Endoscopic Resection of Early Luminal Cancer

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KEYWORDS

- Endoscopic resection • Endoscopic submucosal dissection
- Endoscopic mucosal resection • Early luminal cancer

KEY POINTS

- Early-stage luminal cancers confined to the mucosal layer or superficial submucosal layer can be cured by endoscopic resection.
- Techniques for endoscopic resection include endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD), and endoscopic full-thickness resection (EFTR).
- Various devices are available for performing endoscopic resection. It is essential to be familiary with and use the correct device(s).
- It is essential to understand the potential complications from endoscopic resection and know how to manage any complication that may arise.

INTRODUCTION

For most cancers, early detection is the most important factor in curing the disease. In the case of gastrointestinal (GI) cancers, early diagnosis through endoscopy and early detection through screening increase the cure rate. The survival rate for early-stage gastric and colorectal cancer is reported to be more than 90%.[1,2] In the past, detecting early-stage cancers through endoscopy still necessitated open or laparoscopic surgery for removal. However, advances in therapeutic endoscopy now enable the resection of early-stage GI cancers using endoscopic techniques, when appropriate.

Endoscopic resection (ER) is a minimally invasive technique for removing early cancer or precancerous lesions from the GI tract. GI endoscopic surgery can improve the quality of life of patients and reduce healthcare costs by allowing them to forgo open or laparoscopic surgery for early-stage cancers. The detection of early-stage GI cancer and the advancement of ER techniques have led to a significant increase in cure rates. This has allowed for the successful treatment of many patients with early-stage

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Gastrointest Endoscopy Clin N Am 34 (2024) 51–78
https://doi.org/10.1016/j.giec.2023.07.002
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cancer, leading to a better prognosis and a reduced risk of recurrence. Initially, before the development of the endoscopic electrosurgical knifes, cancers were removed using only endoscopic mucosal resection (EMR), a method that uses a snare. However, the size of the tumor that could be resected was limited by the size of the snare, so it was generally used for tumors 2 cm or smaller because *en bloc* resection is a requirement for an oncologic resection. To address the challenges of EMR, the development of advanced endoscopic surgery instruments such as electrosurgical knives and electrosurgical units (ESUs) has made it possible to perform endoscopic submucosal dissection (ESD). Compared with EMR, ESD allows for the removal of larger and deeper tumors with greater precision, expanding the range of cases that can be treated. Initially used for stomach cancer, ESD has since been applied to other regions of the GI tract, such as the esophagus, duodenum, and colon, offering improved treatment options for patients with dysplasia and early-stage GI cancers.

Depending on the location within the GI tract, different indications and methods are used for ESD. Recently, submucosal tunneling ER (STER) using the tunnel method and endoscopic full-thickness resection (EFTR), a form of hybrid ER, has also been used to resect subepithelial GI tumors. In this article, the principles and procedural methods of EMR/ESD/STER/EFTR for ER for each GI organ with are explained. No matter what method is used, the most important aspect of an oncologic resection is to obtain an *en bloc* R0 resection. The outcomes of ER and the response to postprocedural complications will also be addressed.

NATURE OF THE PROBLEM

ER techniques, such as EMR and ESD, have become popular due to the minimally invasive nature compared with traditional surgical methods. These procedures have revolutionized the treatment of early-stage GI cancers and other benign or premalignant lesions. Despite its numerous advantages, there are inherent challenges associated with the procedure.

The nature of the GI tract presents several technical difficulties during ER. First, the complex and variable anatomy of the GI tract may pose challenges during the procedure, especially in areas with tight angulations or difficult-to-reach locations such as the duodenum and ascending colon. Second, large, flat, or irregularly shaped lesions may be challenging to resect completely. Moreover, lesions in certain locations, such as cardia, pylorus, or ileocecal valve, may be more difficult to manage endoscopically. Third, ER, particularly ESD, requires a high level of expertise and has a long learning curve. Inadequate training or limited experience can lead to incomplete resections or increased risk of complications.

Although ER is minimally invasive, it can still lead to complications such as perforation, which is more likely in ESD than EMR, intraoperative and delayed bleeding, rare instances of postoperative infection, and stricture formation after extensive resections for esophagus or colon cancer. Moreover, ER has limitations like the potential for incomplete removal of larger or complex lesions, being mainly suited for early-stage GI cancers rather than advanced ones, and a limited capacity to evaluate and address lymph node metastasis. To overcome these complications and limitations, it is important to understand the characteristics and anatomy of each region of the GI tract and to be familiar with the relevant indications and techniques to avoid complications.

ANATOMY OF THE GASTROINTESTINAL WALL FOR ENDOSCOPIC RESECTION

A comprehensive understanding of the structural characteristics of each GI organ, particularly those related to the GI tract wall, is essential for performing successful

ERs. Even within the GI tract, there are differences in the wall structure of the esophagus, stomach, duodenum, and large intestine. Here, we aim to explain the anatomic characteristics of each organ relevant to ER techniques, such as ESD. Fig. 1 shows the cross-sectional anatomy of various locations within the GI tract.

