

# Research Progress on Endoscopic Submucosal Dissection for the Treatment of Early Esophageal Cancer and Precancerous Lesions

Xue Xiaoxiao

North Sichuan Medical College, China

**Abstract:** Endoscopic Submucosal Dissection (ESD) is a minimally invasive procedure that has revolutionized the treatment of early esophageal cancer and precancerous lesions. This technique allows for en-bloc resection of tumors while preserving the esophagus, leading to improved patient outcomes and quality of life. Advancements in ESD include the application of new techniques and devices, such as submucosal injection agents and the dual-knife technique, which enhance the safety and effectiveness of the procedure. Operative techniques have also evolved, with the introduction of the dual-dissection technique and countertraction technique, improving surgical outcomes. Furthermore, ESD techniques originally developed for the esophagus have been successfully applied to other anatomical sites, including the stomach, colorectum, and anorectal region, expanding the scope of ESD applications. These advancements continue to refine the field of ESD and offer new possibilities for the management of early-stage gastrointestinal neoplasms.

**Keywords:** Endoscopic Submucosal Dissection; ESD; early esophageal cancer; precancerous lesions; minimally invasive; en-bloc resection; preservation; new techniques; devices; operative techniques; advancements; expanding applications; stomach; colorectum; anorectal region

## 1 Introduction

### 1.1 Background

In recent years, endoscopic submucosal dissection (ESD) has gained widespread attention and research as an innovative surgical technique for the treatment of early esophageal cancer and precancerous lesions. Traditional surgical methods have exhibited certain side effects and complications in the treatment of early esophageal cancer and precancerous lesions, whereas ESD, as a minimally invasive treatment, offers lower trauma and higher treatment efficacy, gradually becoming the preferred therapeutic approach for esophageal diseases. Therefore, this paper aims to systematically review the research progress of ESD in the treatment of early esophageal cancer and precancerous lesions, with the goal of providing reliable evidence for clinical practice.

### 1.2 Research Objectives and Significance

The objective of this study is to comprehensively summarize and analyze the research progress of ESD in the treatment of early esophageal cancer and precancerous lesions, including its principles, technical characteristics, treatment efficacy, and complications. By reviewing existing literature and research findings, the study aims to explore the application prospects and advantages of ESD in the treatment of early esophageal cancer and precancerous lesions, providing scientific basis for clinical decision-making. Additionally, the study aims to analyze the improvements and development trends of ESD, offering insights for enhancing the safety and effectiveness of ESD techniques.

### 1.3 Article Structure

This paper is organized into the following sections:

Introduction, Overview of Early Esophageal Cancer and Precancerous Lesions, Principles and Techniques of ESD, Diagnosis and Evaluation of Early Esophageal Cancer and Precancerous Lesions, Application of ESD in Early Esophageal Cancer and Precancerous Lesions, Improvements and Developments of ESD, Challenges and Issues in Clinical Practice, Conclusion. In the introduction, the research background of ESD in the treatment of early esophageal cancer and precancerous lesions will be introduced, along with an explanation of the research objectives and significance. Subsequently, the relevant content will be elaborated and analyzed in accordance with the aforementioned structure, aiming to comprehensively present the research progress and application prospects of ESD in the treatment of esophageal diseases.

## 2 Overview of Early Esophageal Cancer and Precancerous Lesions

### 2.1 Definition of Early Esophageal Cancer and Precancerous Lesions

Early Esophageal Cancer refers to tumors that occur in the mucosal or submucosal layers of the esophagus, without invasion beyond the submucosal layer and distant lymph node metastasis. Precancerous Lesions refer to abnormal changes in esophageal tissues that have not yet developed into malignant tumors.

### 2.2 Classification of Early Esophageal Cancer and Precancerous Lesions

Based on histological types and the extent of lesions, Early Esophageal Cancer and Precancerous Lesions can be classified into the following categories:

**Squamous Intraepithelial Neoplasia:** including low-grade and high-grade squamous intraepithelial neoplasia.

**Glandular Epithelial Lesions:** including low-grade and high-grade glandular epithelial lesions.

**Carcinoma in Situ:** refers to cancer cells confined to the esophageal epithelium without invasion beyond the submucosal layer.

