depth, an additional bolus of propofol (10-20 mg each) was administered if the sedation was deemed inadequate, as judged by the endoscopist.

All ESD procedures were conducted using a single-channel endoscope (GIF-H290 T; Olympus Optical Co., Ltd., Tokyo, Japan) with a water jet system and electrosurgical generator (VIO3; Erbe, Tubingen, Germany). First, we inserted the endoscope and left an operating overtube while the patient was in the lateral position. Carbon dioxide (CO_2) gas was provided for gastric insufflation in all patients except for those with chronic obstructive pulmonary disease. Next, we observed the targeted gastric lesion

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Figure 3. (**A**) A dual knife for dissecting the submucosal layer. (**B**) Comparison between the ordinary (GIF-H290T, Olympus Optical, Japan) and multi-bending (GIF-2TQ260M, Olympus Optical, Japan) scopes. The multi-bending scope can maintain a better endoscopic angle to handle the lesions in retroflexed positions. *The image editing software used is the Adobe Photoshop software (Adobe Inc., version 25.0).*

using endoscopy and circumferentially dotted it using a dual knife (KL-D650L; Olympus Optical Co. Ltd., Tokyo, Japan) (**Figure 3A**). Before the actual resection, 0.4% sodium hyaluronate acid solution (MucoUp; Seikagaku Co. and Boston Scientific Japan Co., Japan) was injected into the submucosal layer. We generally used the same endoscope; however, we occasionally switched it to a multi-bending scope (GIF-2TQ260M, Olympus Optical, Japan) (**Figure 3B**) based on the attending endoscopists' judgment, particularly in cases where approaching the lesion was deemed challenging. After the circumferential mucosal incision, the targeted mucosa was separated from the normal surrounding mucosa (**Figure 4A**), and an S-O clip was placed at the edge of the peeled mucosa (**Figure 4B**). Another standard clip holding a rubber loop of an S-O clip was attached to the proximal gastric wall contralateral to the lesion (**Figure 4C**). This process effectively provided traction to the layer and enhanced the visibility of the perforating microvessels (**Figure 4D**). Consequently, a better intraoperative view could facilitate the technical tolerability of ESD.

S-O Clip

The S-O clip device consists of a metallic clip with a spring and rubber loop anchored to one side. It passes through the working channel of an endoscope. Attaching the clip to the edge of the specimen and then attaching another clip with a rubber loop in the contralateral direction provided traction at any location desired by the operator without switching to a multi-bending scope (GIF-2TQ260M, Olympus Optical, Japan) (**Figure 1**).

Location of Gastric Neoplasms

Gastric neoplasms were classified by location according to the domestic classification of gastric carcinoma [15]. The upper, middle, and lower third of the stomach were defined as U, M, and L, respectively. Additionally, the circumferential positions were classified as the anterior wall (Ant), posterior wall (Post), lesser curvature (Less), or greater curvature (Gre) of the stomach.

Measurement of Resected Specimens and Tumors

After pinning the resected specimens to a clipboard, the lengths of the longer and shorter axes were measured (mm). The specimen size was defined as the length of the longer axis of the resected sample. Additionally, the tumors were macroscopically measured in the same manner. The areas of the specimens were calculated by multiplying their longer and shorter

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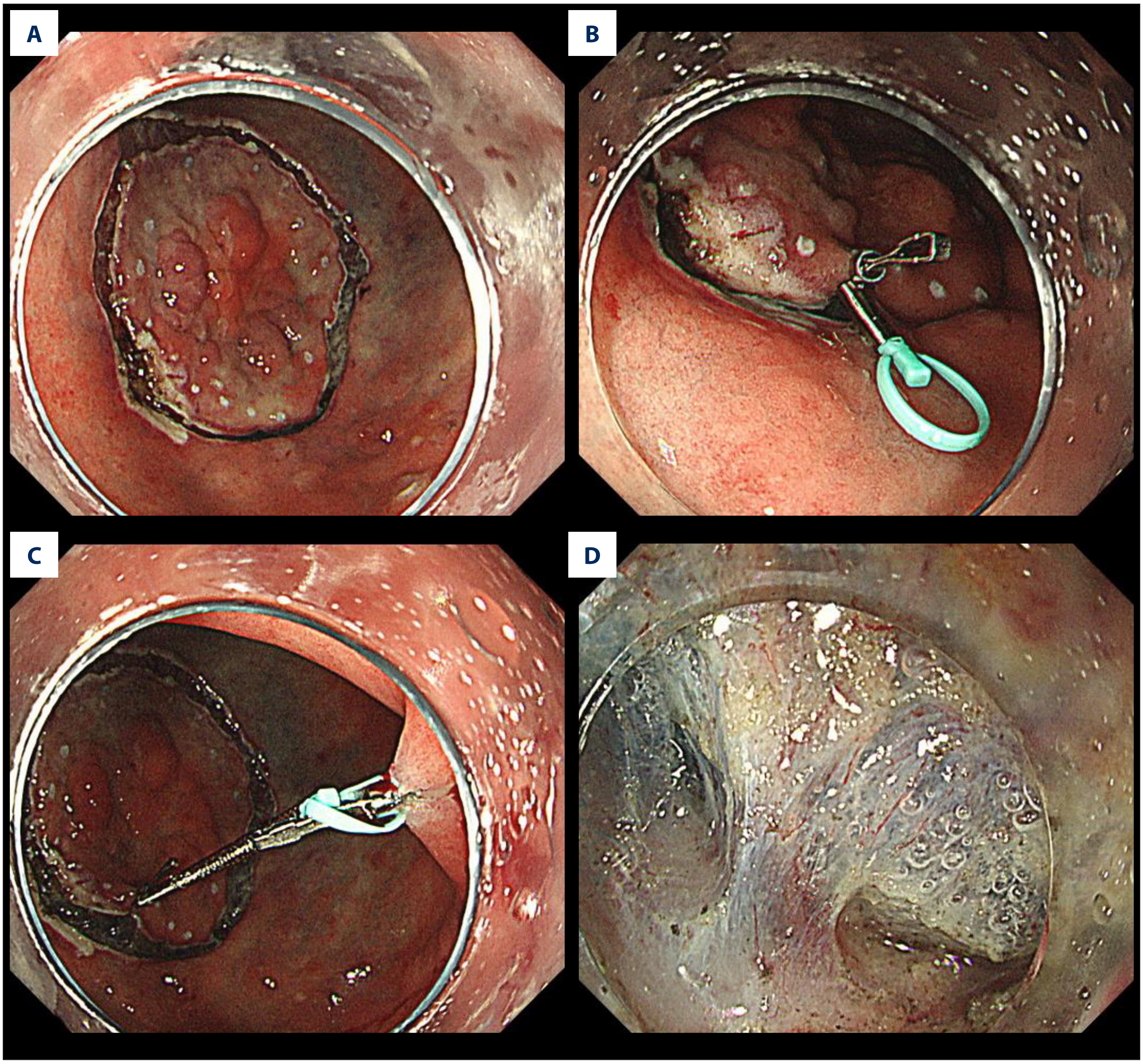