1. Esophagus
   The esophagus consists of four layers: the mucosa (innermost), the submucosa, the muscularis propria, and the adventitia (outermost). The mucosa is composed of epithelial cells (M1), a thin layer of connective tissue called the lamina propria (M2) and a thin layer of muscle called the muscularis mucosae (M3). In the case of squamous cell invasion, there is a possibility of nodal metastasis from M3 invasion onward. The submucosa is the layer beneath the mucosa, made up of connective tissue, blood vessels, nerves, and glands that produce mucus to lubricate the esophagus during swallowing.[3,4]
2. Stomach
   The mucosa of stomach is the most superficial layer of the gastric wall and comprises three sublayers: epithelium, lamina propria, and muscularis mucosae.

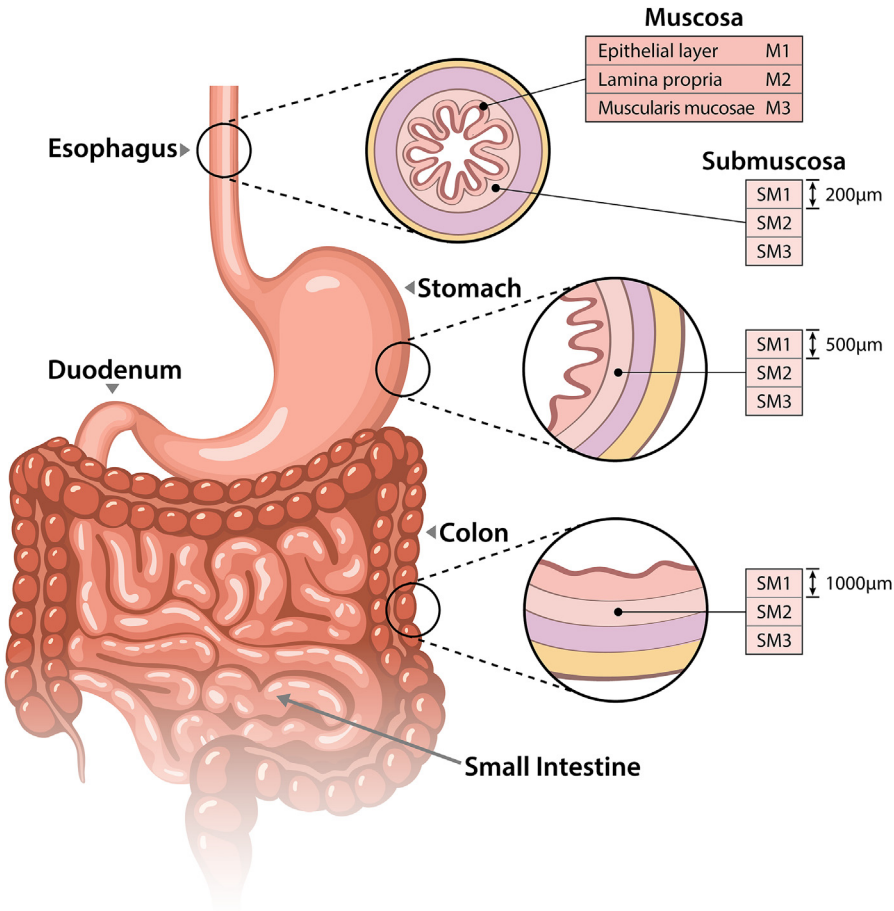

Fig. 1. Anatomy of the gastrointestinal tract for endoscopic resection.

The submucosa is a layer of dense irregular connective tissue situated beneath the mucosa. It contains blood vessels, lymphatic vessels, and nerves. Unlike esophageal ESD, successful gastric ESD requires a greater understanding of the submucosa in the gastric wall structure because the likelihood of lymph node metastasis is related to the depth of submucosal invasion of adenocarcinoma in gastric cancer. The submucosa layer is divided into three parts based on the depth of invasion in increments of 500 μm: Sm1 (less than 500 μm), Sm2 (greater than 500 μm but <1000 μm), and Sm3 (greater than 1000 μm). Proper assessment of these layers and adherence to ESD criteria can lead to successful treatment of early-stage GI neoplasms, reduced complications, and improved patient outcomes. In general, the submucosal layer of the gastric antrum has fewer blood vessels, and the connective tissue is less dense, making dissection relatively easy. On the other hand, the submucosal layer of the gastric body and fundus contains more fibrous tissue and a higher concentration of blood vessels than the antrum, making the dissection of the submucosal layer more challenging.

3. Duodenum

Owing to the duodenum's thin wall, anatomic curvature, and proximity to major blood vessels and the pancreaticobiliary system, the risk of complications, such as perforation and bleeding, is significantly higher compared with ER performed in the stomach or esophagus. Performing ER (such as ESD) in the duodenum requires a detailed understanding of its complex anatomy, including the ampulla of Vater and other important structures that can affect the safety and efficacy of the procedure as well as special caution due to the duodenum's proximity to vital organs such as the pancreas and bile duct.

4. Colon/rectum (colorectum)

ESD can be used to treat early-stage colorectal cancers or large polyps by excising the lesion from the submucosal layer, keeping the muscularis propria intact. In the context of colon ESD, understanding the submucosal layer is crucial, as this is the primary target for dissection. The colon is attached to the posterior abdominal wall through the mesentery, a fold of the peritoneum that supports and anchors the colon. The ascending and descending colon have a retroperitoneal position, meaning that they are fixed to the posterior abdominal wall, whereas the transverse and sigmoid colon are intraperitoneal and have more mobility due to their longer mesenteric attachments. The cecum is the widest part of the colon and has a thinner wall compared with other regions of the colon. ESD in the cecum requires careful dissection to avoid perforation. In addition, the ileocecal valve, the junction between the small intestine and the colon, is anatomically complex, with folds and curves that may make the procedure more challenging. Limited space and maneuverability in the ileocecal valve area may make it more difficult to obtain an optimal endoscopic view and maintain a stable position during the procedure. Appropriate scope handling and patient positioning can help overcome these challenges. The transverse colon and sigmoid colon have longer mesenteries, which provide greater mobility and require caution during endoscopic procedures.