**Early Invasive Cancer:** cancer cells invade the submucosal layer but do not extend into deeper layers of the esophageal wall or lymph nodes.

### 2.3 Epidemiological Data and Incidence

The incidence of Early Esophageal Cancer and Precancerous Lesions varies globally. Based on statistical data and research, the following are some epidemiological data and incidence information:

Squamous cell carcinoma of the esophagus is a common type of cancer in developing countries, particularly in East Asia, Central Asia, the Middle East, and South America. China has the highest incidence rate.

Adenocarcinoma of the esophagus is more common in developed countries but accounts for a smaller proportion of overall esophageal cancer incidence.

Dietary habits play a significant role in the development of esophageal cancer, such as long-term exposure to hot food and beverages, tobacco use, and alcohol abuse.

Improved diagnostic and screening methods for Early Esophageal Cancer and Precancerous Lesions have led to an increasing detection rate at an early stage. Early diagnosis and treatment are crucial for patient prognosis.

## 3 Principles and Techniques of Endoscopic Submucosal Dissection (ESD)

### 3.1 Basic Principles of ESD

Endoscopic Submucosal Dissection (ESD) is a minimally invasive technique for the resection of gastrointestinal epithelial lesions. It involves the complete resection of lesions by creating a submucosal fluid cushion and dissecting the lesions along the submucosal plane. The basic principles of ESD include the following:

**Creating a submucosal fluid cushion:** A solution is injected into the submucosal layer to lift the lesion and create a space for dissection.

**Precise marking:** The lesion and surrounding margins are accurately marked to ensure complete resection.

**Precise dissection:** The lesions are dissected along the submucosal plane using various endoscopic devices, such as electrosurgical knives and scissors.

**Hemostasis:** Bleeding from the dissected vessels is controlled using coagulation techniques, such as hemostatic forceps or hemostatic clips.

### 3.2 Surgical Steps and Procedure of ESD

The surgical steps and procedure of ESD typically include the following:

**Preoperative evaluation:** The lesion is evaluated using endoscopy, endoscopic ultrasound, and other imaging techniques to determine its size, depth, and potential for lymph node metastasis.

**Marking:** The lesion and surrounding margins are marked using electrocautery or tattooing to delineate the resection area.

**Submucosal injection:** A solution (such as saline mixed with a local anesthetic and/or epinephrine) is injected into the submucosal layer to lift the lesion.

**Precise dissection:** The lesion is dissected along the submucosal plane using endoscopic devices, such as knives or scissors.

**Hemostasis:** Bleeding vessels are coagulated using various methods, including electrocautery or hemostatic clips.

**Resection and closure:** The resected specimen is retrieved, and the mucosal defect is closed using endoscopic closure techniques, such as endoloops or clips.

### 3.3 Treatment Efficacy and Complications of ESD

ESD has been shown to be an effective treatment for early gastrointestinal epithelial lesions, offering higher complete resection rates compared to conventional endoscopic resection techniques. The treatment efficacy of ESD depends on factors such as lesion characteristics, operator experience, and patient selection.

However, ESD is associated with certain complications, including bleeding, perforation, and postoperative stricture formation. These complications are more common when operating on larger lesions or lesions located in challenging anatomical sites.

## 4 Diagnosis and Evaluation of Early Esophageal Cancer and Precancerous Lesions

### 4.1 Clinical Presentation and Symptoms

The clinical presentation and symptoms of early esophageal cancer and precancerous lesions may vary but can include the following:

- Dysphagia (difficulty swallowing)
- Odynophagia (painful swallowing)
- Retrosternal chest pain
- Regurgitation of food or acid reflux
- Weight loss
- Loss of appetite
- Anemia (due to chronic bleeding)
- Gastrointestinal bleeding (hematemesis or melena)

### 4.2 Imaging Techniques for Diagnosis

Various imaging techniques can be used for the diagnosis of early esophageal cancer and precancerous lesions, including:

**Barium swallow:** This radiographic procedure uses contrast material and X-rays to visualize the esophagus and detect abnormalities such as strictures or filling defects.

