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Comparative study on different endoscopic submucosal dissection techniques for the treatment of superficial esophageal cancer and precancerous lesions

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Abstract

Background This study aims to compare the effectiveness and safety of traditional endoscopic submucosal dissection (ESD), endoscopic submucosal tunneling dissection (ESTD), and endoscopic submucosal dissection with C-shaped incision (ESD-C) in the treatment of superficial esophageal cancer and precancerous lesions, providing reference and guidance for the treatment of esophageal cancer.

Methods A retrospective analysis was conducted on the clinical data of patients who underwent ESD ($n = 96$), ESTD ($n = 103$), and ESD-C ($n = 98$) for superficial esophageal cancer or precancerous lesions between January 2017 and December 2022. Through comparative analysis, the effectiveness and safety of the three surgical methods were evaluated, and the risk factors for postoperative esophageal stricture were explored.

Results In terms of total operative time and dissection time, the ESD group > ESTD group > ESD-C group; in terms of dissection speed, the ESD group < ESTD group < ESD-C group; in terms of dissection area, the ESD group < ESTD group and ESD-C group; and in terms of wound treatment time, the ESD group > ESTD group and ESD-C group. In terms of surgical outcomes, the en bloc resection rate was 100% in all three groups, with complete resection rates of 86.84%, 90.79%, and 88.16% in the ESD, ESTD, and ESD-C groups, respectively. The risk factors for postoperative esophageal stricture included dissection area, circumferential proportion of the lesion, and injury to the muscularis propria.

Conclusion Among the three surgical approaches, ESD-C demonstrated superior performance in operative time, resection speed, and procedural efficiency. Increased circumferential involvement of the lesion, larger resection area, and greater injury to the muscularis propria were associated with a heightened risk of postoperative esophageal stricture.

Keywords Esophageal superficial neoplasms, Endoscopic submucosal dissection, Treatment

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Introduction

Esophageal cancer is the seventh most prevalent malignant neoplasm globally and the sixth leading cause of cancer-related mortality, with more than 470,000 new cases diagnosed annually [1]. The incidence of this malignancy is escalating at an alarming rate, posing a significant challenge to global health. Within China, the burden of esophageal cancer is particularly pronounced, with the nation accounting for 53.70% of the world's newly diagnosed cases and 55.35% of cancer-related deaths [2]. Regrettably, early-stage esophageal cancer is often asymptomatic, resulting in the majority of patients presenting with advanced disease at the time of diagnosis, which is associated with a poorer prognosis. Recent years have witnessed substantial advancements in the early detection and treatment of gastrointestinal cancers in China, particularly through the implementation of endoscopic screening and therapeutic interventions for esophageal cancer. Since 2010, there has been a sustained decline in the mortality rate associated with esophageal cancer in the country, especially in regions with high incidence rates, highlighting the critical importance of early diagnosis and treatment [3]. Superficial esophageal cancer and its associated precancerous conditions constitute critical phases within the continuum of the disease [4], and the timely identification and management of these conditions are essential for reducing esophageal cancer mortality and enhancing patient survival rates.

Esophagectomy has long been established as the standard therapeutic intervention for patients diagnosed with esophageal cancer. However, due to the associated trauma, substantial complication rates, and increased mortality, recent advancements in medical technology have necessitated a revision of treatment guidelines [5]. These guidelines now advocate for endoscopic resection as the preferred modality for managing early-stage esophageal cancer, including superficial lesions with no lymph node involvement or a minimal risk of metastasis, as well as precancerous conditions. This endoscopic approach demonstrates efficacy comparable to that of traditional surgical techniques, with five-year survival rates surpassing 95% [6, 7].

Among the key endoscopic interventions for superficial esophageal cancer and precancerous conditions are endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD), and mucosectomy with multiple-band ligation (MBM). Notably, ESD offers a superior overall resection and cure rate while maintaining a lower recurrence rate [8]. The primary advantage of ESD is its capacity to yield complete tissue specimens, independent of lesion size, thereby improving the precision of pathological evaluation and staging [9]. Nonetheless, conventional ESD may face challenges such as lumen obstruction due to submucosal dissection in larger lesions, limited

surgical visibility, and restricted workspace, all of which can prolong procedural duration and compromise resection outcomes, increasing the risk of adverse events [10]. To mitigate these concerns, endoscopic submucosal tunneling dissection (ESTD) has been introduced. Drawing on the principles of peroral endoscopic myotomy [11], ESTD facilitates meticulous dissection by creating a submucosal tunnel. This technique offers several advantages, including enhanced visibility, effective hemostasis, and a marked reduction in the dispersion of the injected fluid [12, 13]. To enhance the quality of endoscopic surgery, advanced techniques for endoscopic submucosal dissection have been developed. One such technique is the endoscopic submucosal dissection with C-shaped incision (ESD-C) [14], which entails the execution of partial circumferential incisions on both sides of the lesion prior to submucosal dissection, thereby forming a C-shaped configuration that effectively prevents fluid diffusion into adjacent tissues while preserving a clear surgical field and optimal lesion exposure. Comparative analyses [15] between ESTD and ESD-C have demonstrated that both techniques exhibit comparable efficacy and safety profiles in the treatment of early-stage and superficial esophageal cancer.

Currently, comparative investigations into ESD, ESTD, and ESD-C are relatively sparse, both nationally and internationally. This study presents a retrospective analysis of these techniques employed at our institution for the management of superficial esophageal cancer and precancerous lesions. The primary objective is to evaluate and compare the surgical efficiency, therapeutic efficacy, and safety profiles of ESD, ESTD, and ESD-C.

Materials and methods

Research target

A retrospective analysis was performed on 297 patients diagnosed with superficial esophageal cancer or precancerous lesions who underwent endoscopic submucosal dissection at the Digestive Endoscopy Center of the Affiliated Hospital of North Sichuan Medical College between January 2017 and December 2022. The inclusion criteria comprised: (1) patients diagnosed with low-grade intraepithelial neoplasia, high-grade intraepithelial neoplasia, or superficial esophageal squamous cell carcinoma confirmed by endoscopy or biopsy; (2) preoperative assessments that revealed no evidence of regional lymph node involvement or distant metastasis; and (3) patients who satisfied the criteria for endoscopic resection as outlined in the Japanese guidelines for the diagnosis and treatment of esophageal cancer [16] and who underwent ESD, ESTD, or ESD-C. Exclusion criteria included: (1) patients who did not meet the aforementioned inclusion criteria; (2) individuals with incomplete clinical records; (3) patients with coagulation disorders; (4) those with

significant comorbidities affecting vital organ function that precluded anesthesia and endoscopic procedures; and (5) patients with less than one year of clinical follow-up or those who were lost to follow-up. Informed consent for ESD, ESTD, or ESD-C was obtained from all patients prior to the procedures.

Treatment method

All patients were instructed to discontinue non-steroidal anti-inflammatory drugs (NSAIDs) and anticoagulants one week prior to surgery. Additionally, they underwent fasting and dehydration protocols starting 12 h before the procedure. Preoperative evaluations yielded normal results, and all patients provided informed consent, acknowledging the associated surgical risks. Surgical interventions were performed under general anesthesia by a team of three experienced endoscopists, each having conducted over 200 endoscopic submucosal dissections.

During the study period, the three treatment modalities were applied concurrently, with each treatment being implemented independently to mitigate any potential sequential or transitory effects between the methods. The key criteria utilized by the treating physicians in selecting the appropriate treatment approach are summarized as follows: (1) ESD: This procedure was typically favored when preoperative evaluation via magnifying endoscopy or ultrasound endoscopy confirmed that the lesion was confined to the mucosal or submucosal layers (stage T1a) and had a diameter of less than 2–3 cm, particularly in the case of bulging, flat, or superficial lesions. (2) ESTD: This procedure was preferred for lesions exhibiting a ring, curved, or irregular morphology, particularly when located in the esophageal curvature or in challenging areas such as the upper and lower esophagus. Lesions that were confirmed to have invaded the submucosa, but not extended into deeper layers, were also typically managed with ESTD. (3) ESD-C: This procedure was employed for larger, more extensive, or morphologically complex lesions, particularly those located in the esophageal curvature. The C-shaped incision technique used in ESD-C allowed for effective resection in these cases. Moreover, for tumors in the upper or lower esophagus, which require more delicate manipulation due to their anatomical location, ESD-C provided a flexible and precise peeling method, making it the preferred option for these challenging lesions.

