Loop9 closure technique for mucosal defects after colorectal endoscopic submucosal dissection (with video)

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ABSTRACT

Background and study aims Mucosal defect closure after colorectal endoscopic submucosal dissection (ESD) has the potential to reduce the occurrence of delayed adverse events (AEs) such as bleeding and perforation. This study aimed to assess the feasibility and effectiveness of the Loop9 method for closing mucosal defects following colorectal ESD.

Patients and methods A retrospective single-center study was conducted using prospectively collected data from May 2020 to March 2023. Loop9 was deployed through a single instrument channel and anchored with clips at the defect site. Closure was accomplished by tightening the loop and deploying additional conventional clips as needed for complete closure. The primary outcome was complete closure rate, with secondary outcomes including the sustained closure rate at 4 to 5 days post-ESD, closed defect size, closure time, number of additional clips, and incidence of delayed AEs.

Results This study included 118 cases. Complete closure was achieved in 96.6% of cases (114/118) with a sustained closure rate of 93.9% (107/114). The median size of the closed mucosal defects was 30 mm (interquartile range [IQR]: 25–38, range: 15–74). The median closure time was 14 minutes (IQR: 11.25–17), and the median number of additional clips deployed was six (IQR: 4–7). Stenosis requiring balloon dilatation was observed in one patient; however, there were no instances of post-ESD bleeding or delayed perforation.

Conclusions The Loop9 method proved feasible and effective for closing mucosal defects following colorectal ESD, achieving high rates of complete and sustained closure.

Introduction

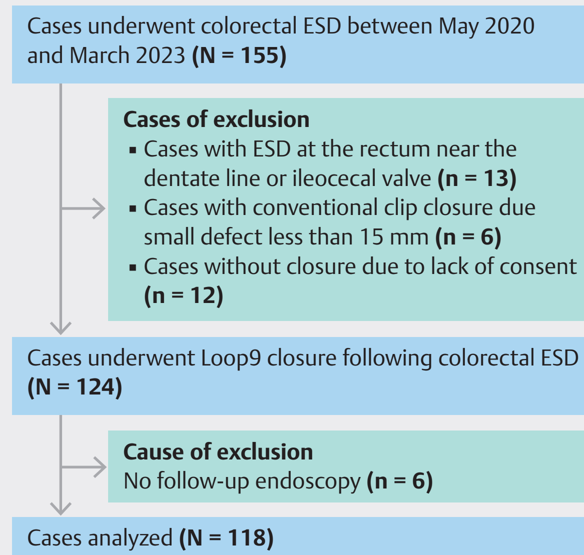
Endoscopic submucosal dissection (ESD), which has revolutionized the treatment of colorectal neoplasms, is known for its minimal invasiveness, high en bloc resection rates, precise histological evaluations, and low local recurrence rates. Evolution in ESD-related instruments and techniques has established it as a core treatment for colorectal cancer. However, delayed adverse events (AEs) such as bleeding and perforation continue to pose significant patient safety concerns [1]. Recent multicenter randomized trials have highlighted that prophylactic clip closure of mucosal defects after resection of large (> 20 mm) non-pedunculated colon polyps can significantly reduce the risk of post-procedure bleeding [2, 3]. Compared with endoscopic mucosal resection (EMR), ESD is usually performed for larger lesions, resulting in larger mucosal defects and requiring more thermal energy than simple polypectomy. For complete closure of large mucosal defects after ESD, several techniques and advanced devices have been developed [4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15]; however, there is still no standard approach because of the complexity of the approach and the need for expensive equipment.

The technique reported by Matsuda et al. in 2004 for completely closing large defects post-EMR was innovative but had limitations, such as the need for a double-channel endoscope or reinsertion of the endoscope [8]. Based on the principle of this technique, we developed and reported about a novel single-channel endoscopic closure technique, "Loop9," using a single-channel endoscope and readily commercially available materials [16]. In this study, we assessed the technical feasibility and efficacy of the Loop9 method, and the attainability of sustained closure after colorectal ESD.