**Endoscopy:** This direct visualization technique allows for the detection and biopsy of esophageal lesions. It may include white light endoscopy, narrow-band imaging (NBI), chromoendoscopy, or confocal laser endomicroscopy.

**Endoscopic ultrasound (EUS):** Combining endoscopy and ultrasound, EUS can provide detailed imaging of the esophageal wall layers and detect invasion depth of lesions.

**Computed tomography (CT) scan:** CT scans can help assess the local extent of the tumor, identify lymph node involvement, and detect distant metastases.

### 4.3 Cytological and Histological Examination

Cytology and histology examinations are important for the diagnosis and evaluation of early esophageal cancer and precancerous lesions. These methods include:

**Endoscopic biopsy:** Tissue samples are obtained during endoscopy using biopsy forceps or brushes. The samples are then sent for pathological examination to determine the presence of dysplasia or malignancy.

**Brush cytology:** Cytology specimens can be obtained by brushing the surface of the esophageal mucosa during endoscopy. The collected cells are examined under a microscope to identify abnormal cells.

**Endoscopic mucosal resection (EMR):** EMR is a technique that removes superficial lesions and allows for the examination of the entire lesion under a microscope.

## 5 Application of ESD in Early Esophageal Cancer and Precancerous Lesions

### 5.1 Indications and Contraindications of ESD

Endoscopic Submucosal Dissection (ESD) is a valuable technique for the treatment of early esophageal cancer and precancerous lesions. Proper patient selection is essential to ensure optimal outcomes and minimize the risk of complications. Here are the expanded indications and contraindications for ESD:

**Indications:**

**Early Esophageal Cancer:** Tumors confined to the mucosal layer (T1a) or superficial submucosal layer (T1b) without lymph node metastasis. Well-differentiated or moderately differentiated adenocarcinoma or squamous cell carcinoma. Tumors with a low risk of lymphovascular invasion and high-risk factors for surgical resection.

**Precancerous Lesions:** High-grade dysplasia (HGD) or intramucosal carcinoma (IMC) in Barrett's esophagus. High-grade intraepithelial neoplasia or intramucosal carcinoma in cases of squamous cell dysplasia.

**Other Lesions:** Non-cancerous superficial lesions, such as submucosal tumors, leiomyoma, or inflammatory polyps, that can be removed en-bloc.

**Contraindications:**

**Advanced Esophageal Cancer:** Tumors extending beyond the submucosal layer (T2 or higher) or with lymph node metastasis. Invasion of adjacent organs or distant metastasis.

**Severe Comorbidities:** Uncontrolled bleeding disorders or coagulopathy that cannot be corrected. Severe cardiopulmonary conditions that pose a high anesthetic risk. Unstable general condition or poor nutritional status.

**Technical Limitations:** Lesions located in anatomically difficult areas, such as the upper esophagus or gastroesophageal junction, where precise dissection may be challenging. Large lesions that cannot be completely resected by endoscopic means. Endoscopic findings suggestive of deep invasion or lymph node metastasis.

**Inadequate Endoscopic Expertise:** Lack of experience or insufficient training in performing ESD procedures. Inability to manage potential complications or access to immediate surgical backup if needed.

It is crucial to evaluate each patient individually, considering

their overall health condition and tumor characteristics, to determine the suitability for ESD. Multidisciplinary discussions involving endoscopists, surgeons, and pathologists are beneficial to make informed decisions and provide optimal treatment options for patients with early esophageal cancer and precancerous lesions.

### 5.2 Treatment Efficacy and Prognosis of ESD

Endoscopic Submucosal Dissection (ESD) is an effective treatment modality for early esophageal cancer and precancerous lesions. The treatment efficacy of ESD is influenced by various factors, including tumor characteristics, operator experience, and patient-related factors. Here are the expanded details on treatment efficacy and prognosis of ESD:

**Treatment Efficacy:**

**En-bloc Resection:** ESD allows for en-bloc resection, which means the tumor is removed as a single piece. En-bloc resection is associated with higher rates of complete resection and lower rates of local recurrence compared to piecemeal resection.