Ultimately, the selection of the endoscopic treatment modality was determined by the treating physician's comprehensive assessment, taking into account lesion characteristics, personal expertise, and the patient's preferences.

Conventional ESD: Initially, the lesion was marked using electrocoagulation with a Dual knife approximately 5 mm from the lesion's edge. Subsequently, a submucosal injection was administered adjacent to the marking point

to ensure adequate mucosal elevation. The mucosal layer was then incised along the lateral margin of the marked area, employing both the Dual knife and IT knife alternately to dissect into the submucosal layer. Following the completion of dissection, the surgical site was thoroughly inspected and managed appropriately (Fig. 1).

ESTD Group: After marking and submucosal injection, the mucosa on the anal side of the lesion was incised first, followed by incision of the mucosa on the oral side, thus creating a tunnel connecting the two sides. Peeling was performed along both sides of this tunnel, with subsequent steps mirroring those utilized in the ESD approach (Fig. 2).

ESD-C Group: Following the labeling and submucosal injection, mucosal incisions were made on both the oral and anal sides of the lesion. The incision on the oral side served as the starting point, from which dissection proceeded along the outer edge of the lesion to the anal-side incision, forming a "C" shape. Submucosal dissection was then conducted from the oral to the anal side, followed by incisions of the remaining mucosa lateral to the lesion. The submucosal layer on the contralateral side was dissected in a similar fashion, and finally, the submucosal layer at the lesion's center was removed, with subsequent steps conforming to the conventional ESD methodology (Fig. 3). No intraoperative traction techniques or external assistance with traction were employed during any of the three surgical procedures described.

Postoperative management and follow-up

Patients should be instructed to maintain a semi-recumbent position and to abstain from oral intake for a period of 24 to 48 h following surgery. Concurrently, it is imperative to implement a regimen aimed at suppressing gastric acid secretion, controlling hemorrhage, preventing infection, and ensuring electrolyte homeostasis. Continuous monitoring of vital signs is critical, along with vigilant assessment for clinical manifestations including chest pain, fever, acid reflux, heartburn, abdominal pain, hematemesis, and melena. In cases where lesions extend beyond three-quarters of the circumference of the esophagus, oral prednisone therapy should be initiated post-fasting. The recommended starting dose is 30 mg per day for the initial two weeks, followed by a tapering dose of 25 mg per day for the subsequent two weeks. Thereafter, the dose should be further reduced by 5 mg weekly until cessation of therapy. Postoperative gastroscopy is advised at 3, 6, and 12 months to evaluate wound healing, assess for residual lesions, monitor recurrence, and identify any postoperative strictures. Additionally, chest enhanced CT scans should be performed biannually, with a transition to annual imaging thereafter.

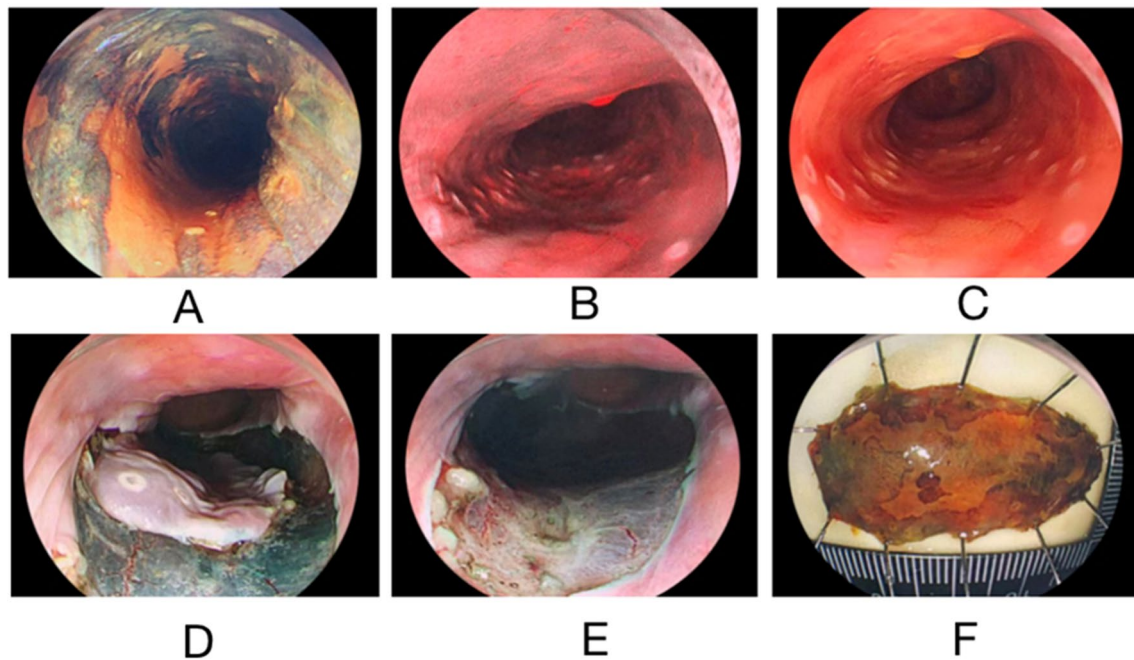


Fig. 1 Procedure of ESD. **A:** Iodine staining to define the extent of the lesion. **B:** Observation of the lesion under Narrow Band Imaging (NBI). **C:** Marking the boundaries of the lesion. **D:** Circumferential incision around the lesion. **E:** Wound after complete excision of the lesion. **F:** Measurement of the specimen size

Observational indicators and definitions

Name, gender, age, location of the lesion, lesion size, morphology of the lesion, postoperative pathology, surgical approach, total duration of the surgery, duration of lesion dissection, area of dissection, duration of wound management, en bloc resection (EnR) rate, complete resection rate, intraoperative complications (bleeding, muscular layer injury), postoperative complications (delayed bleeding, perforation, incidence of stricture), and major postoperative adverse symptoms (chest pain, throat discomfort, acid reflux, heartburn, fever, abdominal pain).

The findings of this investigation encompass several key metrics: en bloc resection (EnR) rate, complete resection rate, total surgical time, dissection time, dissected area, dissection speed, wound management time, and both intraoperative and postoperative adverse events. Adverse events include muscular layer injury, bleeding, and perforation. The total surgical duration is defined as the interval from the initial endoscopic examination to the conclusion of the procedure, which includes the withdrawal of the endoscope. Dissection time is delineated as the duration from the marking of the lesion to its complete excision. The area of the dissected lesion and the size of the lesion are calculated using the formula: $\text{Area [cm}^2\text{]} = (\text{transverse diameter}/2) \times (\text{longitudinal diameter}/2) \times \pi$. Dissection speed, expressed in cm^2/min , is determined by dividing the dissection area by the dissection time. En bloc resection is characterized as the

complete excision of the lesion under endoscopic guidance, yielding a single specimen. Complete resection is defined as the excision of a specimen that exhibits tumor-free vertical and horizontal margins, thus precluding the risk of lymph node metastasis [17]. Muscular layer injury is defined by the exposure, damage, or rupture of the muscular layer during the dissection process. Intraoperative bleeding is categorized as any event necessitating electrocautery or hemostatic clips for hemostatic control. Delayed bleeding is identified by the presence of hematemesis or melena, or a decrease in hemoglobin levels of 20 g/L or greater within 30 days following the procedure. Esophageal stricture is characterized by the failure of a standard 11 mm endoscope to traverse the constricted region. Perforation is indicated by subcutaneous emphysema in the anterior chest or neck, with chest X-ray or CT imaging revealing free air in the mediastinum or cervical region.