Patients and methods

A retrospective single-center study was conducted using prospectively collected data from May 2020 to March 2023 at Showa University Koto Toyosu Hospital, a tertiary referral center in Tokyo, Japan. The selection process is shown in ▶ **Fig. 1**. Among 155 colorectal ESDs performed at our center during this period, exclusions were made for lesions located in the lower rectum near the dentate line (n = 11) and lesions in the cecum including the ileocecal valve (n = 2) due to the expected higher risk of stenosis associated with these locations. In addition, cases that underwent conventional clip closure for small defects less than 15 mm (n = 6) were also excluded. Twelve patients were excluded due to lack of consent. After these exclusions, 124 patients underwent defect closure using the Loop9 method. A further six patients were excluded because of lack of follow-up endoscopy, leading to a final cohort of 118 cases for analysis. The ESD procedures and subsequent closures were conducted by nine endoscopists, including three experts and six trainees. An expert is defined as having performed over 100 cases of colorectal ESD, whereas trainees are defined as having conducted fewer than 50 cases. We adhered to the Japan Gastroenterological Endoscopy Society (JGES) guidelines for colorectal ESD indications [17]. All targeted lesions were preoperatively diagnosed as either colorectal adenoma or adenocarcinoma, with invasion depths limited to the mucosa or submucosa (< 1000 μm). Management of antithrombotic agents was guided by established guidelines for gastroenterological endoscopy in patients receiving antithrombotic treatment [18]. Regarding post-ESD management, patients who did not experience AEs started drinking water 1 hour after the procedure, and a soft meal diet was initiated on postoperative day 2.

The study complied with the Declaration of Helsinki and received approval from the Institutional Review Board of Showa University (approval number 2023–008-A). Written informed consent was obtained from all participants.



▶ **Fig. 1** Flowchart of patient selection and exclusion criteria for the study on colorectal ESD using loop9 closure method.

Loop9 closure method

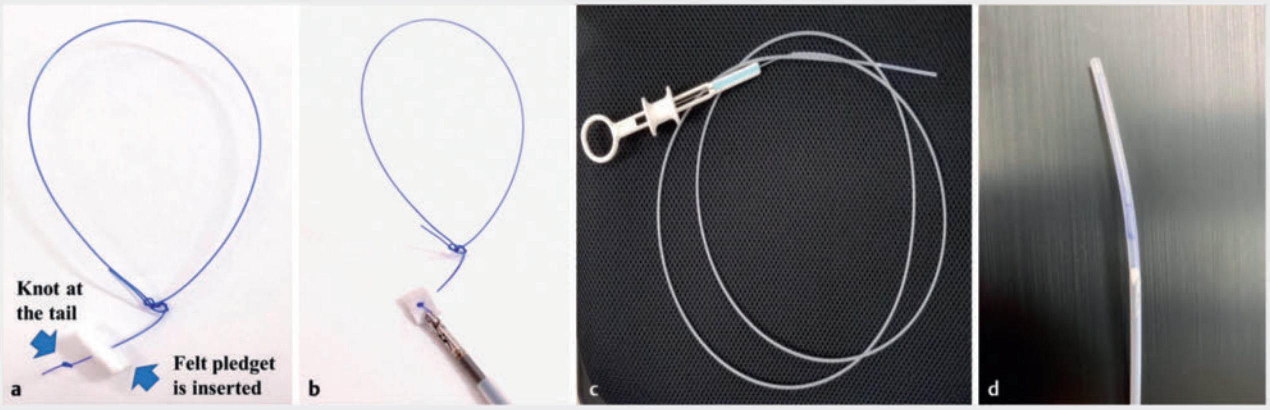
Preparation

For Loop9 closure, we used specific equipment and accessories: a single-channel endoscope (PCF-290TI, Olympus, Tokyo, Japan); a 4–0 absorbable monofilament surgical suture (PDS-II, Ethicon EndoSurgery, Cincinnati, Ohio, United States); a felt pledget; an outer sheath from the QuickClip Pro Clip Fixing Device (HX-202LR, Olympus); and a disposable biopsy forceps (Radial Jaw4, Boston Scientific) suitable for a 2.0-mm scope channel (▶ **Fig. 2** and ▶ **Video 1**). We crafted a self-made slip knot loop resembling the figure of a '9' with the 4–0 absorbable suture. At the loop's tail, a single knot was tied, and an anchor (square-shaped felt pledget piece commonly used in cardiovascular surgery) was pierced between the knot and loop. The outer sheath served dual purposes: loop delivery and closure. The biopsy forceps were used to grab the felt pledget anchor and retract it into the sheath. The preparation time was approximately 5 minutes. A detailed video demonstrating the preparation process is provided.