**Curative Resection:** ESD can achieve curative resection in selected cases. Curative resection is defined as complete removal of the lesion with negative horizontal and vertical margins. It is crucial for achieving long-term disease control and favorable outcomes.

**Lymph Node Metastasis:** ESD is suitable for tumors that have a low risk of lymph node metastasis based on preoperative evaluation. Tumor size, depth of invasion, and histological features play a role in assessing the risk of lymph node involvement.

**Margin Assessment:** ESD allows for accurate evaluation of horizontal and vertical margins, providing valuable information on the completeness of resection. Adequate margin assessment minimizes the risk of residual or recurrent disease.

**Prognosis:**

**Recurrence Rate:** The risk of local recurrence after ESD depends on factors such as tumor size, depth of invasion, histological differentiation, lymphovascular invasion, and margin status. Long-term follow-up is necessary to monitor for recurrence and manage any potential residual or metachronous lesions.

**Survival Outcomes:** The prognosis of patients undergoing ESD for early esophageal cancer is generally favorable, especially for those with curative resection. The overall survival rates at 5 years range from 80% to 95% for mucosal tumors and 60% to 80% for superficial submucosal tumors.

**Surveillance and Follow-up:** After ESD, regular surveillance endoscopy is essential to detect any local recurrence or metachronous lesions. The frequency and duration of surveillance depend on various factors, including the initial tumor stage, histology, and patient risk factors.

**Quality of Life:** ESD offers several advantages over traditional surgical resection, including reduced invasiveness, shorter hospital stays, and faster recovery. Preservation of the esophagus maintains normal swallowing function, resulting in improved quality of life for patients.

It is important to note that individual patient characteristics and tumor factors can influence treatment efficacy and prognosis. Close collaboration between physicians, pathologists, and other healthcare professionals is crucial to ensure optimal treatment outcomes and long-term follow-up care for patients undergoing ESD for early esophageal cancer and precancerous lesions.

### 5.3 Comparison of ESD with Traditional Surgical Methods

Endoscopic Submucosal Dissection (ESD) is a minimally invasive treatment option for early esophageal cancer and precancerous lesions. It offers several advantages compared to traditional surgical methods. Here is an expanded comparison between ESD and traditional surgical methods:

**Minimally Invasive Approach:** ESD is an endoscopic procedure that involves accessing the esophagus through the mouth, eliminating the need for an open surgical incision. This leads to reduced trauma, less postoperative pain, and faster recovery compared to traditional surgery, which involves larger incisions and longer hospital stays.

**Organ Preservation:** ESD allows for en-bloc resection of tumors while preserving the esophagus. This is particularly advantageous for patients with early-stage tumors, who may avoid the need for esophagectomy (surgical removal of the esophagus) and its associated complications, such as postoperative dysphagia and changes in eating habits.

**Improved Quality of Life:** Due to the preservation of the esophagus and the minimally invasive nature of the procedure, ESD has a positive impact on the patient's quality of life. Patients can maintain normal swallowing function and experience fewer dietary restrictions compared to those who undergo esophagectomy.

**Accurate Pathological Staging:** ESD allows for precise evaluation of tumor stage and histological features as the resected specimen is intact. The accurate assessment of the tumor's depth of invasion and lymphovascular involvement helps guide further management decisions and improves patient prognosis.

**Reduced Complications:** ESD is associated with a lower risk of complications compared to open surgical procedures. The incidence of postoperative complications, such as wound infections, anastomotic leaks, and respiratory complications, is generally lower in ESD. However, it is important to note that ESD carries its own set of procedure-related risks, including bleeding and perforation, which require skilled endoscopists and proper patient selection.

**Limited Surgical Morbidity:** ESD eliminates the need for thoracotomy or laparotomy, reducing the risk of surgical complications such as postoperative pain, scarring, and long-term functional impairments associated with traditional surgical methods.

**Cost-Effectiveness:** Compared to traditional surgical approaches, ESD may incur lower overall healthcare costs, considering shorter hospital stays and reduced postoperative care requirements. However, the cost-effectiveness may vary depending on factors such as the expertise of the endoscopist and the availability of specialized equipment.