It is important to avoid putting undue tension on the mesentery and its blood supply to prevent complications such as ischemia or damage to the surrounding structures. Owing to the lower blood flow in part of colon compared with other abdominal organs, colonoscopy poses a risk for colon ischemia, which can have multiple causes such as splanchnic circulation impairment, bowel

preparation, sedative drugs, bowel wall ischemia due to insufflation or barotrauma, and the introduction of the endoscope.[5]

The rectum is located in the pelvic cavity and is surrounded by various pelvic structures, such as the prostate or uterus, seminal vesicles, and urinary bladder. During ESD in the rectum, it is essential to consider these neighboring structures to avoid damaging them inadvertently. In addition, the rectum has a relatively consistent diameter and straight configuration, making endoscope navigation and lesion visualization easier. However, its more abundant blood supply may pose a higher risk of bleeding, requiring extra care to avoid injury to larger vessels. The rectal wall is generally thicker than the colonic wall. This thickness difference affects the dissection process during ESD. In the rectum, the thicker wall may provide more stability and reduce the risk of perforation, whereas in the colon, the thinner wall requires a more delicate approach to prevent accidental damage to muscle layer.

INDICATIONS FOR ENDOSCOPIC RESECTION

Indication for Endoscopic Resection of Esophageal Cancer

Early-stage esophageal cancer confined to the mucosal layer or submucosal layer is referred to as superficial esophageal cancer. Most of these cases are in the initial stages, allowing for long-term survival after treatment. The detection rate of early esophageal cancer is increasing in some regions, and advancements in endoscopic local treatments are significantly improving esophageal cancer care.[6]

One of the most important considerations in endoscopic treatment of esophageal cancer is that the histopathological characteristics are significantly different from those of gastric cancer. Although dividing the mucosal layer into M1, M2, and M3 in gastric cancer may not be very meaningful, it is extremely important in squamous cell esophageal cancer.[7] The reason for the detailed classification of the mucosal layer in esophageal cancer is that the risk of lymph node metastasis dramatically increases with involvement of M3.

In esophageal cancer, SM1 refers to up to 200 μm (**Fig. 1**). The American Gastroenterological Association (AGA) Institute Clinical Practice Update provides separate ESD indications for squamous cell carcinoma and Barrett's esophagus[8] (**Table 1**).

Table 1
Indication for esophageal endoscopic submucosal dissection in the United States

Condition	Indications for Esophageal ESD
Squamous cell carcinoma	High-grade dysplasia (HGD) to well-differentiated (G1) or moderately differentiated (G2) squamous cell carcinoma
	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
Barrett's esophagus	HGD to moderately differentiated (G1 or G2) T1a (m1–m3) lesions ≥ 15 mm (not amenable to *en bloc* resection by EMR)
	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

Recently, the Japan Gastroenterological Endoscopy Society (JGES) provided guidelines for esophageal cancer ESD, which are based on the depth of invasion, size, and circumferential extent. For clinical T1a-epithelium/lamina propria mucosa (N0M0) cancer, ER can be performed for non-circumferential lesions, whereas for whole circumferential lesions, ER is recommended for those up to 5 cm and surgical resection or chemoradiotherapy for those larger than 5 cm. If an esophageal cancer is staged as T1a-MM or T1b-SM1, ER can be performed for non-circumferential lesions, followed by pathologic assessment to determine if the resection was curative. For circumferential lesions, surgical resection or chemoradiotherapy is recommended.[9]

Indication for Endoscopic Resection of Gastric Cancer

The indications for gastric ESD are generally based on the risk of lymph node metastasis and the likelihood of achieving complete resection. In gastric cancer ESD, absolute indications and expanded criteria have been suggested in Japan by Gotoda, and various countries have presented ESD indications suitable by their respective national gastroenterological endoscopy societies[8,10] (**Tables 2** and **3**).

The criteria for lesions that can be determined by preoperative endoscopy are somewhat subjective. It is difficult to accurately distinguish between M cancer (mucosal cancer) and SM (submucosal) cancer through endoscopic findings alone. Although endoscopic ultrasound (EUS) can be used to assess the depth of invasion before EMR or ESD, it is not always capable of accurately diagnosing very small submucosal invasions. As a result, conducting EUS before EMR/ESD can provide useful information, but it is not considered an essential prerequisite for these procedures. In gastric cancer, ESD is indicated for absolute indications including intramucosal

Table 2
Indication for gastric cancer endoscopic submucosal dissection

Depth	Mucosal cancer				Submucosal cancer	
	Ulceration		No ulceration		Sm1(invasion depth ≤ 500um)	Sm2,3 (Invasion depth ≥ 500 um)
Lesion size	≤2cm	>2cm	≤3cm	>3cm	≤3cm	Any size
Differentiated carcinoma						
Undifferentiated carcinoma						