Statistical methods

Statistical analyses were conducted utilizing SPSS software version 26.0 (IBM SPSS Inc., Chicago, IL). Continuous variables that adhered to a normal distribution are presented as means \pm standard deviations. For comparisons among multiple groups, one-way analysis of variance (ANOVA) was employed, with subsequent post hoc analyses performed using the Bonferroni t-test. Categorical variables are reported as rates or proportions and were analyzed using Pearson's chi-square test,

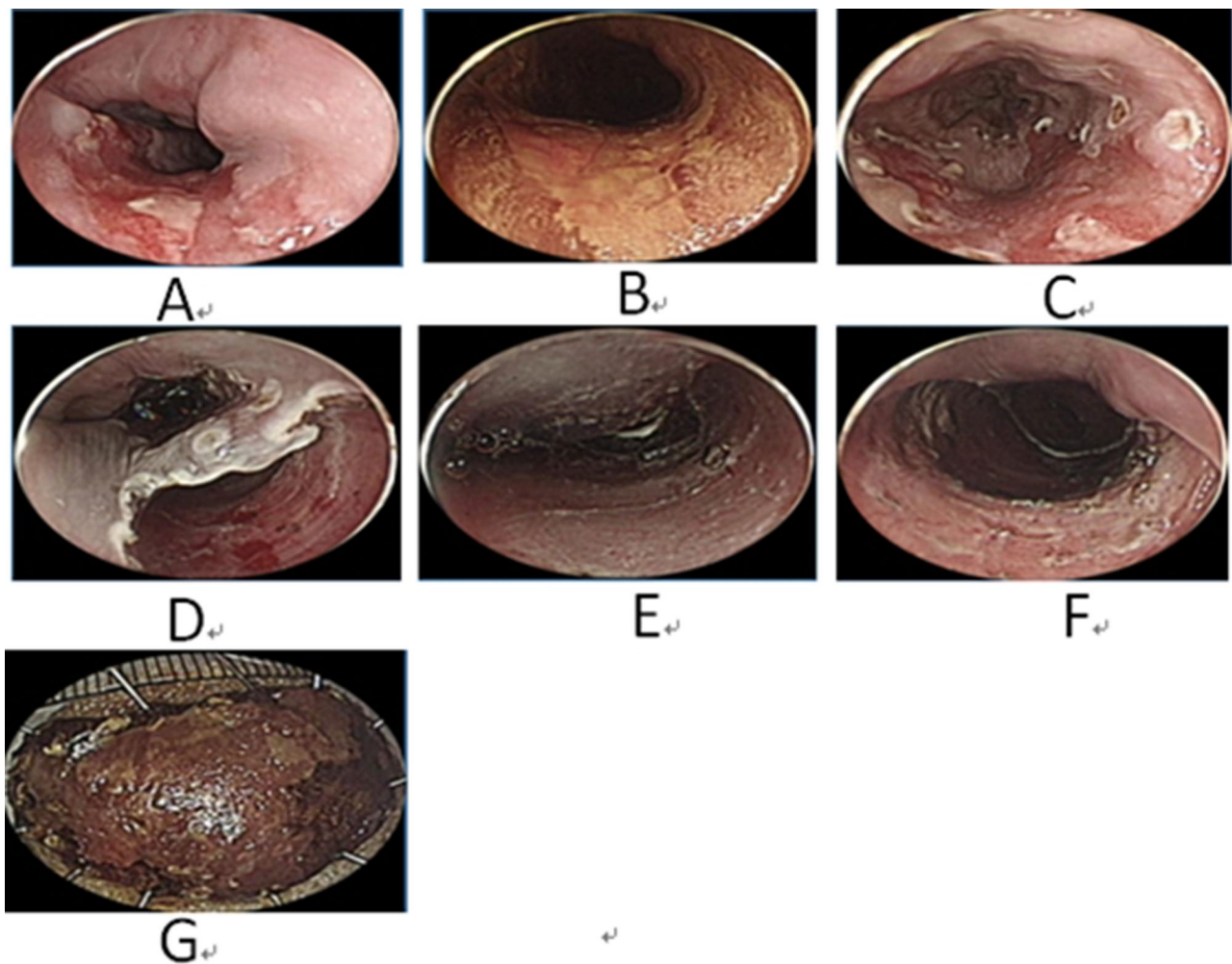


Fig. 2 Procedure of ESTD. **A:** Lesions identified during endoscopy; **B:** Iodine staining used to determine the extent of the lesions; **C:** Marking the boundaries of the lesions; **D:** Establishing a tunnel; **E:** Dissection within the tunnel; **F:** Complete dissection of the lesions; **G:** Measuring the size of the specimen

continuity-corrected chi-square test, or Fisher's exact test as appropriate. A p -value of less than 0.05 was deemed statistically significant; for post hoc multiple comparisons, significance was determined using the Bonferroni adjustment, where $p < 0.05/3 = 0.017$ was considered significant. Additionally, both univariate and multivariate regression analyses were conducted to identify risk factors associated with postoperative esophageal stricture.

In this study, we employed multi-group propensity score matching (PSM) using the `mnp`s function from the R package `twang`. The `mnp`s function, which implements polynomial propensity scores, was adapted to accommodate comparisons across more than two subgroups. The Average Treatment Effect (ATE) was selected as the estimand within the `mnp`s function, which quantifies the average treatment effect across the entire population. Specifically, the ATE represents the difference in the outcome when the treatment is applied to the entire population, as opposed to when the control is applied. By

estimating the ATE, we derived the average propensity score weight for each sample. These weights were then used to partition the data into distinct subgroups, with the samples sorted by their propensity scores in descending order. The highest-weighted sample from each group was subsequently selected, and the matched datasets were then combined to generate the final results.

Results

Baseline patient characteristics

A total of 297 patients with superficial esophageal cancer and precancerous lesions were enrolled in this study in accordance with the predefined inclusion and exclusion criteria. The baseline characteristics of these patients are summarized in Table 1. To mitigate potential bias arising from differences in patient characteristics between the groups, propensity score matching (PSM) was utilized to match patients in a 1:1:1 ratio across the three treatment groups: ESD, ESTD, and ESD-C. Ultimately, 76 patients

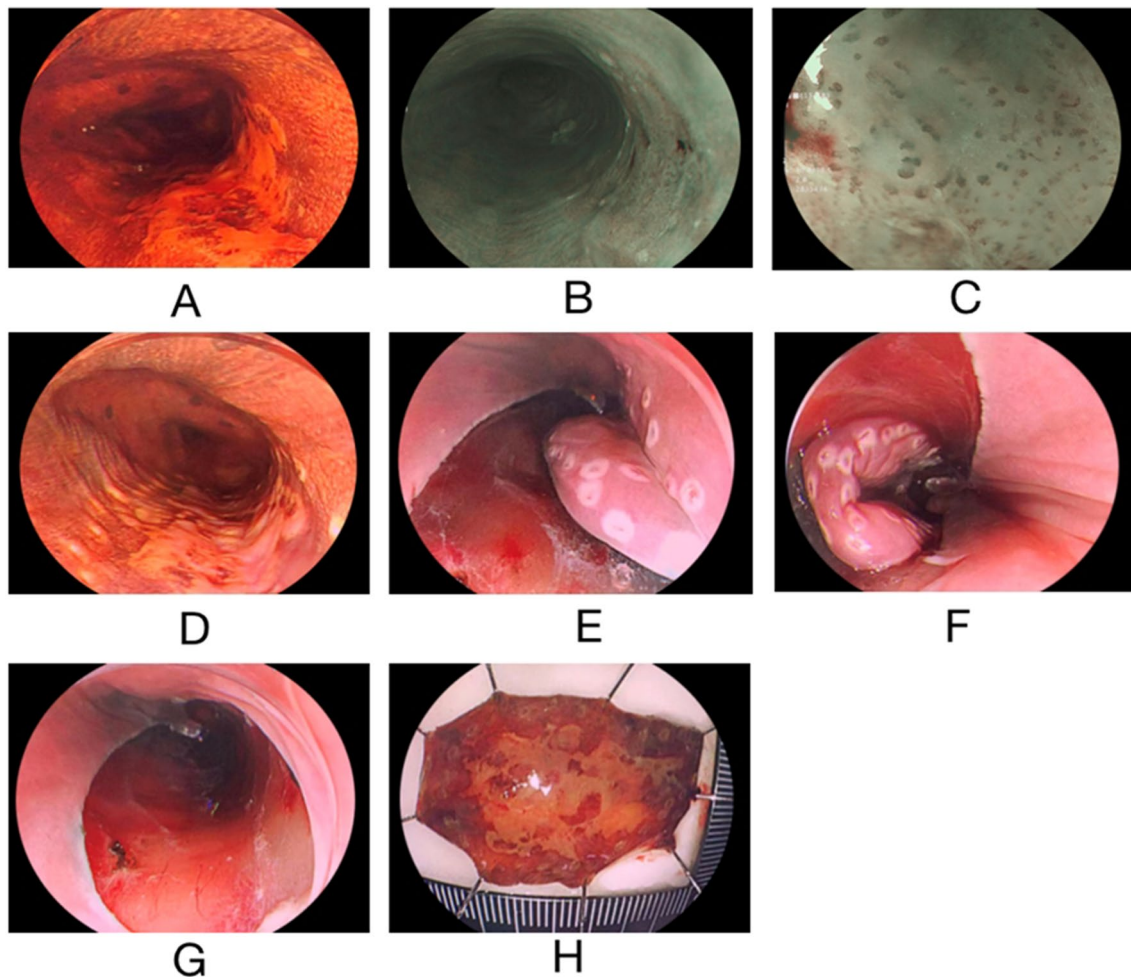


Fig. 3 Procedure of ESD-C. **A:** Iodine staining to determine the extent of the lesion; **B-C:** Observation of the lesion under Narrow Band Imaging (NBI); **D:** Marking the boundaries of the lesion; **E:** C-shaped incision and submucosal dissection; **F:** Completion of C-shaped incision and submucosal dissection on both sides; **G:** Wound after dissection of the lesion; **H:** Measurement of the specimen size

