Endoscopic Submucosal Dissection (ESD) for Treatment of Gastrointestinal Lesions

Saowanee Ngamruengphaong, M.D
Assistant Professor of Medicine
Division of Gastroenterology & Hepatology
Johns Hopkins Medicine

What is Endoscopic Submucosal Dissection (ESD)?

ESD is an advanced endoscopic technique that allows en bloc resection of the superficial neoplasias within the lumen of the gastrointestinal (GI) tract regardless of the lesion’s size. The technique entails 1 mucosal marking outside the lesion; 2 submucosal injection using saline or other viscous solutions; 3 mucosal incision outside of the marking dots and 4 submucosal dissection using specialized endoscopic electrocautery knives (Figure 1).

What are benefits of ESD over endoscopic mucosal resection (EMR)?

Prior to introduction of ESD, endoscopic mucosal resection (EMR) was the mainstay endoscopic resection technique for luminal GI lesions. When performing endoscopic resection, En bloc resection (resection of the targeted lesion in a single specimen) is desirable because it enables precise histological assessment of the histologic complete resection, allow accurate assessment of curability by endoscopic resection and minimize local recurrence. However, EMR cannot reliably archive en bloc resection, particularly for lesions larger than 1.5 - 2 cm. ESD was first developed in Japan to overcome technical limitations of EMR.

Other advantages of ESD over EMR include:

1. Higher chance of endoscopic cure after endoscopic resection, thus decrease the need for repeated endoscopic therapy and subsequent surgery

2. In cases that endoscopic resection is performed for pathologic tumor staging, ESD has been shown to be associated with a greater proportion of upgraded diagnoses and more accurate disease staging. Accurate tumor staging enables appropriate decision-making and treatment planning after endoscopic resection.

3. ESD can be a salvage treatment for recurrent or residual neoplasms that are not amendable for EMR.

4. Lesions with underlying fibrosis such as in the setting of chronic inflammation, snare resection with EMR is often not feasible. ESD has been shown to be an effective endoscopic option for these lesions.
However, the main disadvantages of ESD are longer procedure times, and an increased risk of bleeding and perforation, particularly during endoscopists’ early experience with the ESD procedures.

**What are indications for ESD?**

ESD is a minimally invasive option for treatment of superficial neoplasia with a negligible risk of lymph node metastasis because it is a local therapy without lymph node dissection. Therefore, careful endoscopic evaluation using high definition endoscopy with digital and/or chromoendoscopy and accurate preprocedural diagnosis are critical steps for proper patient and lesion selection for ESD. For example, en bloc resection of lesions suspected containing superficial invasive cancer is desirable. ESD is also a valuable technique for the lesions with “non-lifting” or severe submucosal fibrosis from previous endoscopic intervention or chronic inflammation. On the other hand, ESD should not be performed for lesions which are obviously deeply invasive cancers.

The 2019 American Gastroenterological Association (AGA) Institute Clinical Practice Update suggested various indications for ESD in the United States (Table 1). [https://www.cghjournal.org/article/S1542-3565(18)30807-3/fulltext](https://www.cghjournal.org/article/S1542-3565(18)30807-3/fulltext)

**What are challenges in performing ESD in the United States?**

Although ESD has become a standard treatment for superficial neoplasia in Asia, the adoption of ESD in the West has been slow. ESD is a technically demanding procedure. The endoscopists are required to precisely manipulate endoscopes and needle knives in the desired depth and direction during procedure to efficiently dissect the lesion away from the GI wall and avoid muscle injury. Therefore, ESD requires optimal training and proper case selection, starting from small lesions (<30mm) in the gastric antrum, to lesions in the proximal stomach, esophagus, and colorectum. In the West, because of low prevalence of early gastric cancer, there is a lack of appropriate cases for early phase of ESD adoption.

Moreover, accurate endoscopic assessment of lesions’ margins and predicted depth of invasion are mandatory to achieve satisfactory outcomes of ESD. However, these skills are difficult to obtain due to a limited training in advanced endoscopic diagnosis. In addition, the clinicians should have access to experts in gastrointestinal pathology who are experienced in interpretation of ESD specimens and can provide all the relevant information required to assess curability and risk of lymph nodes metastasis (which will determine whether further treatment are needed).