Figure 4. (**A-D**) An example of the endoscopic procedure for gastric endoscopic submucosal dissection (ESD). The procedural sequence from the marking of a lesion to the completion of ESD is shown. *The image editing software used is the Adobe Photoshop software (Adobe Inc., version 25.0).*

diameters by an approximate value based on the assumption that the shape of the specimen was rectangular.

Tumor Depth

Tumor depth was classified as M, SM1, or SM2, according to the domestic classification [3,15]. M denotes tumor invasion in situ. SM indicates tumor confined to the submucosa. SM is subclassified as SM1 (tumor invasion is within 0.5 mm of the muscularis mucosae) or SM2 (tumor invasion is 0.5 mm or more deep into the muscularis mucosae).

Procedure Time

The procedure time (min) was measured from the injection of hyaluronic acid to the complete resection of the specimen. The dissection speed (mm^2/min) was calculated by dividing the specimen area (mm^2) by the procedure time (min).

En Bloc and Complete Resection

En bloc resection was defined as the excision of the tumor lumped together as an intact piece. Complete resection was defined as en bloc resection without any pathologically positive margins on the horizontal or vertical cut surface. Each

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resection rate was expressed as the percentage (%) of cases that achieved en bloc or complete resection.

Requirement for the Multi-Bending Scope

We switched the ordinary scope (GIF-H290 T; Olympus Optical Co., Ltd., Tokyo, Japan) to a multi-bending scope (M-scope) (GIF-2TQ260M, Olympus Optical, Japan) (**Figure 3B**), particularly in cases where approaching the lesion was challenging. The M-scope can maintain a better angle, particularly in the retroflexion position, during ESD. Therefore, we evaluated the required rate (%) of the M-scope in each group.

Requirement of a Snaring Device

ESD can be achieved as much as possible without a snaring device; however, a snaring device (Snare Master; SD-210U-15; Olympus, Tokyo) was used in cases where the attending endoscopist judged that the submucosal incision of the lesion was challenging. Therefore, we evaluated the required rate (%) of snaring device usage in each group.

Evaluation of Fibrosis in the Submucosal Layer

Fibrosis in the submucosal layer can occur due to various factors, including pre-treatment biopsies, prior endoscopic treatments, inflammation of the mucosa, and submucosal tumor invasion. In general cases, the submucosal layer appears translucent, allowing the underlying structures to be visible (**Figure 4D**). However, severe fibrosis manifests as a thick, white, ridged structure, complicating the visibility and dissection process in ESD. The presence or absence of fibrosis in the submucosal layer was determined macroscopically by endoscopists based on intraoperative and postoperative endoscopic images. The presence of fibrosis in the submucosal layer was shown in both groups (%).

Gastric Perforation

Gastric perforation was endoscopically identified during ESD. Specifically, this was determined by observing the external tissue through the gastric serosa during ESD. We also regarded subdiaphragmatic intra-abdominal free gas on radiography in the upright position, routinely performed on postoperative day (POD) 1 of ESD, as gastric perforation. Computed tomography (CT) was not routinely conducted to identify potential abdominal complications following ESD. Patients with delayed gastric perforation were also included, and the rate of gastric perforation (%) was compared between the groups.

Post-ESD Bleeding

Post-ESD bleeding was defined as a bleeding occurring post-ESD that necessitated endoscopic hemostasis. The occurrence rate of post-ESD bleeding (%) was compared between the groups.

Hematological Examinations Before and After ESD

Screening blood tests were routinely performed preoperatively and on PODs 1 and 4. We assessed serum hemoglobin (Hb) (g/dL) and C-reactive protein (CRP) (mg/dL) levels to monitor perioperative inflammation or anemia during the postoperative period, comparing them to preoperative data. Both postoperative parameters were selected as the worst data, regardless of the number of PODs.