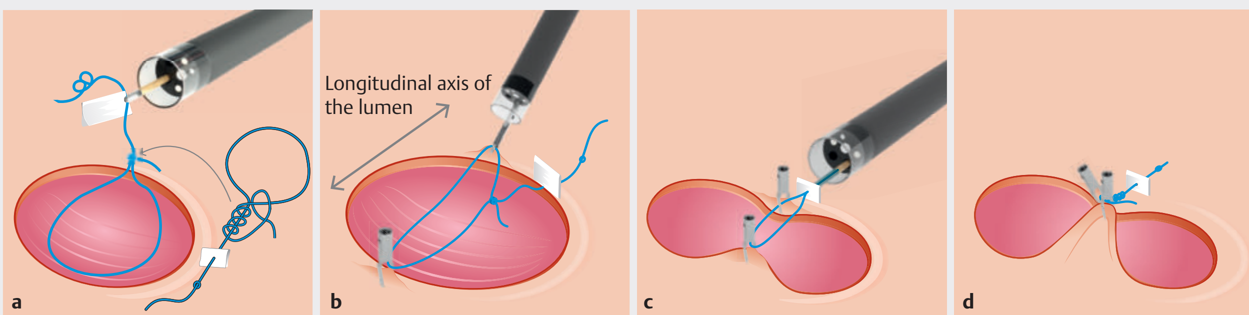
Procedure steps

The Loop9 closure involves three key steps – insertion and release, anchoring, and closure and tightening – which are shown in ▶ **Fig. 3**, ▶ **Fig. 4**, and ▶ **Video 1**.

First, the sheath containing the loop9 is inserted through the endoscope's instrument channel and released into the lumen at the defect site (▶ **Fig. 3a**). Next, SureClip (RC30411, Micro-Tech, Cheshire, Connecticut, United States) clips are used to anchor the loop to the edges of the defect, positioned on opposite sides (▶ **Fig. 3b**). This step is crucial for approximating the defect along the longitudinal axis of the lumen. Effective anchoring requires grasping as much tissue as possible, includ-

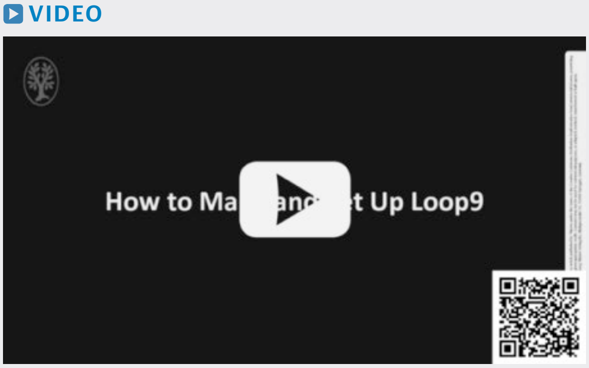


▶ **Fig. 2** Preparation of Loop9. **a** Loop9 made by conventional surgical suture with a slip knot. A knot is made at the distal end of the suture. A felt pledget is placed between the slip knot and the knot. **b** The felt pledget is grabbed and pulled inside the outer sheath using a biopsy forceps. **c** The biopsy forceps is inserted through the outer sheath. **d** The sheath with the Loop9 drawn inside.



▶ **Fig. 3** Schematic illustration of the loop9 closure method. **a** Delivery and release of the loop9 through the channel to the targeted site. **b** After releasing the loop9, clips are placed at opposite edges of the defect. Placement of the clips at the proximal and distal sides of the lumen is preferable. **c** A knot at the distal end of the loop9 is grabbed using a biopsy forceps and pulled inside the sheath. The felt pledget works as an anchor to tighten up the loop. **d** Loop closure and approximation of the mucosal edges are complete.