Table 1 Summary of general information for 297 patients

General information	Number of cases (n = 297)
Gender	
Male n(%)	182(61.28%)
Female n(%)	115(38.72%)
Age(years), mean ± SD	63.26 ± 7.36
Lesion location	
Upper n(%)	32(10.78%)
Middle n(%)	199(67.00%)
Lower n(%)	66(22.22%)
Postoperative pathology	
LGIN n(%)	28(9.43%)
HGIN n(%)	138(46.46%)
SC n(%)	131(44.11%)

Legend: Table 1 summarizes the general demographic and clinical information for the 297 patients included in the study. The table includes the following variables: Gender, Age, Lesion location, Postoperative pathology

Lesion location is the location of the esophagus where the lesion is located

Postoperative pathology is the pathologic type of tissue removed after surgery

were matched in each group. Following matching, no statistically significant differences were observed in baseline characteristics, including gender, age, lesion location, Paris classification, lesion size, circumferential involvement, and postoperative pathology ($P > 0.05$, Table 2).

Treatment outcomes

The analysis revealed statistically significant differences in total surgical time, dissection time, dissection speed, dissection area, and wound management time among the three groups ($P < 0.05$, Table 3). Pairwise comparisons indicated that the total surgical time in the ESD-C group was significantly less than that observed in both the ESTD and ESD groups ($P < 0.05$). Additionally, the total surgical time in the ESTD group was also shorter than that in the ESD group ($P < 0.05$) (Fig. 4). In terms of dissection time, the ESD-C group exhibited a notable advantage, with dissection times significantly shorter than those in both the ESTD and ESD groups ($P < 0.05$).

Table 2 Comparison of general information among the three groups

General information	Pre-PSM			P	Post-PSM			P
	ESD(n=96)	ESTD(n=103)	ESD-C(n=98)		ESD(n=76)	ESTD(n=76)	ESD-C(n=76)	
Gender				0.326				0.310
Male n(%)	55(57.29)	69(66.99)	58(59.18)		43(56.58)	51(67.11)	43(56.58)	
Female n(%)	41(42.71)	34(33.01)	40(40.82)		33(43.42)	25(32.90)	33(43.42)	
Age (years), mean ± SD	62.05 ± 7.45	63.87 ± 7.35	63.79 ± 7.19	0.098	63.00 ± 6.42	63.71 ± 7.14	64.80 ± 7.06	0.273
Lesion location				0.827				0.944
Upper n(%)	9(9.38)	14(13.59)	9(9.18)		8(10.53)	10(13.16)	7(9.21)	
Middle n(%)	64(66.67)	67(65.05)	68(69.39)		50(65.79)	48(63.16)	52(68.42)	
Lower n(%)	23(23.96)	22(21.36)	21(21.43)		18(23.68)	18(23.68)	17(22.37)	
Postoperative pathology				0.769				0.868
LGIN n(%)	7(7.29)	10(9.71)	11(11.22)		5(6.58)	7(9.21)	7(9.21)	
HGIN n(%)	47(48.96)	44(42.72)	47(47.96)		38(50.00)	32(42.11)	36(47.37)	
SC n(%)	42(43.75)	49(47.57)	40(40.82)		33(43.42)	37(48.68)	33(43.42)	
Circumferential extent				<0.01				0.292
< 1/2 n(%)	56(58.33)	31(30.10)	28 (28.57)		36(47.37)	28(36.84)	24(31.58)	
1/2–3/4 n(%)	29(30.21)	48(46.60)	50 (51.02)		29(38.16)	36(47.37)	35(46.05)	
> 3/4 n(%)	11(11.46)	24(23.30)	20 (20.41)		11(14.47)	12(15.79)	17(22.37)	
Paris classification				0.881				0.949
0-Ila n(%)	11.00 (11.46)	11.00 (10.68)	10.00(10.20)		9(11.84)	8(10.53)	8(10.53)	
0-Ilb n(%)	65.00 (67.71)	66.00 (64.08)	61.00(62.24)		49(64.47)	52(68.42)	48(63.16)	
0-Ilc n(%)	12.00 (12.50)	14.00 (13.59)	12.00(12.24)		10(13.16)	7(9.21)	12(15.79)	
Others n(%)	8.00 (8.33)	12.00 (11.65)	15.00(15.31)		8(10.53)	9(11.84)	8(10.53)	
Lesion size, mean ± SD	2.76 ± 1.59	3.27 ± 2.01	3.28 ± 2.03	0.228	2.69 ± 1.62	3.31 ± 2.01	3.27 ± 1.95	0.143

Legend: Table 2 shows the comparison of the general information of patients in the ESD, ESTD and ESD-C groups after PSM. The table includes the following variables: Gender, Age, Lesion location, Postoperative pathology, Circumferential extent, Paris classification, Lesion size

Lesion location is the location of the esophagus where the lesion is located

Postoperative pathology is the pathologic type of tissue removed after surgery

Circumferential extent is the proportion of esophageal circumference occupied by the lesion

Paris classification is a system used to categorize the types of superficial esophageal and gastric lesions, particularly in the context of endoscopic procedures. It classifies lesions into five categories based on their appearance, shape, and characteristics, helping guide clinical decision-making and treatment approaches

Lesion size refers to the physical dimensions (length, width, and sometimes depth) of a lesion

Furthermore, the dissection time in the ESTD group was less than that in the ESD group ($P < 0.05$) (Fig. 5). Concerning dissection area, both the ESD-C and ESTD groups demonstrated larger dissection areas compared to the ESD group ($P < 0.05$), while no significant difference in dissection area was found between the ESD-C and ESTD groups ($P > 0.05$) (Fig. 6). The ESD-C group exhibited the highest dissection speed, significantly surpassing that of both the ESTD and ESD groups ($P < 0.05$), with the ESTD group also showing a higher dissection speed compared to the ESD group ($P < 0.05$) (Fig. 7). Lastly, in terms of wound management time, both the ESD-C and ESTD groups required less time than the ESD group ($P < 0.05$), although there was no significant difference in wound management time between the ESD-C and ESTD groups ($P > 0.05$) (Fig. 8).

A total of 228 patients underwent surgical procedures, resulting in a complete specimen resection rate of 100%. The complete resection rates for the three cohorts—specifically the ESD group, ESTD group, and ESD-C group—were 86.84%, 90.79%, and 88.16%, respectively. Statistical

analysis revealed that these differences were not statistically significant ($P > 0.05$, Table 4). Among the 26 lesions classified as non-complete resections, 5 patients subsequently underwent additional surgical intervention, 5 received radiation therapy, and 16 were monitored through endoscopic follow-up.

Analysis of complications

During the surgical procedures, no perforations were observed in any of the cohorts: ESD, ESTD, and ESD-C. The incidence rates of intraoperative bleeding and muscular layer damage were recorded as 23.68% and 17.11%, respectively, in the ESD group; 18.41% and 17.11% in the ESTD group; 17.11% and 15.79% in the ESD-C group. Notably, the ESD group exhibited higher rates of intraoperative bleeding compared to the ESTD and ESD-C groups; however, the differences in the incidence of these intraoperative complications among the three groups did not reach statistical significance ($P > 0.05$, Table 5). Among the 45 cases of intraoperative bleeding, hemostasis was effectively achieved using electrocautery or

Table 3 Comparison of surgical efficiency among the three groups after PSM

Surgical efficiency	ESD(n=76)	ESTD(n=76)	ESD-C(n=76)	P
Total surgical time(min)	56.09±7.32	48.59±8.33	45.28±9.34	<0.001
Dissection time(min)	47.11±6.96	41.54±7.79	38.05±7.92	<0.001
Dissection area(cm ²)	6.83±1.28	11.68±2.25	11.49±2.37	<0.001
Dissection speed(cm ² /min)	0.15±0.03	0.29±0.07	0.31±0.06	<0.001
Wound management time(min)	8.98±1.48	7.05±2.28	7.23±2.14	<0.001

Legend: Table 3 compares the surgical efficiency of patients in the ESD, ESTD, and ESD-C groups after PSM. The following variables are included in the comparison:

The total surgical time is defined as the interval from the initial endoscopic examination to the conclusion of the procedure, which includes the withdrawal of the endoscope

Dissection time is delineated as the duration from the marking of the lesion to its complete excision.