S-O Clip Device-Related Adverse Events

Device-related adverse events were defined as complications due to the device during or after S-O clip placement in 141 procedures using S-O clips. Specifically, the S-O clip occasionally required reattachment during ESD treatment. These were minor issues and did not require treatment; however, they could influence procedure time. Therefore, we retrospectively investigated the breakdowns and causes of the S-O clip reattachment.

Length of Hospital Stay

The length of the hospital stay was determined using a clinical pathway, which involved an 8-day schedule of admission on the preoperative day and discharge on POD 7. However, this schedule was postponed by an attending physician if the patient had a prolonged inflammatory response or a higher risk of bleeding.

Statistical Analyses

Descriptive statistics for each continuous variable were calculated and presented as mean±standard deviation. Categorical data were expressed as proportions (%) and analyzed using Fisher's exact or Pearson's chi-squared test. Continuous variables were assessed for normality using the Shapiro-Wilk test and for homoscedasticity using Levene's test and the two-tailed F-test. If the Shapiro-Wilk test had a *P* value of <0.05, the data were determined to not be normally distributed. If Levene's test and the two-tailed F-test had a *P* value of <0.05, it was concluded that there were differences in variance between the groups. Wilcoxon signed-rank test was used for non-normally distributed variables. We applied Welch's *t* test for normally distributed variables that lacked homoscedasticity and the *t* test for normally distributed variables that were homoscedastic. Statistical significance was set at $P<0.05$. All statistical analyses were performed using JMP software (version 14, SAS Institute, Japan).

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Table 1. Patient's backgrounds and demographic data before PSM.

		S-O group (n=141)	Control group (n=149)	*P* value
Age (years old)		73.3±7.6	71.8±8.2	0.0946
Sex (%)	Male	73.8 (n=104)	75.2 (n=112)	0.076
	Female	26.2 (n=37)	24.8 (n=37)	
Body mass index (kg/m²)		23.7±3.5	23.5±3.7	0.4659
Location of the neoplasms (%)	U	18.4 (n=26)	17.5 (n=26)	
	M	37.6 (n=53)	20.8 (n=31)	0.003*
	L	44.0 (n=62)	61.7 (n=92)	
Circumferential position of the neoplasms (%)	Ant	12.1 (n=17)	10.7 (n=16)	0.376
	Post	17.0 (n=24)	25.5 (n=38)	
	Less	46.8 (n=66)	42.3 (n=63)	
	Gre	24.1 (n=34)	21.5 (n=32)	
Endoscopists' expertise (%)	Experts	75.9 (n=107)	81.9 (n=122)	0.211
	Trainees	24.1 (n=34)	18.1 (n=27)	
Antithrombotic therapy (%)		19.9 (n=28)	25.5 (n=38)	0.252
Post ESD (%)		7.1 (n=10)	2.0 (n=3)	0.037*

Data are shown a mean±standard deviation. PSM – propensity score matching. Location of the neoplasms: U – upper one-third of the stomach; M – middle one-third; L – lower one-third. Circumferential position of the neoplasms: Ant – anterior wall of the stomach; Post – posterior wall; Less– lesser curvature; Gre – greater curvature. ESD – endoscopic submucosal dissection. * *P* value <0.05 were regarded as statistically significant.

Propensity Score Matching

From April 2017 to March 2020, 95.9% of the enrolled patients (n=149/156) did not undergo the planned use of the S-O clip (control group), whereas 97.9% of the enrolled patients (n=141/144) underwent scheduled use of the S-O clip (S-O group) between April 2020 and March 2023 (**Figure 2**). The department altered its strategic policy in April 2020; however, we observed a significant difference in the location of the neoplasm between the 2 groups (*P*=0.003) (**Table 1**). Previous reports have included lesion size, lesion location, the presence of ulceration or scarring, and endoscopist experience as factors influencing the technical difficulty of gastric ESD [16-18]. To mitigate the influence of selection bias, we classified the patients into 2 groups based on the use of the S-O clip and conducted propensity score matching (PSM) analysis to further align the background factors. We calculated the propensity score for each case using a logistic regression model that incorporated the following variables: age, sex, body mass index (BMI), the use of antithrombotic therapy, endoscopist expertise level (expert/trainee), fibrosis in the submucosal layer, area of the specimens, location of the neoplasm (U/M/L), and circumferential position of the neoplasm (Ant/Post/Less/Gre). Patients in the S-O and control groups were matched on a one-to-one basis using the nearest neighbor method with a caliper width of 0.05, based on the standard deviation of the propensity score logit.

Results

Patient Background and Demographic Data Before PSM

ESD was performed in 347 patients. The data of 47 patients were excluded due to different types or numbers of gastric neoplasms or operative conditions of the stomach. Furthermore, 7 patients treated with S-O clips from April 2017 to March 2020 and three treated without S-O clips from April 2020 to March 2023 were also excluded. Therefore, data were collected from 290 patients, and 141 procedures were performed using an S-O clip. The mean age and male/female constitutions in both groups did not significantly differ (*P*>0.05). Concerning the circumferential position of the lesions, no significant difference was found between the groups (p>0.05); however, the locational distribution of the neoplasms was significantly different (p<0.05). The experts-to-trainee ratio and patients under

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Table 2. Histological outcomes of ESD with or without the S-O clip before PSM.