It is important to note that the selection of treatment modality should be based on individual patient characteristics, tumor factors, and the expertise of the treating team. Multidisciplinary discussions among endoscopists, surgeons, and other healthcare professionals are crucial to determine the most appropriate treatment approach for each patient with early esophageal cancer or precancerous lesions.

## 6 Advancements and Developments in ESD

Endoscopic Submucosal Dissection (ESD) has undergone significant advancements and developments over the years, leading to improved outcomes and expanded applications. Here are the expanded details on some of the advancements in ESD:

### 6.1 Application of New Techniques and Devices

New techniques and devices have been developed to enhance the safety and effectiveness of ESD procedures. Here are some notable advancements:

**Submucosal Injection Agents:** Various submucosal injection agents, such as hyaluronic acid, glycerol, and sodium hyaluronate, have been introduced to improve submucosal lifting during ESD. These agents help create a submucosal cushion, facilitating dissection and reducing the risk of perforation.

**Dual-Knife Technique:** The dual-knife technique involves the use of two different knives, such as the IT knife and the hook knife, in combination to achieve precise and efficient dissection during ESD. This technique allows for improved maneuverability and increased safety during the procedure.

**HybridKnife:** The HybridKnife is a versatile electrosurgical knife that combines monopolar and bipolar energy modes. It offers the advantages of both cutting and coagulation, allowing for more efficient and controlled dissection during ESD.

**Over-the-Scope Clipping (OTSC):** OTSC is a device that can be used to achieve hemostasis or close perforations that may occur during ESD. It consists of a clip delivery system that allows for secure closure and promotes faster healing.

### 6.2 Improvement in Operative Techniques

ESD techniques have evolved to enhance safety and improve outcomes. Here are some notable improvements in operative techniques:

**Dual-Dissection Technique:** The dual-dissection technique, also known as the "step-by-step" technique, involves a systematic approach to dissection. It aims to reduce the risk of complications, such as perforation or bleeding, by dissecting the lesion in multiple steps rather than attempting complete resection in a single step.

**Countertraction Technique:** The countertraction technique involves the use of additional instruments, such as graspers or retractors, to provide counterpressure outside the mucosa. This technique enhances visualization and helps stabilize the target area, facilitating safer and more efficient dissection.

**Pocket Creation Technique:** The pocket creation technique involves the initial creation of a submucosal pocket adjacent to the lesion before the actual dissection. This technique creates a space that allows better maneuverability and improved visualization during subsequent dissection steps.

### 6.3 Application of ESD in Sites Beyond the Esophagus

ESD techniques originally developed for esophageal lesions have been successfully applied to other anatomical sites. Here are examples of ESD applications beyond the esophagus:

**Stomach:** ESD has been widely used for the treatment of early gastric cancer, enabling en-bloc resection and sphincter preservation. It has also been applied to the treatment of gastric subepithelial tumors and gastric precancerous lesions.

**Colorectum:** ESD has been increasingly utilized for the treatment of early colorectal neoplasia. It offers the advantage of en-bloc resection for large lesions, reducing the need for surgical resection and preserving the colon.

**Anorectal Region:** ESD has shown promise in the treatment of early-stage rectal cancers and larger adenomas in the anorectal region. It allows for precise and complete resection while

maintaining anal sphincter function.

Other Sites: ESD techniques have been explored and applied in various other sites, including the duodenum, small intestine, and even the bronchial tree for the treatment of early-stage neoplasms.

These advancements and developments in ESD techniques, devices, and expanding applications have contributed to improved treatment outcomes, expanded indications, and increased adoption of this minimally invasive procedure. Ongoing research and innovation continue to refine and advance the field of ESD, offering new possibilities for the management of early-stage gastrointestinal neoplasms.

## 7 Challenges and Issues in Clinical Practice

### 7.1 Learning Curve and Training in ESD

The learning curve for ESD is steep and requires specialized training and experience to achieve proficiency. Here is some data and related information about the learning curve and training:

#### Learning Curve:

The learning curve for ESD is often described as having an initial period of difficulty followed by rapid improvement.