Dissection area is calculated using the formula: Area [cm²] = (transverse diameter/2) × (longitudinal diameter/2) × π

Dissection speed, expressed in cm²/min, is determined by dividing the dissection area by the dissection time

Wound management time refers to the time spent on handling and managing the wound or tissue defect created during the procedure

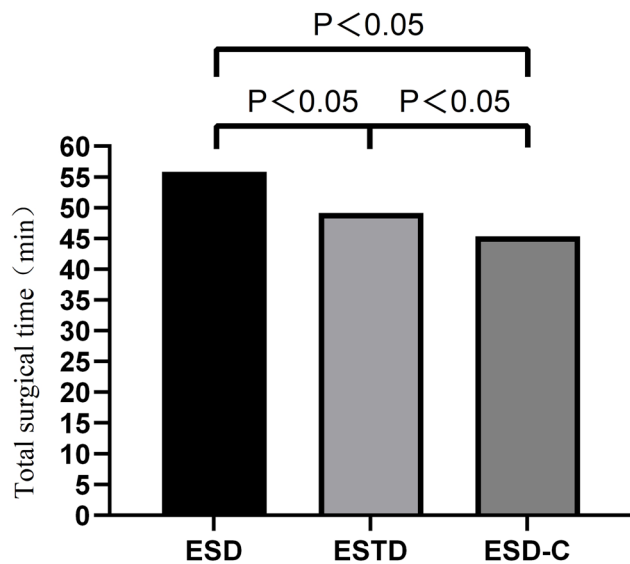


Fig. 4 Pairwise comparisons of total surgical time

hemostatic clips, with no instances necessitating surgical intervention for major bleeding. Additionally, 38 cases of muscular layer damage were addressed intraoperatively using titanium clips to mitigate the risk of postoperative perforation.

The postoperative stricture rates for ESD, ESTD, and ESD-C were 7.90%, 14.47%, and 14.47%, respectively. The ESD group exhibited a lower incidence of postoperative stricture compared to the other two groups; however, no statistically significant differences were observed

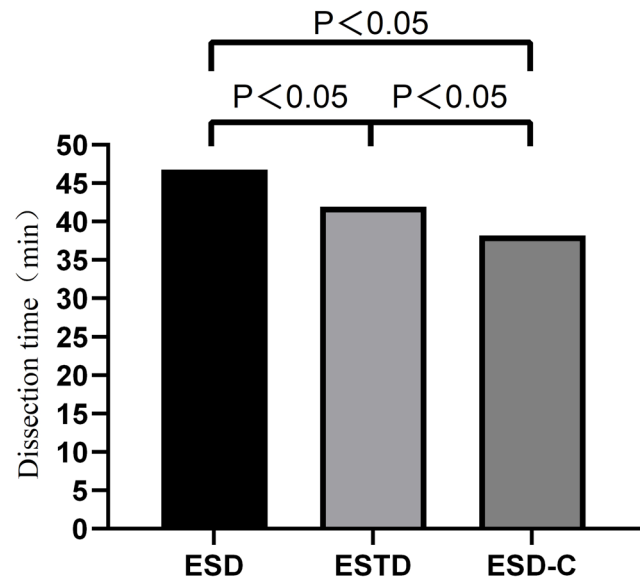


Fig. 5 Pairwise comparisons of dissection time

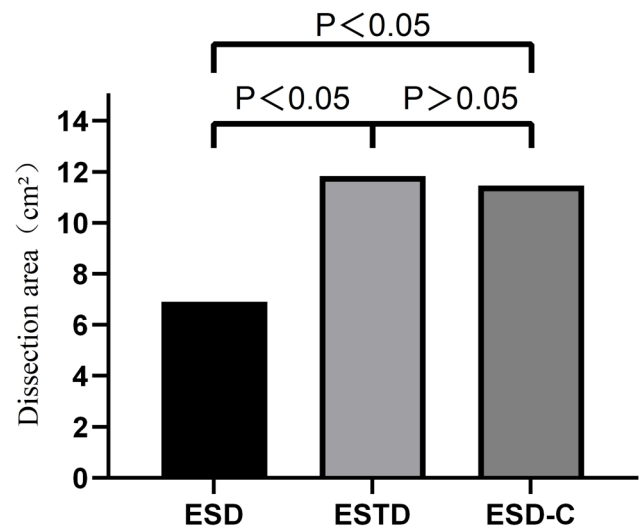


Fig. 6 Pairwise comparisons of dissection area

in the rates of postoperative stricture, delayed bleeding, or perforation ($P > 0.05$, Table 6). Among the three cases of delayed postoperative bleeding, two presented with melena 2–3 days after the procedure, and one with hematemesis, with estimated blood loss ranging from 50 to 200 mL. Endoscopic hemostasis was successfully achieved in one case, while the other two cases resolved with conservative management. Four cases of postoperative perforation were identified, with chest radiographs revealing subcutaneous emphysema in the neck or mediastinum. All patients improved following conservative treatment, including fasting, gastrointestinal decompression, and antimicrobial therapy, with no life-threatening complications. The incidence of postoperative adverse events did not differ significantly among the three groups

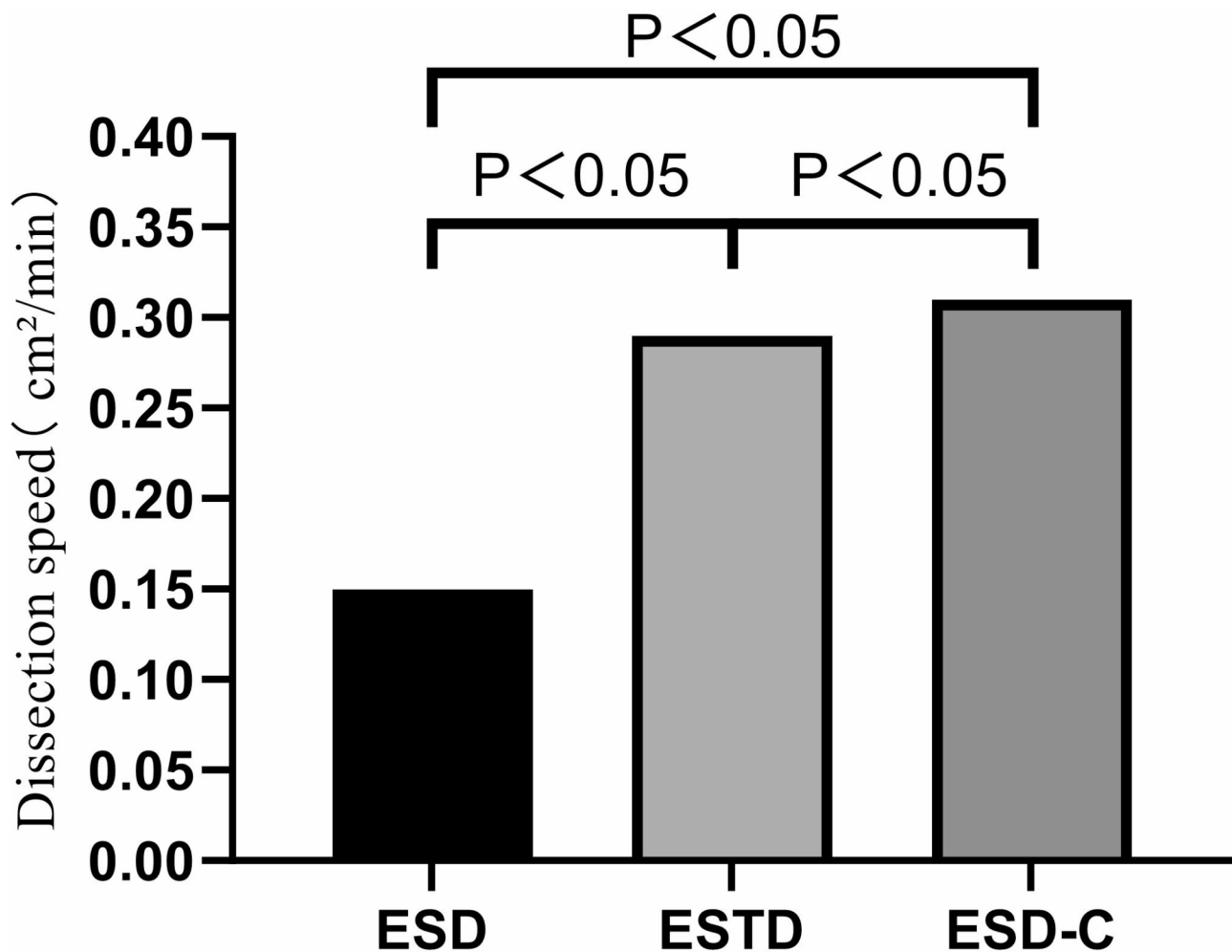


Fig. 7 Pairwise comparisons of dissection speed

($P > 0.05$, Table 7), with all patients showing improvement or responding to appropriate treatment.