VIDEO



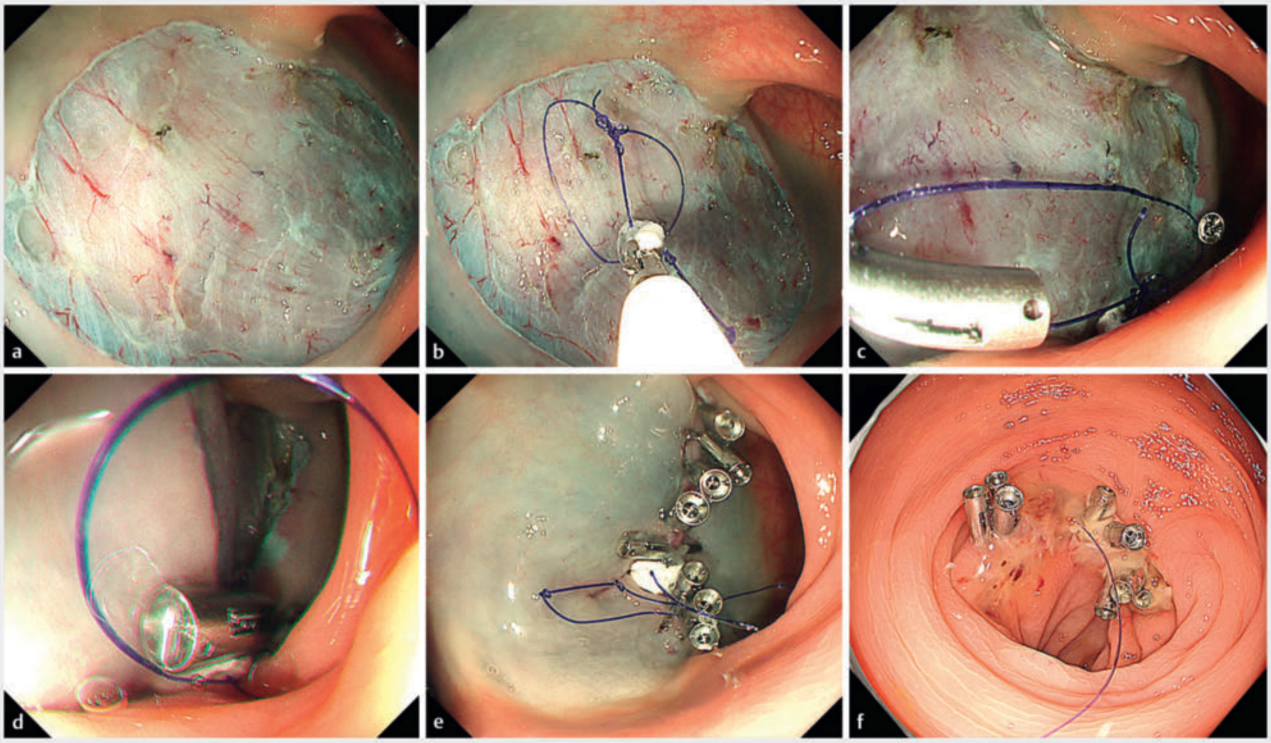
▶ **Video 1** How to create the Loop9 and apply the Loop9 closure method in colorectal ESD.

ing the mucosa-submucosa and muscle layer, to ensure a secure and durable closure. Finally, biopsy forceps, sheathed, are then inserted through the scope channel to grasp the tail knot of the loop, pulling it into the sheath. A felt pledget acts as a pusher, tightening the slip knot and further approximating the borders of the defect. Additional SureClip clips are applied as needed to ensure complete closure of the defect (▶ **Fig. 3c**, ▶ **Fig. 3d**).

The entire Loop9 closure process is performed immediately following ESD, efficiently without the need for withdrawing and reinserting the endoscope. If a muscle layer injury is observed during ESD, it is initially sealed using a conventional clip; subsequently, the Loop9 is applied to achieve comprehensive closure of the defect.

Study outcomes and definition

The primary outcome of this study was the complete closure rate. Secondary outcomes were the sustained closure rate, closed defect size, closure time per defect, time taken for each



▶ **Fig. 4** Case presentation of Loop9 closure technique for a post-ESD mucosal defect. **a** 40-mm mucosal defect in the sigmoid colon following ESD. **b** Delivery and release of the Loop9 device through the endoscopic channel. **c** Anchoring of the Loop9 with clips at the opposite edges of the defect. **d** Complete apposition of the mucosal edges confirmed after tightening the loop. **e** Achievement of complete closure with the addition of more clips to secure the defect. **f** Sustained closure confirmed via endoscopy four days post-ESD.