Guideline criteria for EMR
Surgery
Expanded criteria for ESD
possible surgery or ESD

Table 3
American Gastroenterological Association recommendation for gastric cancer endoscopic submucosal dissection

Indications	Type	Differentiation	Size	Ulceration	Invasion
Absolute	Mucosal adenocarcinoma (and lesions with HGD), intestinal type	G1 or G2	$\leq$ 2 cm	No	mucosa
Expanded	Adenocarcinoma, intestinal type	G1 or G2	Any size	No	mucosa
	Adenocarcinoma, intestinal type	G1 or G2	-	-	SM < 500 μm
	Adenocarcinoma, intestinal type	G1 or G2	$\geq$ 3 cm	Yes	mucosa
	Adenocarcinoma, diffuse type	G3 or G4	$\leq$ 2 cm	No	mucosa

gastric adenocarcinoma (cT1a) with differentiated histology, lesion size $\leq$ 2 cm, no evidence of ulceration (UL0), and no lymphovascular invasion, whereas expanded indications encompass larger lesions, undifferentiated histology, and submucosal invasion up to 500 μm with favorable prognostic factors.

It is essential to note that the indications for gastric ESD may vary among countries and institutions, as they are influenced by factors such as clinical expertise and local guidelines. In addition, patient factors, such as age, overall health, and comorbidities, should be considered when determining the suitability of gastric ESD.

Indication for Endoscopic Resection of Duodenal Lesions

EMR or ESD can be performed in the duodenum, but it is less common and more technically challenging compared with gastric or esophageal ESD. The indications for duodenal ESD include early-stage duodenal cancers or precancerous lesions, such as large adenomas, which are limited to the mucosa or superficial submucosa layers without evidence of lymph node metastasis or distant metastasis.

However, due to the duodenum's thin wall, anatomic curvature and proximity to major blood vessels and the pancreaticobiliary system, the risk of complications, such as perforation and bleeding, is significantly higher compared with ESD performed in the stomach or esophagus. Therefore, the decision to perform ESD in the duodenum should be made on a case-by-case basis, considering factors such as lesion size, location, histology, and the patient's overall health. In addition, the procedure should be performed by experienced endoscopists who are skilled in managing potential complications.

Indications for Endoscopic Resection of Colorectal Cancers

EMR is typically suitable for lesions smaller than 20 mm and those with a low risk of lymph node metastasis. ESD is a more advanced technique used to achieve *en bloc* resection of larger lesions or those difficult to remove with EMR, such as lesions with significant submucosal fibrosis. ESD involves the dissection of the submucosal layer beneath the lesion, allowing for more precise removal of the tumor while minimizing the risk of recurrence. ESD is indicated for lesions with superficial submucosal invasion, minimal lymph node metastasis risk, and lateral spreading tumors (LSTs) larger than 20 mm. The AGA has published indications for colon ESD, which are summarized in **Table 4**.[8]

The choice between EMR and ESD depends on factors such as lesion size, location, morphology, and the endoscopist's skill level. If the lesion to be resected is suspected

Table 4
American Gastroenterological Association recommendation for colorectal endoscopic submucosal dissection

Risk Factor	Description (Paris)	Size
***En bloc* Resection for Lesions at Risk for Submucosally Invasive Cancer:**		
Type V Kudo pit pattern	-	-
Depressed component	0–IIc	-
Complex morphology	0–Is or 0–IIa + Is	-
Rectosigmoid location	-	-
Nongranular LST (adenomas)	-	$\geq$ 20 mm
Granular LST (adenomas)	-	$\geq$ 30 mm
Residual or recurrent adenomas		

to be a malignancy, it is essential that the lesion be resected *en bloc* for histopathologic evaluation. The decision to perform either ESD or EMR should take this into consideration. Both techniques aim to provide effective treatment while preserving the patient's quality of life and minimizing complications.

The indications for ER of malignant colorectal polyps may vary depending on whether the polyp is pedunculated or non-pedunculated. Pedunculated polyps are polyps with a stalk, whereas non-pedunculated polyps do not have a stalk and are sessile or flat.

According to the US Multi-Society Task Force on Colorectal Cancer (the American Society for Gastrointestinal Endoscopy (ASGE), the American College of Gastroenterology (ACG), and the AGA) guidelines on the management of malignant colorectal polyps, non-pedunculated malignant polyps should be considered high risk for residual or recurrent cancer if they have any of the following features: poor tumor differentiation, lymphovascular invasion, submucosal invasion depth greater than 1 mm, tumor involvement of the cautery margin, or tumor budding. For pedunculated malignant polyps, the ASGE guidelines recommend that they are considered high risk for residual or recurrent cancer if they have poor tumor differentiation, lymphovascular invasion, or tumor within 1 mm of the resection margin.[11]

In general, ER (either EMR or ESD) can be considered for malignant colorectal polyps that meet certain criteria, such as tumor is resected *en bloc*, no evidence of deep submucosal invasion, no evidence of lymphovascular invasion, and negative resection margins. However, for polyps with high-risk features or larger size, surgical resection with lymph node dissection may be recommended.

PROCEDURAL APPROACH

Endoscopic Mucosal Resection

EMR is primarily used for the removal of polypoid tumors in the GI tract. However, recent advances have led to the utilization of modified EMR techniques such as piecemeal EMR, EMR-L, and EMR with cap-assisted technique (EMR-C) for lesions with LSTs and fibrosis.