Analysis of factors associated with postoperative esophageal stricture

A total of 228 patients who underwent endoscopic treatment were included in this study after PSM, of which 28 developed postoperative esophageal strictures. To identify the factors associated with the development of esophageal stricture post-treatment, we conducted both univariate and multivariate regression analyses. The univariate analysis indicated significant associations between esophageal stricture and several variables, including the circumferential ratio of the lesion, the area of dissection, the dissection speed, and damage to the muscularis propria ($P < 0.05$, Table 8). In the initial regression analysis, a substantial multicollinearity was observed between the variables “stripping speed” and “stripping area,” as indicated by a Variance Inflation Factor (VIF) of 18.594, which exceeds the threshold value of 10. Such high multicollinearity can lead to unstable regression coefficients

and inflated standard errors, thereby compromising the model’s reliability and explanatory power. To mitigate the impact of multicollinearity, the variable “stripping speed” was subsequently excluded from the model. This modification resulted in enhanced model stability, with more robust regression coefficient estimates and minimal impact on the significance of the remaining independent variables. Consequently, based on these statistical findings, we conclude that the removal of “stripping speed” contributes to the improved reliability and interpretability of the model. The subsequent multivariate analysis identified the circumferential ratio of the lesion, area of dissection, and intraoperative damage to the muscularis propria as independent risk factors for postoperative esophageal stricture. Notably, an increased circumferential ratio of the lesion, a larger dissection area, and more extensive damage to the muscularis propria were correlated with a heightened risk of developing postoperative esophageal stricture (Table 9).

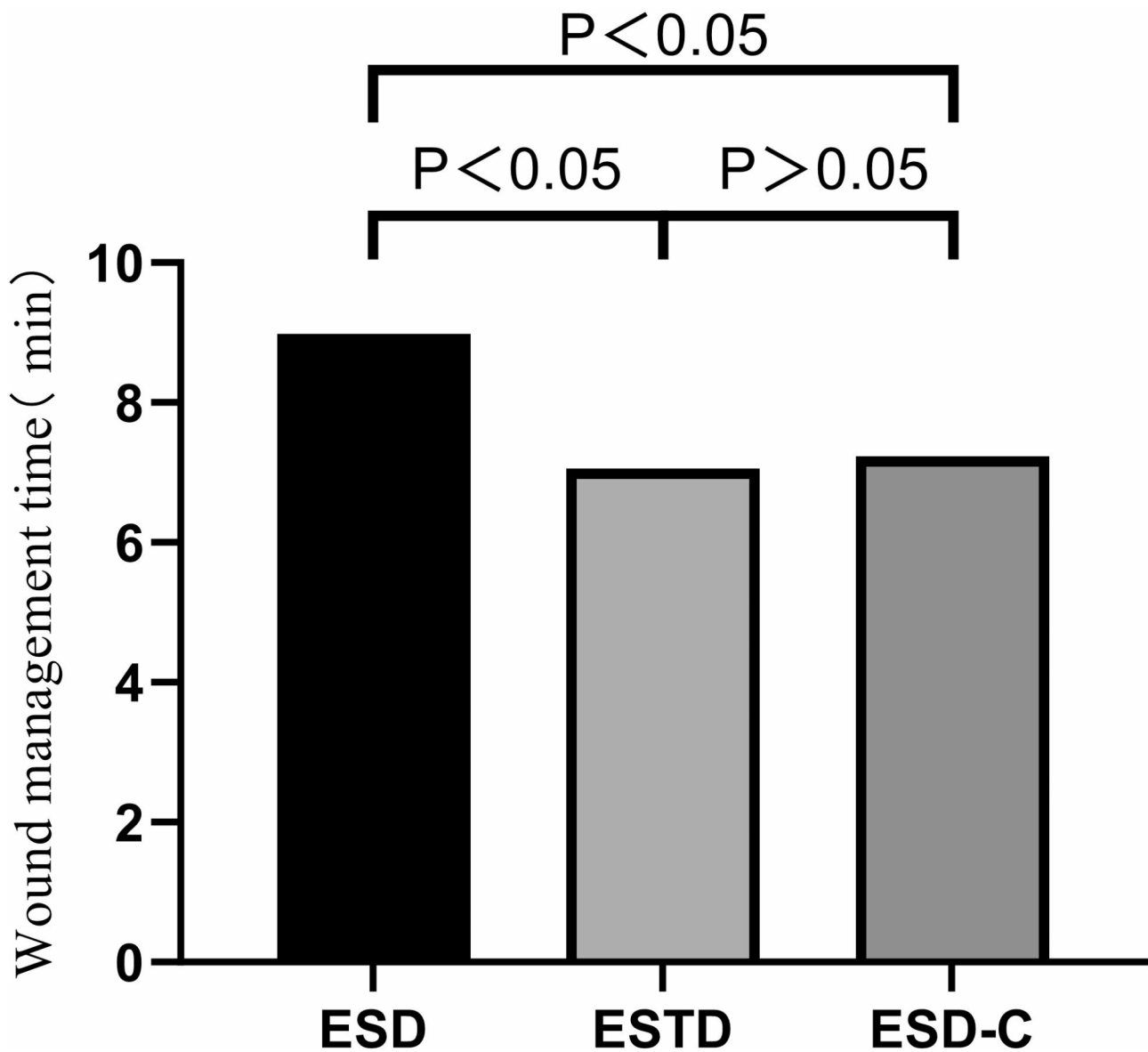


Fig. 8 Pairwise comparison of wound management time

Table 4 Comparison of surgical outcomes among the three groups after PSM

Outcomes	ESD(n = 76)	ESTD(n = 76)	ESD-C(n = 76)	P
En bloc resection, n(%)	76(100.00)	76(100.00)	76(100.00)	1
Complete resection				0.738
Yes n(%)	66(86.84)	69(90.79)	67(88.16)	
No n(%)	10(13.16)	7(9.21)	9(11.84)	

Legend: Table 4 shows a comparison of the surgical outcomes of patients in the ESD, ESTD and ESD-C groups after PSM. The following outcomes are compared:

En bloc resection is characterized as the complete excision of the lesion under endoscopic guidance, yielding a single specimen

Complete resection is defined as the excision of a specimen that exhibits tumor-free vertical and horizontal margins, thus precluding the risk of lymph node metastasis

Table 5 Comparison of intraoperative complications among the three groups after PSM

Intraoperative complications	ESD(n = 76)	ESTD(n = 76)	ESD-C(n = 76)	P
Intraoperative bleeding n(%)	18(23.68)	14(18.41)	13(17.11)	0.559
Muscular injury n(%)	13(17.11)	13(17.11)	12(15.79)	0.969
Total complications n(%)	31(40.79)	27(35.52)	25(32.89)	0.849

Legend: Table 5 compares intraoperative complications in the ESD, ESTD, and ESD-C groups of patients after PSM. The table includes the following complication types:

Intraoperative bleeding is categorized as any event necessitating electrocautery or hemostatic clips for hemostatic control

Muscular layer injury is defined by the exposure, damage, or rupture of the muscular layer during the dissection process

Table 6 Comparison of postoperative complications among the three groups after PSM

Postoperative complications	ESD(n=76)	ESTD(n=76)	ESD-C(n=76)	P
Delayed bleeding n(%)	1(1.32)	1(1.32)	1(1.32)	1.000
Perforation n(%)	0(0.00)	3(3.95)	1(1.32)	0.168
Stricture n(%)	6(7.90)	11(14.47)	11(14.47)	0.361
Total complications n(%)	7(9.21)	15(19.74)	13(17.11)	0.411