Loop9 closure, the number of additional clips used, length of hospital stay post-ESD, and delayed AEs such as bleeding, perforation, and post-ESD electrocoagulation syndrome (PECS). Complete closure was defined when the post-ESD mucosal defect was closed without any space and the closure time was calculated as the time from insertion of the Loop9 in the sheath into the endoscope to completion of the whole defect closure. Closed defect size was determined by comparing the shape of the resected specimen with the shape of the mucosal defect. Because all colorectal ESD defects were approximated along the longitudinal axis of the lumen, the length of the defect along the longitudinal axis of the lumen was adopted as the closed defect size. Sustained closure was defined as complete apposition of mucosal defect edges, confirmed by follow-up endoscopy conducted 4 to 5 days post-ESD. Delayed bleeding was characterized as bleeding necessitating endoscopic hemostasis or transfusion or presenting with a hemoglobin loss of ≥ 2 g/dL post-ESD [19]. Delayed perforation was identified by detection of free air on abdominal computed tomography scans post-procedure in patients without perforation during ESD. PECS was defined as localized abdominal pain and fever (> 37.6°C, leukocytosis > 10,000/μL), or elevated C-reactive protein levels (> 0.5 mg/dL) occurring post-ESD without clear evidence of perforation [20].

Statistical analysis

All statistical analyses were conducted using JMP software (SAS Institute, Cary, North Carolina, United States). Categorical data were represented as frequencies and percentages, while continuous and nonparametric variables were presented as medians with interquartile ranges or overall ranges.

Results

Patient characteristics and outcomes are detailed in ▶ **Table 1** and ▶ **Table 2**. The median patient age was 72 years (interquartile range [IQR]: 60–78) with a male-to-female ratio of 75:43. Oral antithrombotic agents were used by 18.6% of patients (22/118). Lesion locations were distributed across the colon as follows: cecum (12.7%), ascending colon (25.4%), transverse colon (28.8%), descending colon (4.2%), sigmoid colon (16.9%), and rectum (11.9%). Median lesion size was 25 mm (IQR: 20–35). Perforation during ESD occurred in 8.5% of cases. Median size of the closed defect length was 30 mm (IQR 25–38, range 15–74). Immediate complete closure was achieved in 96.6% of cases (114/118), with a sustained closure rate of 93.9% (107/114) as confirmed by follow-up endoscopy 4 to 5 days post-ESD. Median time required for complete closure was 14 minutes per defect, and 4 minutes per Loop9 closure. Median number of additional clips used was six (IQR: 4–7). Median

▶ **Table 1** Patient and lesion characteristics (N = 118).

Characteristics	Values
Age, median (IQR, range), years	72 (60–78, 29–88)
Gender, male/female	75/43
Use of oral antithrombotic agent, n (%)	
▪ None	96 (81.4%)
▪ Antiplatelet	16 (13.6%)
▪ Oral anticoagulant	1 (0.8%)
▪ Direct oral anticoagulant (DOAC)	8 (6.8%)
Location, n (%)	
▪ Cecum	15 (12.7%)
▪ Ascending colon	30 (25.4%)
▪ Transverse colon	34 (28.8%)
▪ Descending colon	5 (4.2%)
▪ Sigmoid colon	20 (16.9%)
▪ Rectum	14 (11.9%)
▪ Rectosigmoid	4 (3.4%)
▪ Ra	7 (5.9%)
▪ Rb	3 (2.5%)
Size of the lesion, median (IQR, range), mm	25 (20–35, 10–104)
Histology, n (%)	
▪ Sessile serrated lesion	17 (14.4%)
▪ Low grade tubular adenoma	11 (9.3%)
▪ High grade tubular adenoma ~ intramucosal cancer	77 (65.3%)
▪ Submucosal cancer	13 (11.0%)

ESD, endoscopic submucosal dissection; IQR, Interquartile range; Ra, rectum above the peritoneal reflection; Rb, rectum below the peritoneal reflection.

▶ **Table 2** Closure technique results.

Closure technique results	Values
Size of the closed defect, median (IQR, range), mm	30 (25–38, 15–74)
Complete closure rate, n (%)	114/118 (96.6%)
Sustained closure rate, n (%)	107/114 (93.9%)
Complete closure time, median (IQR), min	14 (11.25–17)
Closure time per one loop, median (IQR), min	4 (4–5)
Number of loops used, median (IQR)	1 (1–1)
Number of additional clips used, median (IQR)	6 (4–7)
Post-procedural adverse events	
Delayed perforation, n (%)	0 (0%)
Bleeding, n (%)	0 (0%)
Post-ESD electrocoagulation syndrome, n (%)	2 (1.7%)
Stenosis, n (%)	1 (0.8%)
C-reactive protein level (mg/dl) at post-ESD day1, median (IQR)	0.56 (0.17–1.33)
Hospital stays after ESD, days, median (IQR)	5 (4–5)