Studies have shown that the operator's skills and outcomes significantly improve after completing 50 to 100 cases of ESD.

One study found that after performing 30 cases of ESD, there was a significant reduction in the procedure time and the occurrence of complications.

Another study found that after completing 50 cases of ESD, the operator's success rate significantly increased.

#### Training and Education:

Structured training programs are helpful in providing sufficient education and skill development. Here are some common training methods:

Hands-on practice: Trainees gain experience by participating in actual ESD procedures under experienced guidance.

Simulator training: Simulated training using simulators allows operators to practice procedural skills and problem-solving.

On-site guidance: Experienced mentors provide guidance and supervision during the learning process, ensuring patient safety and optimizing surgical outcomes.

Research has shown that through structured training programs and appropriate guidance, operators can significantly improve their technical proficiency after completing a certain number of ESD procedures.

Below is a table showing the relationship between the number of ESD procedures, procedure time, and success rate:

Number of ESD Procedures	Average Procedure Time (minutes)	Success Rate (%)
1-10	120-180	70-80
11-30	90-120	80-90
31-50	60-90	90-95
50+	<60	>95

### 7.2 Prevention and Management of Complications

ESD is associated with potential complications, and their

prevention and management are important considerations. Some common complications include:

Perforation: Perforation can occur during ESD due to unintended full-thickness injury. Techniques such as the creation of mucosal incisions and careful dissection can help minimize the risk of perforation.

Bleeding: Bleeding can occur during or after the procedure. The use of electrocautery, hemostatic agents, and prophylactic coagulation can help control bleeding.

Stricture formation: ESD may lead to the development of strictures, especially in the esophagus. Measures such as the use of steroid injections or the placement of stents can help prevent or manage strictures.

### 7.3 Postoperative Surveillance and Follow-up

Postoperative surveillance and follow-up are crucial for detecting and managing recurrent or metachronous lesions. Key considerations include:

Surveillance endoscopy: Regular follow-up endoscopies are recommended to monitor for recurrence or new lesions. The frequency and duration of surveillance depend on the individual patient's risk factors and the characteristics of the resected lesion.

Histopathological evaluation: Accurate histopathological evaluation of the resected specimen is essential for determining the need for additional treatment and assessing the risk of recurrence.

Multidisciplinary collaboration: Collaboration between gastroenterologists, pathologists, radiologists, and oncologists facilitates comprehensive patient care and decision-making during surveillance and follow-up.

## 8 Conclusion

### 8.1 The Position of ESD in the Treatment of Early Esophageal Cancer and Precancerous Lesions

ESD has established itself as a valuable treatment modality for early esophageal cancer and precancerous lesions. Its minimally invasive nature, high en-bloc resection rate, and low recurrence rate make it an attractive option. ESD allows for precise pathological staging and enables organ preservation, particularly in cases where surgical resection may be associated with significant morbidity. With appropriate patient selection and skilled operators, ESD has shown promising results in achieving curative resection and long-term survival. However, careful consideration should be given to individual patient characteristics and tumor factors when determining the optimal treatment strategy.

### 8.2 Outlook for Future Development

The future of ESD in the treatment of early esophageal cancer and precancerous lesions looks promising. Ongoing advancements in endoscopic imaging technologies and instruments are expected to further enhance the safety and efficacy of ESD procedures. Improvements in endoscopic training programs and the development of simulation models will help shorten the learning curve and ensure the widespread adoption of ESD. Collaboration between endoscopists, surgeons, and pathologists is crucial for the multidisciplinary management of esophageal neoplasms. Additionally, long-term follow-up studies and clinical trials are needed to evaluate the oncological outcomes and compare

the effectiveness of ESD with other treatment modalities. The integration of molecular biomarkers and targeted therapies may also play a role in personalized treatment strategies for esophageal neoplasms.

In conclusion, ESD has emerged as an important treatment

option for early esophageal cancer and precancerous lesions. Its potential for organ preservation, coupled with ongoing advancements, holds promise for improving patient outcomes and expanding its indications in the future.

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