		S-O group (n=141)	Control group (n=149)	*P* value
Tumor size (mm)		15.1±9.3	14.7±0.1	0.766
Specimen size (mm)		33.1±11.3	29.7±11.0	0.005*
Area of specimens (mm²)		991.9±732.9	778.5±689.2	0.0004*
Histological type (%)	Adenoma	2.8 (n=4)	0.7 (n=1)	0.620
	Differentiated	92.9 (n=131)	95.3 (n=142)	
	Undifferentiated	4.3 (n=6)	4.0 (n=6)	
Macroscopic type (%)	Elevated	54.6 (n=77)	49.0 (n=73)	0.338
	Flat or depressed	45.4 (n=64)	51.0 (n=76)	
Tumor depth (%)	M	85.8 (n=121)	92.6 (n=138)	0.168
	SM1	7.1 (n=10)	3.4 (n=5)	
	SM2	7.1 (n=10)	4.0 (n=6)	
En block resection rate (%)		98.6 (n=139)	97.3 (n=145)	0.449
Complete resection rate (%)		97.9 (n=138)	92.6 (n=138)	0.037*

Data are shown a mean±standard deviation. ESD – endoscopic submucosal dissection; PSM – propensity score matching; M – tumor invasion in situ; SM – tumor confined to the submucosa. SM is subclassified as SM1 (tumor invasion is within 0.5 mm of the muscularis mucosae) or SM2 (tumor invasion is 0.5 mm or more deep into the muscularis mucosae). * *P* value <0.05 were regarded as statistically significant.

Table 3. Clinical outcomes of ESD with or without the S-O clip before PSM.

	S-O group (n=141)	Control group (n=149)	*P* value
Procedure time (min)	44.4±23.9	61.1±40.9	0.0008*
Dissection speed (mm²/min)	25.1±17.4	14.7±9.3	<0.001*
Gastric perforation (%)	0.7 (n=1)	0.7 (n=1)	0.964
Post-ESD bleeding (%)	2.8 (n=4)	5.4 (n=8)	0.279
Maximal serum CRP level (mg/dl)	2.13±2.6	1.47±1.7	0.0452*
Decreased hemoglobin level (g/dl)	-0.58±0.8	-0.50±0.7	0.632
Length of hospital stay (days)	8.70±1.8	8.35±1.9	0.0302*
Requirement of M-scope (%)	7.09 (n=10)	15.4 (n=23)	0.025*
Requirement of snare (%)	1.4 (n=2)	12.8 (n=19)	<0.001*
Fibrosis in submucosal layer (%)	22.0 (n=31)	18.1 (n=27)	0.410

Data are shown a mean±standard deviation. ESD – endoscopic submucosal dissection; PSM – propensity score matching; CRP – C-reactive protein; M-scope – multi-bending scope. * *P* values <0.05 were regarded as statistically significant.

antithrombotic therapy were not significantly different between the groups (both *P*>0.05). **Figure 2 and Table 1** present the patient backgrounds and demographic data.

S-O clip Device-Related Adverse Events

In total, 6 of the 141 patients (4.2%) required the reattachment of the S-O clip. The reasons for reattachment were as follows: a shortage of traction force due to directionally ineffective traction,

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Table 4. Selected 9 matching factors.

		S-O group (n=93)	Control group (n=93)	*P* value
Age (years old)		72.2±7.9	72.7±7.3	0.997
Sex (male) (%)		75.3 (n=70)	73.1 (n=68)	0.738
Body mass index (kg/m^2)		23.5±3.2	23.8±3.8	0.693
Antithrombotic therapy (%)		20.4 (n=19)	20.4 (n=19)	1.000
Endoscopists' expertise (expert) (%)		76.3 (n=71)	80.7 (n=75)	0.475
Fibrosis in submucosal layer (%)		21.5 (n=20)	22.0 (n=21)	0.860
Area of specimens (mm^2)		932.8±79.4	833.7±79.4	0.159
Location of the neoplasm (%)	U	22.6 (n=21)	19.3 (n=18)	0.745
	M	22.6 (n=21)	26.9 (n=25)	
	L	54.8 (n=51)	53.8 (n=50)	
Circumferential position of the neoplasms (%)	Ant	11.8 (n=11)	14.0 (n=13)	0.768
	Poss	20.4 (n=19)	16.1 (n=15)	
	Less	41.9 (n=39)	47.3 (n=44)	
	Gre	25.9 (n=24)	22.6 (n=21)	

Data are shown a mean±standard deviation. Location of the neoplasms: U – upper one-third of the stomach; M – middle one-third; L – lower one-third. Circumferential position of the neoplasms: Ant – anterior wall of the stomach; Post – posterior wall; Less – lesser curvature; Gre – greater curvature.

a large size of the specimen, failure to attach the S-O clip (1 (0.7%) patient each), and slipping off the S-O clip (3 (2.1%) patients). All events were resolved by the additional reattachment of an S-O clip.

Histological Outcomes of ESD with or without the use of S-O Clips Before PSM

Although the tumor size was not significantly different between groups (*P*>0.05), the specimen size and area significantly differed between the 2 groups (both *P*<0.05). Pathological parameters, such as histological type, macroscopic type, or depth of tumor invasion, did not significantly differ between the groups (both *P*>0.05). The number of ESDs with en bloc resection did not significantly differ (*P*>0.05); however, the complete resection rate was significantly higher in the S-O group than in the control group (*P*<0.05). **Table 2** presents the histological outcomes of both groups.