A recent survey study reported that the main factors slowing adoption of ESD in the U.S include limited availability of structured training opportunities, concerns over procedural length, lack of adequate number of lesions, and potential for serious adverse events. In addition, costs associated with equipment or devices and lack of reimbursement are seldom cited (<7%) as a reason to impede start-up of ESD program.
How can physicians acquire ESD training in the United States?

ESD training has not been standardized. However, the trainees can acquire ESD training at the high-volume, advanced endoscopy centers, and training courses in and outside the U.S. The two major stages of ESD training are pre-procedural theoretic knowledge and hands-on training.

1. The trainees should first gain knowledge and skills in advanced imaging diagnosis, learn optimal treatment strategy, know how to interpret the histopathology findings of the ESD specimens and their implications, and how to manage potential adverse events of ESD.

2. The training should include: observe ESD procedures performed by experts, assist experts performing the procedure, practice in animal models and then perform ESD procedure under expert supervision.

The European Society of Gastrointestinal Endoscopy (ESGE) have developed a curriculum for ESD practice in the Western setting [7] https://www.esge.com/esd-training-curriculum/

What are technologies that could make ESD more efficient and safer?

Given the inherent technical difficulty of ESD, several modified techniques and devices have been developed to facilitate safe and effective ESD. Some of these technologies have been used in clinical practices and some are still under development.

- Modified ESD techniques such as pocket creation method, tunneling technique, saline immersion [10, 11, 12]
- Devices:
  - Electrosurgical knives with water-jet function [13, 14]
  - Scissor type knives [15]
  - Traction methods: such as clip-with-line method, clip-and-snare method, S-O clip. Magnetic-assisted traction devices have been reported in clinical cases [16]
  - Overtube system: these devices provide stability of the scope during ESD which make the ESD safer and more efficient.
- Solutions for submucosal injection that provide an immediate and long-lasting cushion beneath the lesion. Example of viscous solutions that are available in the US market are ORISE gel® and Eleview.

Future Directions

Given the widespread use of diagnostic GI endoscopy, precancerous and cancerous lesions will be increasingly detected. Many of these lesions might be amenable to endoscopic resection by ESD. To increase dissemination of ESD in the West, the efforts are dedicated in developing novel techniques and accessories that make ESD both safer and easier. It is expected that ESD will become more popular and accessible to the patients in the US in the near future because of its proven value in treatment of GI lesions. Increased availability of ESD training with standardized curriculum are needed to ensure high quality training and satisfactory outcomes of ESD.
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<th>Organ</th>
<th>Indications for ESD</th>
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| **Esophagus**                 | HGD to well (G1) to moderately (G2) differentiated  
Paris 0–II lesions  
Absolute indications: m1–m2 involvement with two thirds or less of the esophageal circumference  
Expanded indications: m3 or sm <200 μm involvement, any size, clinically N0  
HGD to moderately (G1 or G2) differentiated T1a (m1–m3) lesions ≥15 mm (not amenable to en bloc resection by EMR)  
Patients with Barrett’s esophagus and the following features:  
• Large or bulky area of nodularity  
• Equivocal preprocedure histology  
• Intramucosal carcinoma  
• Suspected superficial submucosal invasion  
• Recurrent dysplasia  
• EMR specimen showing invasive carcinoma with positive margins |
| **Stomach**                   | Absolute indications:  
Mucosal adenocarcinoma (and lesions with HGD), intestinal type, G1 or G2 differentiation, size ≤2 cm, no ulceration  
Expanded indications:  
• Adenocarcinoma, intestinal type, G1 or G2 differentiation, any size, without ulceration  
• Adenocarcinoma, intestinal type, G1 or G2 differentiation, sm-invasive (<500 μm)  
• Adenocarcinoma, intestinal type, G1 or G2 differentiation, ≤3 cm, with ulceration  
• Adenocarcinoma, diffuse type, G3 or G4 differentiation, size ≤2 cm, without ulceration |
| **Colon and rectum**          | En bloc resection for lesions at risk for submucosally invasive cancer:  
• Type V Kudo pit pattern  
• Depressed component (Paris 0–IIc)  
• Complex morphology (0–I or 0–IIa+IIb)  
• Rectosigmoid location Nongranular LST (adenomas), ≥20 mm in size  
• Granular LST (adenomas), ≥30 mm in size  
• Residual or recurrent colorectal adenomas |
## References


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ENDO-766909-AA