Legend: Table 6 presents a comparison of postoperative complications among the ESD, ESTD, and ESD-C groups after PSM. The table includes the following types of postoperative complications:

Delayed bleeding is identified by the presence of hematemesis or melena, or a decrease in hemoglobin levels of 20 g/L or greater within 30 days following the procedure

Perforation is indicated by subcutaneous emphysema in the anterior chest or neck, with chest X-ray or CT imaging revealing free air in the mediastinum or cervical region

Esophageal stricture is characterized by the failure of a standard 11 mm endoscope to traverse the constricted region

Table 7 Comparison of postoperative adverse symptoms among the three groups after PSM

Adverse symptoms	ESD(n=76)	ESTD(n=76)	ESD-C(n=76)	P
Chest pain n(%)	14(18.42)	19(25.00)	15(19.74)	0.575
Throat discomfort n(%)	29(38.16)	29(38.16)	25(32.90)	0.739
Acid reflux n(%)	4(5.26)	8(10.53)	12(15.79)	0.107
Heartburn n(%)	5(6.58)	8(10.53)	9(11.84)	0.520
Fever n(%)	12(15.79)	19(25.00)	13(17.11)	0.298
Abdominal pain n(%)	6(7.90)	13(17.11)	11(14.47)	0.224

Legend: Table 7 compares the postoperative adverse symptoms experienced by patients in the ESD, ESTD, and ESD-C groups after PSM. The table includes the following categories of adverse symptoms:

Throat discomfort after surgery is often caused by surgical manipulation or tracheal intubation during anesthesia. This usually resolves on its own within 3–5 days

Acid reflux and heartburn: Patients experiencing acid reflux or heartburn typically have a history of gastroesophageal reflux disease (GERD). Their symptoms can be alleviated by increasing the use of acid-suppressing medications

Chest pain and abdominal pain: All patients with chest or abdominal pain undergo a chest X-ray to rule out perforation. If no perforation is found, no special treatment is necessary

Fever: Most patients with fever respond to prophylactic antibiotics and physical cooling measures. Their body temperature generally returns to normal within 3 days. If the fever persists, it is important to suspect wound infection and consider upgrading antibiotic therapy

Discussion

The continuous evolution of endoscopic instruments and techniques has established ESD as the preferred therapeutic approach for superficial esophageal cancer and precancerous lesions [18]. While ESD is not inherently constrained by lesion size, larger lesions can adversely affect the operator’s working space and visibility during the dissection, thereby elevating the risk of significant complications such as hemorrhage and perforation [19]. To enhance the efficacy and safety of ESD, several

innovative techniques have emerged, notably ESTD and ESD-C. A total of 297 patients were enrolled in this study. Propensity score matching (PSM) was applied to balance the groups in a 1:1:1 ratio, resulting in 76 patients per group, for a final cohort of 228 patients. The mean age of the participants was 63.26±7.36 years, with the majority being male. The lesions were primarily localized in the mid-esophagus, consistent with the demographic characteristics commonly associated with esophageal cancer [20]. In terms of surgical efficiency, the total procedural time, dissection time, and wound management duration were significantly shorter for the ESTD and ESD-C groups compared to the ESD group. Additionally, both the dissection area and speed were superior in the ESTD and ESD-C cohorts relative to the ESD group, corroborating findings from prior studies [15, 21]. Potential explanations for these observations include: (1) The creation of a tunnel in ESTD and the circumferential incision in ESD-C may mitigate the efflux of injected fluid in the submucosa, thereby reducing the necessity for multiple injections; (2) ESTD affords a larger operational space within the tunnel, employing a transparent cap to facilitate blunt dissection; ESD-C utilizes a longitudinal, arc-shaped cutting technique that accelerates dissection from the lesion side toward the anal side; (3) Both techniques enhance the operator’s capacity to accurately identify submucosal blood vessels and structures, enabling simultaneous dissection and management of exposed vessels; (4) As more lesions are dissected, the operational space available for ESD diminishes, necessitating repeated angle adjustments to complete the procedure. Moreover, this study revealed that the total procedure time and dissection duration for ESD-C were less than those for ESTD, aligning with the results reported by Ribeiro et al. [22]. This difference may be attributed to: (1) The tunnel establishment in ESTD, which is time-intensive and requires repetitive retraction of the endoscope to ensure proper alignment with the lesion; (2) Variations in cutting techniques, where ESD-C’s longitudinal and arc-shaped approach promotes expedited dissection. Nevertheless, it is imperative to underscore that both ESD-C and ESTD techniques necessitate a high level of expertise and should be conducted on the foundation of proficient ESD practice.

This study assessed the effectiveness of three dissection techniques by analyzing rates of en bloc resection and complete resection. Remarkably, the en bloc resection rates for all three groups were found to be 100%. The complete resection rates were 86.84% for the ESD group, 90.79% for the ESTD group, and 88.16% for the ESD-C group, with no statistically significant differences among these rates. A meta-analysis [21] encompassing 15 studies with a total of 776 cases of superficial esophageal cancer treated with ESD reported an overall resection rate of

Table 8 Univariate analysis of factors associated with postoperative esophageal stricture

Factors	overall, N=228 normalcy(n=200) stricture (n=28)			P
Dissection time, mean ± SD	42.23 ± 8.46	42.50 ± 8.40	40.35 ± 8.75	0.231
Total surgical time, mean ± SD	49.99 ± 9.53	50.22 ± 9.37	48.31 ± 10.66	0.374
Dissection area, mean ± SD	10.00 ± 3.03	9.81 ± 2.90	11.39 ± 3.59	0.033
Dissection speed, mean ± SD	0.25 ± 0.09	0.24 ± 0.09	0.29 ± 0.11	0.016
Wound management time, mean ± SD	7.75 ± 2.18	7.73 ± 2.09	7.96 ± 2.79	0.677
Gender				0.452
Male n(%)	137.00 (60.09)	122.00 (61.00)	15.00 (53.57)	
Female n(%)	91.00 (39.91)	78.00 (39.00)	13.00 (46.43)	
Lesion location				0.239
Upper n(%)	25.00 (10.96)	22.00 (11.00)	3.00 (10.71)	
Middle n(%)	150.00 (65.79)	135.00 (67.50)	15.00 (53.57)	
Lower n(%)	53.00 (23.25)	43.00 (21.50)	10.00 (35.71)	
Circumferential extent				0.026
< 1/2 n n(%)	88.00 (38.60)	80.00 (40.00)	8.00 (28.57)	
1/2–3/4 n(%)	100.00 (43.86)	90.00 (45.00)	10.00 (35.71)	
> 3/4 n(%)	40.00 (17.54)	30.00 (15.00)	10.00 (35.71)	
Paris classification				0.635
0-IIa n(%)	25.00 (10.96)	21.00 (10.50)	4.00 (14.29)	
0-IIb n(%)	149.00 (65.35)	129.00 (64.50)	20.00 (71.43)	
0-IIc n(%)	29.00 (12.72)	27.00 (13.50)	2.00 (7.14)	
Others n(%)	25.00 (10.96)	23.00 (11.50)	2.00 (7.14)	
Lesion size, mean ± SD	3.09 ± 1.88	3.13 ± 1.89	2.82 ± 1.82	0.404
Treatment method				0.361
ESD n(%)	76.00 (33.33)	70.00 (35.00)	6.00 (21.43)	
ESTD n(%)	76.00 (33.33)	65.00 (32.50)	11.00 (39.29)	
ESD-C n(%)	76.00 (33.33)	65.00 (32.50)	11.00 (39.29)	
Muscular injury, n (%)				<0.001
No	190.00 (83.33)	175.00 (87.50)	15.00 (53.57)	
Yes	38.00 (16.67)	25.00 (12.50)	13.00 (46.43)	

Legend: After PSM: Table 8 presents the results of a univariate analysis examining factors associated with postoperative esophageal stricture. The table includes the following variables:

Dissection time is delineated as the duration from the marking of the lesion to its complete excision.