Clinical Outcomes of ESD with or without the use of S-O Clips Before PSM

Table 3 presents the clinical outcomes of ESD with and without the use of S-O clips. All ESD procedures were performed without any mortality. Importantly, the mean procedure time was significantly shorter in the S-O group than in the control group (*P*<0.05). The dissection speed was also significantly faster in the S-O group than in the control group (*P*<0.05). However, the major complications of post-ESD bleeding and gastric perforation did not differ significantly between the groups (*P*>0.05).

Regarding the laboratory data, the maximal serum CRP level was significantly increased in the S-O group compared to the control group (p<0.05), whereas the Hb level showed no difference (*P*>0.05). For additional equipment, the rate of use of the M-scope and snaring device was decreased in the S-O group compared to the control group (both *P*<0.05).

Selection of 9 Matching Factors After PSM

PSM was performed for age, sex, BMI, the use of antithrombotic therapy, endoscopist expertise level (expert/trainee), fibrosis in the submucosal layer, specimen area, location of the neoplasm, and circumferential position of the neoplasm. Similar parameters, as in **Table 1**, were evaluated, and all matching factors significantly met the requirements of the S-O and control groups, as shown in **Table 4**.

Clinical Outcomes of ESD with or without the use of S-O Clips After PSM

Table 5 summarizes the clinical outcomes of ESD with and without the use of S-O clips after PSM. S-O clips significantly

Table 5. Clinical outcomes of ESD with or without the S-O clip after PSM.

	S-O group (n=93)	Control group (n=93)	*P* value
Procedure time (min)	42.4±24.4	65.5±42.8	<0.001*
Dissection speed (mm²/min)	14.5±9.5	25.1±18.9	<0.001*
En block resection (%)	97.9 (n=91)	97.9 (n=91)	1.000
Complete resection (%)	96.8 (n=90)	89.3 (n=83)	0.044*
Post-ESD bleeding (%)	2.2 (n=2)	7.5 (n=7)	0.087
Gastric perforation (%)	0.0 (n=0)	1.1 (n=1)	0.316
Maximal serum CRP level (mg/dl)	2.11±2.4	1.59±2.0	0.086
Decreased hemoglobin level (g/dl)	-0.52±0.9	-0.49±0.7	0.930
Length of hospital stay (days)	8.61±1.8	8.60±2.2	0.905
Requirement of M-scope (%)	7.5 (n=7)	17.2 (n=16)	0.045*
Requirement of snare (%)	2.2 (n=2)	11.8 (n=11)	0.009*

Data are shown a mean±standard deviation. ESD – endoscopic submucosal dissection; PSM – propensity score matching; CRP – C-reactive protein; M-scope – multi-bending scope. * *P* values <0.05 were regarded as statistically significant.

decreased the mean procedure time (*P*<0.05), which was a similar result to that before PSM. Dissection speed was also significantly decreased in the S-O group compared to the control group (*P*<0.05). Post-ESD bleeding and gastric perforation did not significantly differ between the groups (*P*>0.05). Regarding the laboratory data, the maximal serum CRP and Hb levels did not significantly differ between the groups (*P*>0.05). For additional instruments), using the S-O clip decreased the required rates of the M-scope and snaring device (both *P*<0.05), which was consistent with data before PSM.

Subgroup Analyses of Procedure Time Between the Disadvantageous Variables for ESD

Table 6 presents the subgroup analyses of procedure time between the disadvantageous variables for ESD. Regarding the expertise level of the endoscopists, both experts and trainees could significantly reduce procedure time with the use of the S-O clip (both *P*<0.05). In cases with fibrosis in the submucosal layer, the procedure time was also significantly decreased with the use of S-O clips (*P*<0.05). Regarding the location of the stomach, the procedure time was significantly shorter with the use of S-O clips in U and L (both *P*<0.05), which was not demonstrated in M (*P*>0.05). Considering the circumferential location, the S-O clips resulted in a significant reduction in procedure time for lesions located at Less and Gre (*P*<0.05) but not at Ant and Post (*P*>0.05).

Discussion

The present study demonstrated that the scheduled use of S-O clips may enhance the procedural process of gastric ESD, retrospectively analyzing data from 290 patients and using propensity score matching. The S-O clip significantly shortened the procedure time of ESD compared to the control group (44.4±23.9 vs 61.1±40.9 minutes, *P*<0.001). Additionally, in contrast to previous reports [10,11], this study also showed that the S-O clip achieved a higher complete resection rate (97.9% vs 92.6%, *P*<0.05) and revealed that the S-O clip significantly reduced procedure time for trainees (40.8±18.3 vs 61.1±35.6 minutes, *P*<0.05), which support that scheduled S-O clip for gastric ESD is an effective method that decreases the degree of technical difficulty for both endoscopists, regardless of expertise in the future.

In 2005, Ono first reported and named the method for en bloc resection for eGNs as ESD [19]. More than 20 years have passed since the development of ESD, and gastric ESD is currently accepted as a standardized strategy for cases with intramucosal malignancies with a low probability of lymph node metastasis [3]. Subsequently, the use of ESD was approved for early-stage neoplasms in the pharynx, esophagus, stomach, duodenum, and large intestine [20]. However, the technical procedure for ESD can be challenging; therefore, ESD should be performed by or with expert endoscopists, implying that ESD can only be performed at a limited number of institutions. The procedure is fundamentally challenging because of the level of endoscopic technique required to maintain clear

Table 6. Subgroup analyses of procedure time between with or without S-O groups concerning disadvantageous variables for ESD.