ESD, endoscopic submucosal dissection; IQR, interquartile range.

hospital stay post-ESD was 5 days (IQR: 4–5). No delayed AEs such as bleeding or perforation were reported. Two cases of PECS in the transverse and descending colon were managed conservatively with antibiotics, with no extension of hospital stay. Asymptomatic stenosis developed in one patient in the transverse colon, which occurred in a large semi-circumferential lesion and necessitated balloon dilation 3 months post-procedure. Immediate complete closure was not achieved in four cases located in the transverse colon due to challenges in scope maneuverability, stability, bowel movement, and lack of working space. During the 4 to 5 days of follow-up, partial dehiscence was observed in seven cases, five of which occurred in the rectosigmoid area. All instances of partial dehiscence occurred at sites of additional clips, with no loosening or detachment of Loop9 closures noted.

Discussion

This study demonstrates the feasibility and efficacy of the Loop9 method for mucosal defect closure following colorectal ESD. We observed high rates of complete closure, sustained closure, and favorable closure times. Notably, sustainability of the closure method is critical to its reliability; however, reports about this aspect are limited. Although second-look colonoscopy is not commonly practiced in routine clinical settings, dehiscence of the defect post-procedure is often encountered even after achieving immediate closure. In our institution, it is routine practice to perform a second-look colonoscopy, and patients are typically discharged on the day of the second-look procedure or the following day. We have implemented use of propofol to minimize patient discomfort during these procedures and have also adjusted bowel preparation to use a reduced amount of laxative or no laxative for sigmoid and rectal defects. This practice allowed us to confirm a sustained closure rate of 93.9%, which underscores the reliability of the Loop9 method and emphasizes one of the key strengths of our study.

Traditional through-the-scope (TTS) clip closures often have limited tissue grasp and low closure force, prompting development of various suturing techniques to prevent delayed AEs [21]. Existing TTS clip closure techniques (▶ **Table 3**) include the hold-and-drag method using repositionable clips [4], the clip-on-clip closure method [5], the underwater clip closure method [6] and the recently reported Origami method (OGM)

▶ **Table 3** Comparison of various mucosal defect closure methods.

Closure method	Features	Requirements
TTS clip alone		
Hold-and-drag method using repositionable clips [4]	Repositionable clips are used to hold and drag the edge of the mucosal defect to the contra-edge	May require advanced endoscopic skills
Clip-on-clip closure method [5]	Utilizes overlapping clips to achieve closure and minimizes muscle layer damage	May require a relatively large number of clips
Underwater clip closure method [6]	Underwater condition reduces pressure in the lumen, decreases the size of the defect, improves visibility, and allows precise clip placement	Requires water irrigation and suction time
Origami method (OGM) [7]	Involves folding the muscle layer to eliminate dead space and enables closing large defects	Requires careful handling to prevent clip penetration of the muscle layer
TTS clip with supplemental materials		
Loop9 method	Purse-string suturing technique that can be done entirely through the endoscopic channel. Free loop in the lumen simplifies the process of fixing loop on the defect edges	Requires crafting of the loop requires familiarity, with 5 minutes of preparation time
Endoloop and clips [8]	Original purse-string suturing technique combining endoloop with clips for strong and reliable defect closure	Usually requires scope reinsertion or a double-channel scope
String clip suturing method [9, 12]	Provides secure closure by pulling the free end of the string; allows flexible adjustment of tissue edges	Requires cutting the string and has a risk of tangling
Line-assisted complete closure technique [10]	Utilizes a clip and line to assist in complete defect closure; enables tight closure by pulling the line directly	Requires cutting the line and has a risk of tangling
Double-loop clip method [14]	Simple method that employs double loops attached to the clip which allows approximation of the defect edges	May leave a gap between mucosal edges during initial approximation due to the fixed loop size
Reopenable clip-over-the-line method [15]	Reopenable clips with line enable repositioning for accurate placement; involves grasping the mucosa and muscle layer with clips and pulling the attached string to reduce dead space between the mucosa and muscle layer	May require a relatively large number of clips

TTS, through-the-scope.