EMR is one of the most commonly used resection techniques for the safe and effective removal of tumors smaller than 20 mm. However, for lesions larger than 20 mm, such as non-pedunculated flat adenomatous polyps, LSTs, submucosal tumors, lesions in difficult-to-access locations due to flexures or folds, lesions with accompanying fibrosis due to prior biopsies or partial resections, and locally recurrent cases

following ER, conventional EMR may have a relatively low *en bloc* resection rate. In such cases, hybrid ESD or ESD should be considered. Generally, for polyps larger than 20 mm, endoscopic piecemeal resection or ESD should be considered based on the possibility of malignancy.

1. Conventional endoscopic mucosal resection
   Conventional-EMR is a method of resection using an endoscope after injecting submucosal injection solution and using a snare. The submucosal injection of the polyp creates a cushion space between the mucosa and the muscularis propria, which can prevent perforation, and there is also a mechanical compression effect on the microvessels of the submucosal layer, allowing for safer removal of the polyp. In addition, if resection is difficult due to the colonic flexure of the GI tract, or if the lesion is not clearly distinguishable from the normal mucosa, making it difficult to capture with adequate margins, submucosal injection can help facilitate polyp resection more easily. Various submucosal injection materials are used, such as normal saline, glycerin, hyaluronic acid, sodium alginate, and hydroxyethyl starch. Generally, solutions containing epinephrine and a small amount of indigo carmine or methylene blue are used to reduce the risk of bleeding and to visualize the injection site. The submucosal solution is preferably injected into the proximal part of the polyp so that the lesion swells in front of the endoscope tip, making it easier to capture, and efforts should be made to inject at an angle of 30 to 45° to penetrate the mucosal barrier as close to vertical as possible. When injecting the submucosal solution into the proximal part of the polyp, slowly pull the needle back while pointing it downward, so the lesion moves to the center of the swelling, making resection easier (**Fig. 2**).
2. Modified EMR (EMR-Cap/EMR-Ligation)
   If the polyp is not captured at once due to factors such as lesion location or swelling shape after submucosal solution injection, EMR using modified method can be considered. Cap-assisted EMR (EMR-C), which involves applying a cap with a snare to the endoscope tip and sufficiently aspirating the lesion into the cap, and ligation-assisted EMR (EMR-Ligation, EMR-L), which uses a cap with a rubber band to capture the lesion and resect it with a snare, can be tried. However, using these devices has the disadvantage of making it difficult to control the capture depth, so they are typically used in rectal lesions with thicker submucosal layers. For lesions with fibrosis where mucosal swelling does not occur well, there is underwater EMR, which is performed by filling the colonic lumen with water instead of air and without using

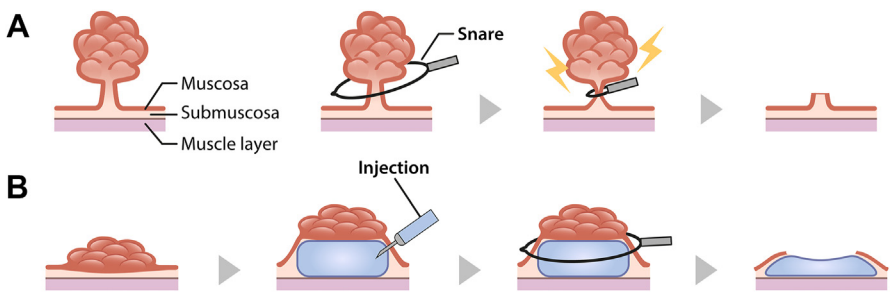

Fig. 2. Conventional endoscopic mucosal resection. (*A*) Cold snare resection without submucosal injection. (*B*) EMR after submucosal injection.

submucosal injection solution. EMR is a minimally invasive technique used to remove GI neoplasms. Several EMR techniques have been developed to treat various types of lesions, EMR-C, and EMR-L.

1. EMR with cap-assisted technique:
   EMR-C, also known as cap-assisted EMR, involves the use of a transparent cap attached to the tip of the endoscope. The cap assists in stabilizing the lesion and provides better visualization. A snare is premounted to the distal end of the cap and advanced to the lesion. After marking the lesion and injecting a solution into the submucosal layer, the lesion is then suctioned into the cap and the snare is then closed around the base of the lesion. The lesion is resected using electrosurgical current, and the specimen is retrieved. This technique allows for easier manipulation of the lesion and can improve the resection rate (**Fig. 3**).
2. EMR with ligation:
   EMR-L, also known as band ligation-assisted EMR, is a technique that combines endoscopic variceal ligation with EMR. After marking the lesion and injecting a solution into the submucosal layer, a ligation device is used to place a rubber band around the base of the lesion, capturing and strangulating it. The lesion, along with a portion of the surrounding tissue, is then resected using a snare and electrosurgical current. The specimen is retrieved by cutting the rubber band (**Fig. 4**). EMR-L is particularly useful for the resection of larger and sessile lesions, as the ligation process reduces the risk of bleeding and perforation.

Each of these EMR techniques has its advantages and limitations, and the choice of the technique depends on factors such as lesion size, location, and morphology as well as the endoscopist's experience and preference. In general, all methods of EMR are limited to lesions less than 20 mm in diameter to achieve an *en bloc* resection.

