

Colorectal endoscopic submucosal dissection defect closure: promising but still evolving

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See “Effect of double-layered suturing for mucosal defect closure after colorectal endoscopic submucosal dissection on postoperative adverse events: a propensity score matched retrospective study in Japan” by Kyohei Nishino, Hiroki Fujita, Takahiro Yuge, et al., Clin Endosc 2025;58:881–889.

Endoscopic submucosal dissection (ESD) has emerged as the preferred technique for the management of large, laterally spreading tumors and early colorectal cancers, with its adoption expanding from East Asia, particularly Japan and Korea, to Western clinical practice. However, colorectal ESD remains technically challenging and is characterized by a steep learning curve, prolonged procedure times often exceeding 1 hour, and relatively high complication rates. Even among experienced endoscopists, certain scenarios, such as lesions involving the anal verge, appendiceal orifice, flexural sites, or areas with pronounced submucosal fibrosis, pose significant procedural difficulties.¹ Consequently, ESD carries a higher risk profile than endoscopic mucosal resection.

Post-ESD complications, including delayed bleeding, delayed perforation, and post-ESD electrocoagulation syndrome (PECS), have driven extensive investigations into preventive strategies.² Among these, prophylactic closure of mucosal

defects has emerged as a rational and potentially effective approach, as immediate closure may protect the ulcer bed, reduce bacterial contamination, and attenuate inflammatory responses. However, routine implementation of prophylactic closure remains controversial. Nishino et al.³ provide valuable insights into the clinical impact of prophylactic double-layer suturing using conventional clips.

Over the past decade, various techniques have been developed to achieve reliable closure of mucosal defects after colorectal ESD. The simplest and most widely adopted approach is closure with conventional through-the-scope clips, which approximate the mucosal edges without requiring scope reinsertion. This method is generally effective in treating small defects (typically <2 cm). However, post-ESD defects are inevitably larger than the original lesions, creating wide gaps that are difficult to close using standard clips alone.

To address these limitations, several modified closure techniques using conventional clips have been introduced, including the hold-and-drag method, closure assisted by small mucosal incisions, and clip-on-clip closure.⁴ These approaches are practical because they rely solely on standard clips without additional devices. However, large defects can be technically challenging and frequently achieve only superficial mucosal approximation rather than durable full-thickness closure. Additional strategies employing threads, bands, or endoloops can enhance closure feasibility but are technically demanding and time-consuming.

Recently, tissue apposition clips have been developed to fa-

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cilitate reliable defect closure. The dual-action tissue (DAT) clip (Micro Tech) has a three-arm design with a fixed central column and two independently operable arms that sequentially grasp opposing edges. In a multicenter prospective study of large nonpedunculated colorectal lesions ≥ 20 mm, the DAT clip, used in combination with conventional clips, achieved complete closure in over 95% of cases, with a delayed bleeding rate of 0.9%.⁵ The Mantis clip (Boston Scientific) is another anchor-pronged device designed to provide secure tissue grasping and minimize slippage, making it particularly suitable for the hold-and-drag technique. In a study involving 52 colorectal ESD cases, Mantis-assisted closure achieved complete defect closure in 98% of cases, with low rates of delayed bleeding (1.9%) and PECS (1.9%).⁶ Although these devices demonstrate high efficacy, their clinical adoption remains limited, with supporting evidence still emerging.

Over-the-scope clips (Ovesco Endoscopy) and padlock clips (Aponos Medical) provide robust closure even for large mucosal defects and are widely used for perforations and fistulas. These devices have demonstrated efficacy in reducing the incidence of post-ESD PECS and other adverse events. However, achieving complete closure of extensive defects can remain challenging, and in many cases, multiple clips are required, leading to increased costs. In addition, their use necessitates scope withdrawal and device reloading, prolongs the procedure time, and requires advanced technical skills, limiting their routine application, particularly in the proximal colon.⁷

Endoscopic suturing is an important strategy in defect closure. The OverStitch platform (Apollo Endosurgery) enables suture-like closure and has demonstrated efficacy for large defects. However, it requires a double-channel endoscope, specialized accessories, and advanced operator training. More recently, single-channel adaptations, such as the OverStitch Sx, have shown feasibility, but available data remain limited, and further studies are needed to validate outcomes in challenging locations and routine clinical practice.⁸ Through-the-scope suturing systems, including endoscopic hand suturing (Olympus Medical Systems), can achieve durable closure using absorbable sutures, yet procedural times are prolonged, and technical demands remain high.⁹

Overall, current closure strategies present a fundamental dilemma: conventional clips are simple, widely available, and easy to deploy but are often inadequate for large defects, whereas advanced closure devices offer more secure and durable outcomes but are limited by cost, availability, and technical com-

plexity. Furthermore, most conventional methods achieve only mucosal apposition, leaving a submucosal dead space that may predispose to bacterial contamination, inflammation, or wound dehiscence. Therefore, durable closure necessitates approximating all layers of the colonic wall, including the muscular layer.

The concept of double-layer closure was first described by Tanaka et al.¹⁰ using standard clips without specialized devices. In this technique, clips are initially applied to the submucosal layer at the ulcer base to reduce defects, followed by clips to close the mucosa. By mimicking surgical principles, this approach eliminates dead space and provides a more durable closure.

Building on this concept, Nishino et al.³ evaluated prophylactic double-layer closure using conventional clips in 370 colorectal ESD cases. Complete double-layer closure was achieved in 197 lesions, compared with partial or no closure. After propensity score matching, complete double-layer closure was associated with a significantly lower overall rate of adverse events (2.2% vs. 9.6%) and reduced postoperative pain. Although the differences in delayed bleeding and PECS did not reach statistical significance individually, the overall reduction in complications and patient discomfort emphasized the clinical value of this approach.

This study had several strengths. It uses a practical approach with conventional clips while adhering to the surgical principle of layered closure. The relatively large sample size, coupled with the use of propensity score matching, enhances its validity. Notably, both adverse events and patient-centered outcomes, such as pain, were evaluated to provide a comprehensive assessment of efficacy. The observation that double-layer closure reduces complications and patient discomfort further emphasizes its clinical relevance.

Several limitations of this study must also be considered. This retrospective, single-center design introduces a risk of bias. The decision to perform closure was left to the discretion of the endoscopist, and defects that were technically easier to close were preferentially selected for complete closure. Residual confounders, such as operator expertise and the presence of submucosal fibrosis, and intraprocedural factors, such as injury to the muscle layer, may also have influenced outcomes. Event rates were relatively low, suggesting limited statistical power to detect differences in individual outcomes.

This study provides clinically meaningful evidence that double-layer closure with conventional clips can effectively manage large post-ESD defects and is feasible in many centers without

the need for specialized equipment. Notably, complete closure of both the mucosal and deeper layers was associated with fewer complications and reduced pain compared with incomplete or no closure, highlighting the critical role of closure quality. However, the procedure required an average of eight clips and approximately 9 minutes, raising concerns regarding cost-effectiveness, procedure duration, and operator fatigue.

Large multicenter randomized trials are needed to validate these findings and identify patients who are most likely to benefit. Cost-effectiveness analyses are essential because the additional use of clips and procedural time must be weighed against potential reductions in complication-related costs. With further studies to strengthen the evidence base and more clearly define the clinical contexts in which closure is most beneficial, such approaches may offer clinicians simpler, more practical, and more effective strategies to prevent complications following high-risk procedures such as colorectal ESD.

Conflicts of Interest

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