	S-O group (n=93)	Control group (n=93)	*P* value
Endoscopists' expertise			
Expert (n=146)	42.9±26.1	66.5±4.2	0.0005*
Trainee (n=40)	40.8±18.3	61.1±35.6	0.0378*
Fibrosis in submucosal layer			
Positive (n=41)	65.8±24.7	124.7±36.8	0.0018*
Negative (n=145)	36.0±20.2	48.2±25.5	0.0007*
Location of the neoplasms			
U (n=39)	59.6±22.2	101.7±45.6	0.0016*
M (n=46)	45.7±30.1	63.7±40.2	0.0832
L (n=101)	34.0±18.4	53.3±36.0	0.0008*
Circumferential position of the neoplasms			
Ant (n=24)	36.4±16.1	45.4±24.4	0.2917
Poss (n=34)	61.3±31.7	81.7±54.6	0.1811
Less (n=83)	44.7±21.2	70.2±43.1	0.0065*
Gre (n=45)	26.6±12.8	56.4±37.3	<0.001*

Data are shown a mean±standard deviation (mm). ESD – endoscopic submucosal dissection. Location of the neoplasms: U – upper one-third of the stomach; M – middle one-third; L – lower one-third. Circumferential position of the neoplasms: Ant – anterior wall of the stomach; Post – posterior wall; Less – lesser curvature; Gre – greater curvature. * *P* values <0.05 were regarded as statistically significant.

visualization of the submucosal dissection plane and maneuver the scalpel horizontally within the submucosal layer [21].

Providing appropriate countertraction to expose the dissection field during ESD is the most intuitive solution. So far, various kinds of traction methods have been developed to obtain good visualization and traction, such as the clip-with-line method [22], the sinker device [23], the external grasping forceps [24], the second thin endoscope [25], the double-channel endoscope [26], and the suture pulley method [27]. Traction devices can be classified into external and internal traction devices [28]. Regarding external traction devices, the clip-with-line method [22] is the most commonly used technique. A recent randomized controlled study confirmed the benefit of a reduction in the procedure time specifically for lesions located in the greater curvature of the upper or middle parts of the stomach [29]; however, the direction of traction was restricted to only the cardiac side, which may not provide optimal traction in all locations. The S-O clip is an internal traction device that allows for flexible traction direction during ESD.

Some reports have demonstrated the effectiveness of S-O clips during ESD for eGNs. In a retrospective cohort study, Hashimoto et al [10] reported that the procedure time was reduced by 25% with the use of S-O clips. Nagata et al [11] demonstrated that the use of the S-O clip could standardize both forward and retroflexed endoscopic positions during ESD, reporting that the average time to attach an S-O clip was merely 2.08 min. The required time to apply the S-O clip is also included in the procedure time; however, this may affect the length of the procedure time by simplifying the dissection process in ESD. Mannen et al [30] showed that prolongation of the procedure time was associated with the risk of perforation. Therefore, the use of the S-O clip may reduce iatrogenic gastric perforation, although no significant difference was observed between the S-O and control groups. Applying S-O clips enables endoscopists to promptly perform submucosal dissection with a better visual field. It eliminates the need to consider perplexing strategies, such as using gravity or trimming the submucosal layer, which are typically necessary with traditional methods. Furthermore, the use of M-scopes and grasping snares was reduced, resulting in a shorter procedure time.

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Notably, our study showed not only a reduction in the procedure time but also an improvement in the complete resection rate. Two retrospective studies reported the application of S-O clips in 48 and 51 cases [10,11], whereas we evaluated the effectiveness of S-O clips in 141 cases. Therefore, our study showed a significant increase in the complete resection rates in ESD using an S-O clip. Regarding the elevated complete resection rate, we could not enumerate the decisive factors contributing to the results; however, we surmise that the S-O clip facilitates submucosal incision by allowing endoscopists to insert the tips of the instruments into the submucosa more easily. Consequently, endoscopists can easily approach the lateral surface and dissect the submucosal layer of the lesions satisfactorily. The S-O clip facilitates easier submucosal incisions in challenging cases, such as lesions located at the greater curvature in the upper stomach, since a tangential approach is needed to dissect the submucosal layer unless the S-O clip is not applied. Furthermore, the S-O clip simplifies the process of performing submucosal incisions in locationally challenging cases [31].

Concerning other outcomes, such as the incidence of gastric perforation and bleeding, maximal serum CRP and decreased Hb levels, and length of hospital stay, no significant differences were observed between the groups after PSM. These outcomes are not dependent on the ESD technique alone; other factors should also be considered. For example, CRP levels may rise due to perioperative aspiration pneumonia [32], and the decreased Hb level and bleeding rate can be influenced by comorbidities, such as heart disease, liver cirrhosis, and chronic kidney disease with or without hemodialysis [33,34]. Regarding the occurrence of gastric perforation, we speculate that the use of an S-O clip might reduce the incidence of perforation if we had evaluated more patients.