Hybrid Endoscopic Submucosal Dissection

Hybrid ESD is a technique in which the lesion is first marked, submucosal injection is performed and then a full circumferential incision is made around the lesion with an electrosurgical knife to create a margin around the lesion. Limited submucosal dissection is performed to expose the submucosal layer circumferentially as well as any areas under the lesion where there is submucosal fibrosis limiting the lifting of the mucosal surface. This step is then followed by injecting a solution into the submucosal layer to elevate the remainder of the mucosal lesion, creating a cushion between the mucosal and deeper layers. After the injection, the lesion is resected using a snare, and the specimen is retrieved. The circumferential incision step allows for precise control of the resection margins and sets the depth of the resection, which may reduce the risk of incomplete resection and local recurrence (**Fig. 5**).

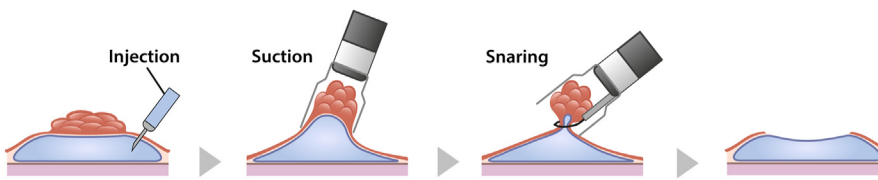

Fig. 3. Endoscopic mucosal resection with cap-assisted technique (EMR-C).

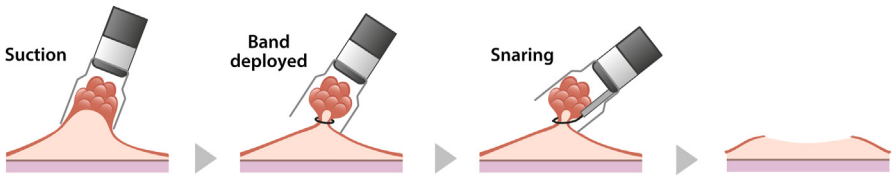

Fig. 4. Endoscopic mucosal resection with ligation (EMR-L).

Endoscopic Submucosal Dissection

ESD was introduced in Japan in the 1990s for the curative resection of early gastric cancer (EGC). Compared with EMR, ESD allows for relatively unrestricted *en bloc* resection regardless of size, location, and shape. It is currently actively used for the complete resection of benign and malignant tumors in the GI tract, including the esophagus, stomach, duodenum, and colon. Regardless of the specific ESD technique used, the fundamental principles of the procedure remain consistent. These basic steps include marking the lesion, administering a submucosal injection, creating a mucosal incision around the lesion, and dissecting the underlying submucosal tissue. By adhering to these core principles, physicians can adapt their approach based on the unique needs of the patient while maintaining the effectiveness of the treatment (Fig. 6).

Once the examination and setting plan for the procedure have been completed, it is helpful to perform mental image preparation for the ESD procedure before starting. After predicting the lesion's location, size, distribution of blood vessels in the submucosal layer, and fibrosis, consider which knife to use, which angle to start the mucosal incision to facilitate visibility in case of bleeding, and where to begin submucosal dissection to maximize the exposure of the submucosal layer with the help of gravity. It is recommended to create a somewhat specific scenario and simulate it.

1. Lesion confirmation
   Before ER of GI lesions, it is essential to accurately confirm the patient's lesion status. Chromoendoscopy using indigo carmine to paint the lesion has been used to accurately assess the margins of the lesion, but recently, image-enhancing endoscopy/electronic chromoendoscopy such as narrow band image (NBI), i-SCAN, and flexible spectral imaging color enhancement have been demonstrated to accurately determine the lesion margins and characterize the lesion. Confirming the lesion helps to accurately determine whether ER is indicated by evaluating the presence of ulcers and lesion size.
2. Choices of ESD devices
   a. Electrosurgical knife
      First, it is necessary to decide which knife to use for the ESD resection. There are various ESD knives currently available, each with its own advantages and disadvantages, and new products are constantly being developed and released.[12,13] Currently, there is no one knife that has the ability to

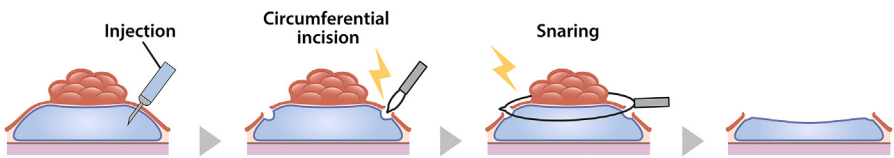

Fig. 5. Hybrid ESD.