Dissection area is calculated using the formula: Area [cm²] = (transverse diameter/2) × (longitudinal diameter/2) × π

Dissection speed, expressed in cm²/min, is determined by dividing the dissection area by the dissection time

Wound management time refers to the time spent on handling and managing the wound or tissue defect created during the procedure

Lesion location is the location of the esophagus where the lesion is located

Circumferential extent is the proportion of esophageal circumference occupied by the lesion

Muscular layer injury is defined by the exposure, damage, or rupture of the muscular layer during the dissection process

Paris classification is a system used to categorize the types of superficial esophageal and gastric lesions, particularly in the context of endoscopic procedures. It classifies lesions into five categories based on their appearance, shape, and characteristics, helping guide clinical decision-making and treatment approaches

Lesion size refers to the physical dimensions (length, width, and sometimes depth) of a lesion

Treatment modalities include ESD, ESTD, ESD-C

Table 9 Logistic regression analysis of factors associated with postoperative esophageal stricture

Predictor	Estimate	SE	Z	P	Odds Ratio	Lower	Upper
Dissection area	0.165	0.074	2.218	0.027	1.179	1.023	1.373
Circumferential extent	1.18	0.567	2.081	0.037	3.254	1.074	10.191
Muscular injury	1.837	0.461	3.985	<0.001	6.277	2.537	15.695

Legend:After PSM: Table 9 shows the results of a logistic regression analysis to identify factors associated with the development of postoperative esophageal stricture. The table includes multivariate analysis of various clinical and procedural factors that may contribute to stricture formation after esophageal surgery. The following variables were considered in the analysis:

Dissection area is calculated using the formula: Area [cm²] = (transverse diameter/2) × (longitudinal diameter/2) × π

Circumferential extent is the proportion of esophageal circumference occupied by the lesion

Muscular layer injury is defined by the exposure, damage, or rupture of the muscular layer during the dissection process

95.1% and a complete resection rate of 89.4%. Another meta-analysis [23] that included 6 studies with 436 cases of superficial esophageal cancer treated with ESTD demonstrated an en bloc resection rate of 98% and a complete resection rate of 87.6%, findings that align closely with the treatment effectiveness observed in our ESD and ESTD groups. At present, there are no meta-analyses specifically evaluating ESD-C; however, one study [22] has indicated that the complete resection rate for ESD-C is comparable to that of ESTD, thereby corroborating the conclusions of the present investigation.

The esophagus is characterized by a narrowed lumen, thin walls, and the proximity of abundant submucosal blood vessels to major cardiac vessels, all of which contribute to the occurrence of complications during endoscopic interventions [24]. Intraoperative complications frequently encountered include hemorrhage and damage to the muscular layer. Notably, the incidence of intraoperative bleeding in the ESD cohort was observed to be 23.68%, slightly surpassing the 18.41% and 17.11% reported in the ESTD and ESD-C groups. Contributing factors include: (1) suboptimal visibility during ESD, which can impede surgical efficacy and increase the risk of hemorrhage; repeated electrocautery used for hemostasis may further compromise the muscular layer, and (2) prolonged surgical duration can lead to an accumulation of gas within the esophagus and submucosal tunnel, resulting in increased pressure [25, 26]. However, the differences in overall complication rates among the three groups were not statistically significant ($P > 0.05$).

Additionally, no statistically significant differences were observed in the incidence of major postoperative complications among the three surgical groups ($P < 0.05$), with all adverse symptoms improving following observation and appropriate management. Delayed hemorrhage, perforation, and stricture are commonly encountered complications after esophageal endoscopic submucosal dissection (ESD). The observed rates of delayed bleeding, perforation, and stricture in the three groups were consistent with those reported in the existing literature [27–30]. Furthermore, Statistical analysis revealed no significant differences in the rates of delayed hemorrhage, perforation, or stricture ($P > 0.05$). However, the incidence of stricture was lower in the ESD group (7.90%) compared to both the ESTD group (14.47%) and the ESD-C group (14.47%). This difference may be attributed to the tendency for surgeons to select ESTD or ESD-C for larger lesions, thereby introducing a selection bias. Consequently, the increased risk of postoperative stricture is likely associated with the larger lesion size in these cases [31].

From a clinical standpoint, esophageal strictures following endoscopic submucosal dissection considerably impair the quality of life in affected patients. Thus,

there is an urgent necessity to investigate and develop effective preventive and therapeutic strategies. Research conducted by Chen et al. and Gwang et al. [32, 33] indicates that the occurrence of postoperative esophageal stricture is significantly correlated with factors such as the size of resected lesions, the extent of submucosal dissection, and the degree of injury to the muscular layer. This study aims to analyze the determinants associated with esophageal stricture and identifies key risk factors, including the resection area, the circumferential ratio of lesions, and the extent of muscular layer damage. Notably, it is observed that an increased circumferential ratio of lesions correlates with a larger resection area and greater intraoperative injury to the muscular layer, thereby elevating the likelihood of developing esophageal strictures postoperatively, corroborating findings from previous studies. Consequently, precise assessment and delineation of lesion boundaries during ESD is critical to minimize unnecessary resection of normal mucosa and to prevent damage to the muscular layer, thereby reducing the incidence of postoperative esophageal strictures while ensuring the complete excision of malignant lesions. In this study, patients exhibiting a circumferential lesion ratio exceeding three-quarters were administered oral prednisone postoperatively to mitigate the risk of esophageal stricture. Yamaguchi et al. [34] were pioneers in demonstrating the efficacy of this approach, attributing its success to the anti-inflammatory and antifibrotic properties of glucocorticoids. Further investigations [35] have revealed that adjunctive strategies, including localized triamcinolone injection, preventive endoscopic balloon dilation, endoscopic placement of self-expanding metal stents, autologous esophageal mucosal grafting, and the application of polycaprolactone and carboxymethyl cellulose sheets, can effectively reduce the incidence of postoperative strictures.

Limitations of the Study: This investigation is a single-center retrospective study that relied on a medical record database to extract clinical case information for the patients involved. As a result, certain patient data may be incomplete or missing. The grouping in this analysis was non-randomized, with the selection of endoscopic treatment modalities influenced by the procedural habits of the operating physicians and the characteristics of the lesions. This non-randomized design may introduce inherent biases, highlighting the need for subsequent prospective studies to corroborate these findings. Endoscopic interventions were not performed by a single surgeon in this study; therefore, variations in the proficiency of different surgeons could affect the surgical outcomes reported. Furthermore, the study lacks long-term follow-up data necessary for evaluating patient recurrence and survival rates, which are critical for assessing the long-term efficacy of endoscopic treatments.

Conclusions

In conclusion, the findings from this comprehensive analysis indicate that ESD, ESTD and ESD-C are all safe and effective modalities for the treatment of superficial esophageal cancer and its precancerous lesions. Importantly, ESD-C has demonstrated advantages over both ESTD and ESD by reducing operative time and accelerating the rate of lesion resection, thus enhancing overall surgical efficiency. Nevertheless, it is imperative to acknowledge that the risk of postoperative esophageal stricture is exacerbated by an increased circumferential extent of the lesion, larger dissection areas, and damage to the intrinsic muscular layer that may occur during the procedure.

Abbreviations

ESD	Endoscopic submucosal dissection
ESTD	Endoscopic submucosal tunneling dissection
ESD-C	Endoscopic submucosal dissection with C-shaped incision
EMR	Endoscopic mucosal resection
MBM	Mucosectomy with multiple-band ligation
NSAIDs	Non-steroidal anti-inflammatory drugs
NBI	Narrow Band Imaging
EnR	En bloc resection
LGIN	Low-grade intraepithelial neoplasia
HGIN	High-grade intraepithelial neoplasia
SC	Superficial cancer

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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Not applicable.

Author contributions

Xianfei Wang, Shuanghong Jiang, Zichen Luo, Xiuyu Liu designed the study; Xianfei Wang, Shuanghong Jiang, Zichen Luo, Xiuyu Liu analyzed the data; Xian-fei Wang, Shuanghong Jiang Zichen Luo, Xiuyu Liu drafted the article; Xianfei Wang, Shuanghong Jiang, Zichen Luo, Xiuyu Liu critically revised the article; Xian-fei Wang finally approved the article; Shuanghong Jiang, Zichen Luo, Xiuyu Liu, Yutong Cui, Haiyang Guo, Shiqi Liang, Xinrui Chen, Ji Zuo provided the study materials or patients. All authors read and approved the final manuscript.

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Data availability

Data is provided within the manuscript or supplementary information files.

Declarations

Ethics approval and consent to participate

The present study was performed at The Affiliated Hospital of North Sichuan Medical College under the Declaration of Helsinki. This retrospective analysis was approved by the The Affiliated Hospital of North Sichuan Medical College's Ethics Committee, which waived the requirement for informed

consent due to the study's retrospective design. (ethical batch number: 2024ER143-1).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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