The most important point emphasized in our study is that endoscopists who undertake gastric ESD may benefit from the technical merits of using the S-O clip. The subgroup analysis revealed that the use of the S-O clip improved the procedure time in gastric ESD, even when performed by trainees. Currently, ESD is standardized in Japan; therefore, the institutions capable of performing ESD should not be limited. However, a tendency for disparities exists between low- and high-volume centers in terms of accessibility to advanced instruments, such as M-scopes or S-O clips. Expert-led training programs may also differ at the educational level. A report indicated that the widespread use of ESD has been limited by technical challenges, lengthy procedures, and issues related to the availability and standardization of training [27]. S-O clips play an important role in solving the differences in ESD outcomes between trainees and experts by improving the endoscopic visibility of the submucosal layer. This is the first study to demonstrate the utility of S-O clips for trainees. To the best of our knowledge, only a few reports exist on the effectiveness of internal traction devices for trainees in gastric ESD [27,35-37]. For example, reports on the multi-loop traction device have been limited to ex vivo studies. The multi-loop traction device is an internal traction device with multiple rings that enables redirection or retention during ESD when the countertraction is insufficient [35]. However, the S-O clip incorporates a spring mechanism, which can maintain a strengthened traction. As shown in the subgroup analyses, the S-O clip is significantly useful when handling lesions located in the upper third of the stomach (U) and lesions at the circumferential location of the lesser and greater curvatures of the stomach (Less and Gre). We believe that the S-O clip guarantees benefits in handling lesions on the lesser curvature (Less) of the cardia or the greater curvature (Gre) of the upper body of the stomach, where maintaining traction strength is crucial. From the standpoint of the medical economy, the S-O clip, which costs approximately $35 (¥5000) without resorting to other expensive alternatives, might be more cost-effective. Therefore, the scheduled S-O clip has advantages and disadvantages in terms of cost reduction. However, further prospective studies on cost-effectiveness are essential to validate whether S-O clips contribute to the spiraling medical economy.

The scheduled application of S-O clips in gastric ESD, the main method in this study, had several limitations. First, attaching the S-O clip properly to the specimen and detaching it from the contralateral gastric mucosa after completing ESD is a skilled technique that requires familiarity. Second, the S-O clip can interfere with the endoscope, particularly in the retroflex position. Therefore, selecting the anchoring site of the S-O clip is important to prevent any interference during the procedure when using the retroflex endoscopic position. Finally, the S-O clip is only available in limited countries at present; therefore, the facilities that can use the S-O clip are restricted.

Our study had some limitations. First, this was not a prospective randomized controlled trial but a retrospective study conducted at a single endoscopic center. Second, we used PSM analysis to mitigate selection bias; however, matching all background factors of the cases was impossible. Third, the usefulness of the S-O clip for trainees was only demonstrated in the subgroup analysis. In the present study, we did not evaluate whether the S-O clip reduced the burden on the medical economy in the present study. Therefore, further research on whether S-O clips could reduce the medical economy and whether indications should be selected based on the location or circumferential location of the stomach is desirable.

Conclusions

The scheduled application of S-O clips in gastric ESD is effective in improving procedural time and complete resection rates, benefiting endoscopists across all experience levels, even in challenging cases with difficult locations and submucosal fibrosis. This is because the S-O clip facilitates submucosal incision by allowing endoscopists to insert the tips of the instruments into the submucosa more easily and provides optimal countertraction to better expose the submucosal dissection field.

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Declaration of Figures' Authenticity

All figures submitted have been created by the authors, who confirm that the images are original with no duplication and have not been previously published in whole or in part.

References:

1. Gotoda T, Kondo H, Ono H, et al. A new endoscopic mucosal resection procedure using an insulation-tipped electrosurgical knife for rectal flat lesions: report of two cases. Gastrointest Endosc. 1999;50(4):560-63
2. Ono H, Kondo H, Gotoda T, et al. Endoscopic mucosal resection for treatment of early gastric cancer. Gut. 2001;48(2):225-29
3. Japanese Gastric Cancer Association. Japanese Gastric Cancer Treatment Guidelines 2021 (6th edition). Gastric Cancer. 2023;26(1):1-25
4. Gotoda T, Yanagisawa A, Sasako M, et al. Incidence of lymph node metastasis from early gastric cancer: Estimation with a large number of cases at two large centers. Gastric Cancer. 2000;3(4):219-25
5. Vasconcelos AC, Dinis-Ribeiro M, Libânio D. Endoscopic resection of early gastric cancer and pre-malignant gastric lesions. Cancers (Basel). 2023;15(12):3084
6. Park CH, Yang DH, Kim JW, et al. Clinical practice guideline for endoscopic resection of early gastrointestinal cancer. Clin Endosc. 2020; 53(2):142-66
7. Teoh AY, Chiu PW, Wong SK, et al. Difficulties and outcomes in starting endoscopic submucosal dissection. Surg Endosc. 2010;24(5):1049-54
8. Sakamoto N, Osada T, Shibuya T, et al. The facilitation of a new traction device (S-O clip) assisting endoscopic submucosal dissection for superficial colorectal neoplasms. Endoscopy. 2008;40(Suppl. 2):E94-E95
9. Ritsuno H, Sakamoto N, Osada T, et al. Prospective clinical trial of traction device-assisted endoscopic submucosal dissection of large superficial colorectal tumors using the S-O clip. Surg Endosc. 2014;28(11):3143-49
10. Hashimoto R, Hirasawa D, Iwaki T, et al. Usefulness of the S-O clip for gastric endoscopic submucosal dissection (with video). Surg Endosc. 2018;32(2):908-14
11. Nagata M. Internal traction method using a spring-and-loop with clip (S-O clip) allows countertraction in gastric endoscopic submucosal dissection. Surg Endosc. 2020;34(8):3722-33
12. Niu C, Zhang J, Vallabhajosyula S, et al. The impact of traction methods on endoscopic submucosal dissection efficacy for gastric neoplasia: A systematic review and meta-analysis. J Gastrointest Cancer. 2024;55(1):129-42
13. Oda I, Odagaki T, Suzuki H, et al. Learning curve for endoscopic submucosal dissection of early gastric cancer based on trainee experience. Dig Endosc. 2012;24(Suppl. 1):129-32
14. Obara K, Haruma K, Irisawa A, et al. Guidelines for sedation in gastroenterological endoscopy. Dig Endosc. 2015;27:435-49
15. Japanese Gastric Cancer Association. Japanese classification of gastric carcinoma: 3rd English edition. Gastric Cancer. 2011;14(2):101-12
16. Nagata S, Jin YF, Tomoeda M, et al. Influential factors in procedure time of endoscopic submucosal dissection for gastric cancer with fibrotic change. Dig Endosc. 2011;23(4):296-301
17. Chung IK, Lee JH, Lee SH, et al. Therapeutic outcomes in 1000 cases of endoscopic submucosal dissection for early gastric neoplasms: Korean ESD Study Group multicenter study. Gastrointest Endosc. 2009;69(7):1228-35
18. Yano T, Hasuike N, Ono H, et al. Factors associated with technical difficulty of endoscopic submucosal dissection for early gastric cancer that met the expanded indication criteria: Post hoc analysis of a multi-institutional prospective confirmatory trial (JCOG0607). Gastric Cancer. 2020;23(1):168-74
19. Ono H. Endoscopic submucosal dissection for early gastric cancer. Chin J Dig Dis. 2005;6(3):119-21
20. Bhatt A, Abe S, Kumaravel A, Vargo J, Saito Y. Indications and techniques for endoscopic submucosal dissection. Am J Gastroenterol. 2015;110(6):784-91
21. Turiani Hourneaux de Moura D, Aihara H, Jirapinyo P, et al. Robot-assisted endoscopic submucosal dissection versus conventional ESD for colorectal lesions: Outcomes of a randomized pilot study in endoscopists without prior ESD experience (with video). Gastrointest Endosc. 2019;90(2):290-98
22. Oyama T. Counter traction makes endoscopic submucosal dissection easier. Clin Endosc. 2012;45(4):375-78
23. Saito Y, Emura F, Matsuda T, et al. A new sinker-assisted endoscopic submucosal dissection for colorectal cancer. Gastrointest Endosc. 2005;62(2):297-301
24. Imaeda H, Hosoe N, Ida Y, et al. Novel technique of endoscopic submucosal dissection by using external forceps for early rectal cancer (with videos). Gastrointest Endosc. 2012;75(6):1253-57
25. Ahn JY, Choi KD, Choi JY, et al. Transnasal endoscope-assisted endoscopic submucosal dissection for gastric adenoma and early gastric cancer in the pyloric area: A case series. Endoscopy. 2011;43(3):233-35
26. Neuhaus H, Costamagna G, Devière J, et al. Endoscopic submucosal dissection (ESD) of early neoplastic gastric lesions using a new double-channel endoscope (the 'R-scope'). Endoscopy. 2006;38(10):1016-23
27. Ge PS, Thompson CC, Jirapinyo P, Aihara H. Suture pulley countertraction method reduces procedure time and technical demand of endoscopic submucosal dissection among novice endoscopists learning endoscopic submucosal dissection: A prospective randomized ex vivo study. Gastrointest Endosc. 2019;89(1):177-84
28. 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(4):361-89
29. Yoshida M, Takizawa K, Suzuki S, et al. Conventional versus traction-assisted endoscopic submucosal dissection for gastric neoplasms: A multicenter, randomized controlled trial (with video). Gastrointest Endosc. 2018;87(5):1231-40
30. Mannen K, Tsunada S, Hara M, et al. Risk factors for complications of endoscopic submucosal dissection in gastric tumors: Analysis of 478 lesions. J Gastroenterol. 2010;45(1):30-36
31. Ueyama H, Murakami T, Matsumoto K, et al. Modified attachment method using S-O clip and multibending scope for gastric ESD at the greater curvature of the fundus. Endosc Int Open. 2021;9(2):E195-E96
32. Saito I, Tsuji Y, Sakaguchi Y, et al. Complications related to gastric endoscopic submucosal dissection and their managements. Clin Endosc. 2014;47(5):398-403
33. Libânio D, Costa MN, Pimentel-Nunes P, Dinis-Ribeiro M. Risk factors for bleeding after gastric endoscopic submucosal dissection: A systematic review and meta-analysis. Gastrointest Endosc. 2016;84(4):572-86
34. Hatta W, Tsuji Y, Yoshio T, et al. Prediction model of bleeding after endoscopic submucosal dissection for early gastric cancer: BEST-J score. Gut. 2021;70(3):476-84
35. Matsui H, Tamai N, Futakuchi T, et al. Multi-loop traction device facilitates gastric endoscopic submucosal dissection: Ex vivo pilot study and an inaugural clinical experience. BMC Gastroenterol. 2022;22(1):10
36. Yang D, Aihara H, Hasan MK, et al. Novel single-operator through-the-scope traction device for endoscopic submucosal dissection: Outcomes of a multicenter randomized pilot ex-vivo study in trainees with limited endoscopic submucosal dissection experience (with video). DEN Open. 2023;3(1):e174
37. He Y, Fu K, Leung J, et al. Traction with dental floss and endoscopic clip improves trainee success in performing gastric endoscopic submucosal dissection (ESD): A live porcine study (with video). Surg Endosc. 2016;30(7):3138-44

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