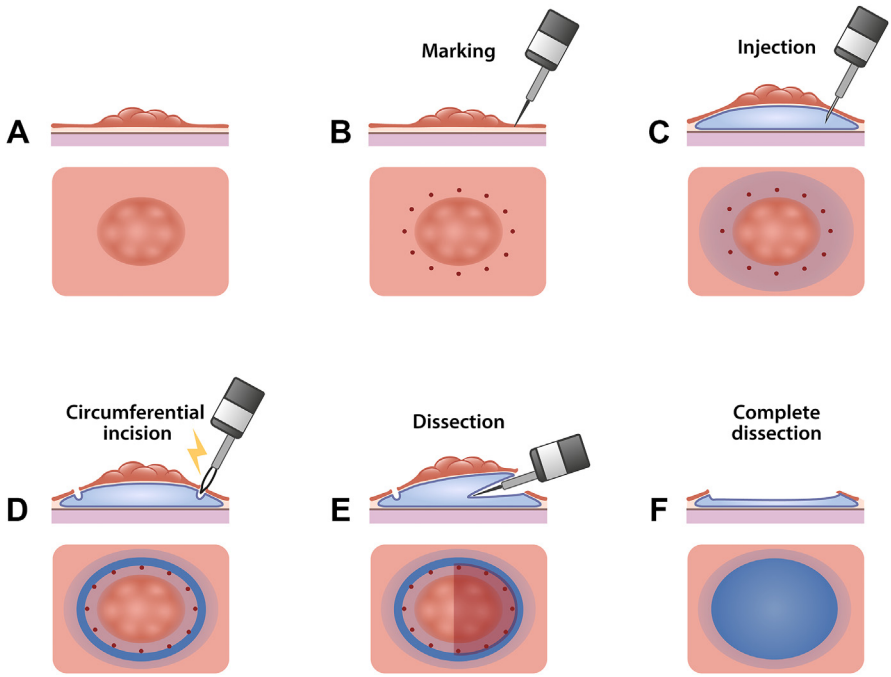

Fig. 6. Endoscopic submucosal dissection. (*A*) Lesion confirmation. (*B*) Marking. (*C*) Submucosal injection. (*D*) Circumferential incision. (*E*) Dissection. (*F*) Complete dissection after retrieval of tissue is resected.

do it all. Therefore, it is important to choose the most appropriate knife for each step of the procedure, and most importantly, whether the operator can handle it comfortably and safely. Because the usage methods differ for each knife, the operator should be well versed in the characteristics and advantages/disadvantages of the knife before starting the procedure. There is little research on which knife is suitable for beginners and has fewer complications. Morphologically, knives can be divided into insulated and non-insulated knives, but recently, knives that combine the advantages of both have also been released (Fig. 7).

b. Electrosurgical unit

A thorough understanding of the ESU is crucial when performing ESD. Operators intending to perform ESD should be well versed in the principles of electrosurgery, particularly the characteristics and application of various cutting and coagulation settings. This theoretic preparation is essential for addressing various situations encountered during ESD and EMR, such as difficulty in dissection due to tissue carbonization, fibrosis with scars, and ineffective resection due to increased resistance in the submucosal layer with abundant adipose tissue, by changing the cutting and coagulation settings.

c. Endoscopic caps/hoods

The ESD procedure often encounters complications such as bleeding and perforation. To reduce these complications, it is important to closely observe the incision and dissection surfaces. However, depending on the location of the lesion, close observation can be challenging due to respiration and cardiac movement. In such cases, attaching a transparent cap to