[7]. Although these methods are accessible and cost-effective, they typically require specific endoscopic skills and training, a relatively larger number of clips, and are generally insufficient for large defects. The OGM, reported by Masunaga et al., showed a median closure time of 17 minutes (range, 9–37 minutes) and a complete closure rate of 94%, with no delayed AEs. This technique, by folding the muscle layer, ensures the closure of all layers, eliminates dead space, and enables reliable closure. Our Loop9 method showed a high sustained closure rate, which can be attributed to the method's ability to effectively grasp and approximate tissue at the edge of the defect, including the submucosal and muscular layers. This technique helps reduce dead space and ensures a tight closure, possibly contributing to durability of the closure.

Techniques that combine TTS clip with supplemental materials (▶ **Table 3**) include the application of the endoloop and clips [8], the string clip suturing method [9, 12], the line-assisted complete closure technique [10], the double-loop clip method [14], and the reopenable clip-over-the-line method [15]. Since Matsuda et al. [8] reported the complete closure of a large defect after EMR by the endoscopic purse-string suturing (EPSS) method utilizing an endoloop and clips in 2004, this technique has been applied in various scenarios, particularly for post-gastric ESD defects [22, 23], and it has proven to be an effective and safe method for closing even large perforations, including those from endoscopic full-thickness resection [24, 25]. However, these applications are predominantly confined to the stomach or distal colon where reinserting the scope poses minimal difficulty. The Loop9 method builds upon the EPSS technique but introduces use of a surgical suture, which is thinner, more flexible, and adjustable. This makes the Loop9 particularly suitable for the proximal colon, where navigating the scope can be more challenging and time-consuming. Although crafting the loop requires familiarity and can be somewhat complex, a significant advantage of the Loop9 method is that the loop remains free within the lumen, simplifying the process of securely fixing it with clips on the defect edges. Unlike methods that use a string through-the-scope channel, which achieve tight closure by pulling the line directly, the Loop9 method avoids complications associated with cutting the string or potential tangling within the channel. Loop9 is safely delivered to the targeted site through a sheath, eliminating risk of tangling and streamlining the procedure, thereby enhancing safety.

Emerging devices such as the OverStitch (Apollo Endosurgery, Inc, Austin, Texas, United States) [26] and the X-Tack endoscopic HeliX tacking system (Apollo Endosurgery, Austin, Texas, United States) [27] show promise for secure closure, yet they face limitations due to device complexity, cost, and availability. In addition, Goto et al. [28] developed an endoscopic hand-suturing device (EHS), and the method can be applied in the colon using a single-channel colonoscope with the aid of an overtube. The EHS provides a closure similar to surgical suturing and the closing force is considerable; however, it has been associated with technical challenges and longer procedure time [13].

When addressing the technique of closure, orienting the closure along the longitudinal axis is advisable. Closing a large defect along the short axis can complicate the procedure due to reduced working space, potentially leading to stenosis. We documented a case of stenosis in a large semi-circumferential lesion that required oblique closure due to technical challenges. Furthermore, during the EPSS, clips may collapse and embed within the tissue, potentially causing muscle injury. We believe that the Loop9 method mitigates risk by using the tip of the sheath to prevent clips from collapsing inward, offering a substantial improvement over the traditional technique.

Although it has not yet been definitively established whether the clip suture prevents post-procedural AEs, our findings indicate that the effect of complete defect closure using the Loop9 method persists for 4 to 5 days following colorectal ESD. Notably, there was no incidence of delayed bleeding, even among a high number of patients on anticoagulants. Achieving complete closure and reducing the exposed defect surface with clips may alleviate stress on the ulcer surface, thereby preventing delayed bleeding or perforation, accelerating ulcer healing, and potentially resulting in fewer AEs.

Despite its advantages, our study has limitations, including its single-center, retrospective design, and lack of comparative analysis with other closure methods. To conclusively demonstrate the efficacy of the Loop9 technique, further prospective, randomized, and comparative studies are required, ideally involving a larger sample size and more diverse clinical settings.

Conclusions

In conclusion, the Loop9 method for closing mucosal defects post-colorectal ESD is both feasible and effective. It offers high complete and sustained closure rates, along with favorable procedure times. The technical ease, reproducibility, and cost-effectiveness of the Loop9 method make it a promising technique for high-risk patients, especially because it does not require expensive devices or double-channel endoscopes and can be performed without the need for scope reinsertion.

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Conflict of Interest

Author H.I. serves as an advisor for Olympus Corporation and Top Corporation. In addition, he has received educational grants from Olympus Corporation and Takeda Pharmaceutical Company. The remaining authors have no conflicts of interest to declare.

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