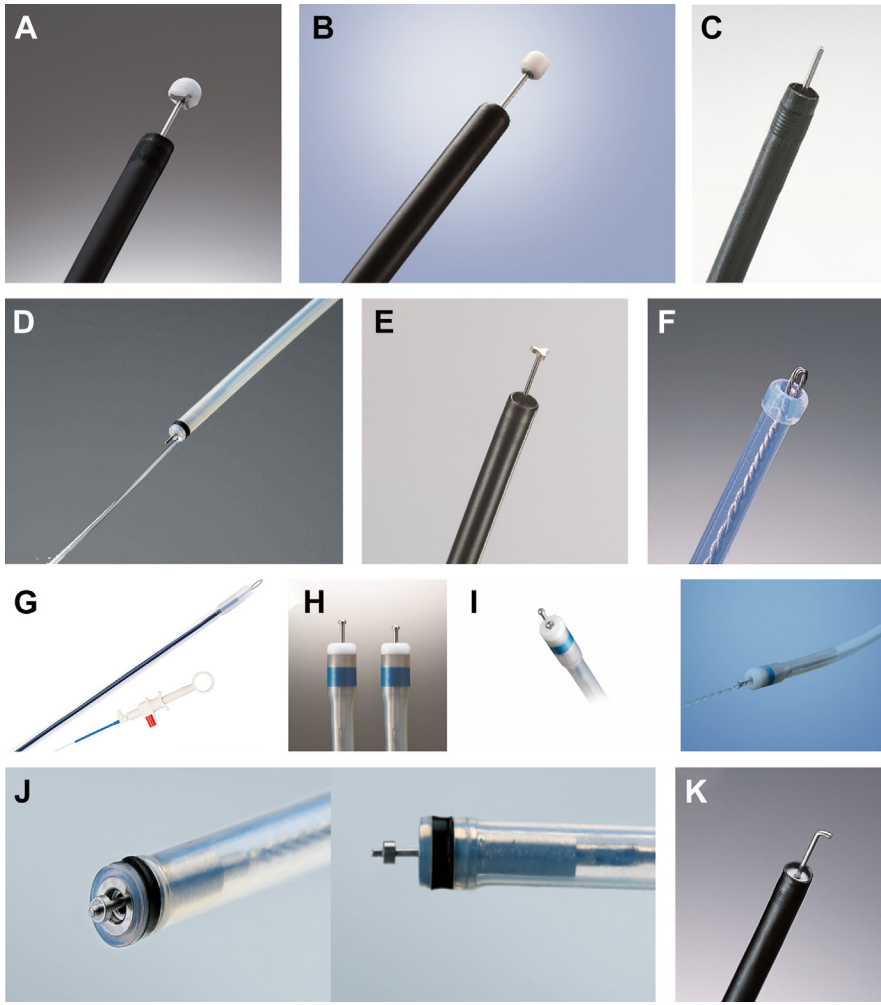

Fig. 7. ESD electroknives. (*A*) IT knife 2 (With permission from Olympus Corporation). (*B*) IT knife nano (With permission from Olympus Corporation). (*C*) Needle knife (With permission from Olympus Corporation). (*D*) Splash knife (Splash M-KnifeTM (PENTAX Medical, HOYA Corporation, Tokyo, Japan). With permission from PENTAX Medical, HOYA Corporation). (*E*) Triangle tip knife (With permission from Olympus Corporation). (*F*). Flex knife (With permission from Olympus Corporation). (*G*) Universal knife (ESD-knife. With permission from MTW Endoskopie Manufaktur). (*H*) Dual knife (With permission from Olympus Corporation). (*I*) Dual knife J (Water jet, With permission from Olympus Corporation). (*J*) Splash M-KnifeTM (PENTAX Medical, HOYA Corporation, Tokyo, Japan). With permission from PENTAX Medical, HOYA Corporation. (*K*) Hook knife (rotatable, With permission from Olympus Corporation).

the end of the endoscope allows a close approach to the lesion, maintaining a consistent distance of about 3 to 4 mm between the lesion's incision and dissection surfaces, greatly aiding in the close observation (Fig. 8).

d. Hemostatic devices

Bleeding can occur at any stage of the ESD procedure. For instance, it can occur during the process of marking around the lesion using electric

Fig. 8. Endoscopic caps (With permission from Olympus Corporation).

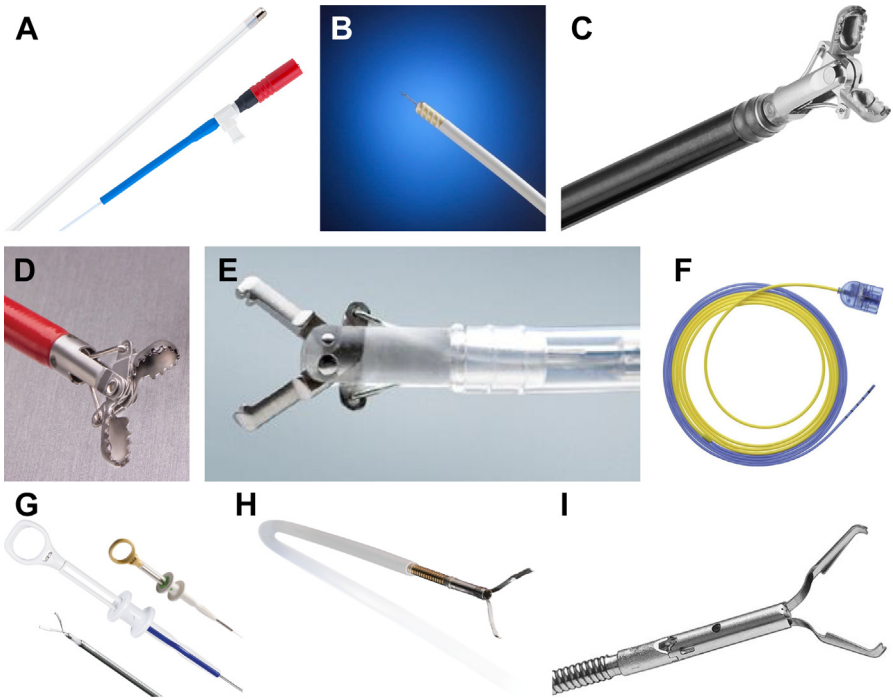

Fig. 9. Hemostatic devices. (*A*) Coagulation probe (With permission from MTW Endoskopie Manufaktur). (*B*) Injection Gold Probe TM (Image provided courtesy of Boston Scientific. ©2023 Boston Scientific Corporation or its affiliates. All rights reserved). (*C*) Coagrasper (With permission from Olympus Corporation). (*D*) Hot biopsy forceps (Image provided courtesy of Boston Scientific. ©2023 Boston Scientific Corporation or its affiliates. All rights reserved). (*E*) Hemostat-Y (HemoStat-YTM (PENTAX Medical, HOYA Corporation, Tokyo, Japan). With permission from PENTAX Medical, HOYA Corporation). (*F*) Argon plasma coagulation probe (ERBE, Germany). (*G*) EZ Clip (With permission from Olympus Corporation). (*H*) QuickPro (With permission from Olympus Corporation). (*I*) Resolution clip (Image provided courtesy of Boston Scientific. ©2023 Boston Scientific Corporation or its affiliates. All rights reserved).

coagulation current or argon plasma coagulation (APC), the submucosal injection process, the process of making an incision around the lesion, and the process of performing submucosal dissection. When bleeding occurs, it is important to know which hemostatic device to use (Fig. 9).

3. Marking

Various methods, such as a cutting knife or APC, can be used to mark the cutting line for lesion resection. Typically, marks are made on the normal mucosa about 5 mm to 1 cm away from the lesion's border using a coagulation current.

4. Submucosal injection

The submucosal injection is performed 2 to 3 mm outside the marked resection area. Typically, the injection is started from the distal part of the lesion or the difficult to resect part in the endoscopic view, then the incision is made, and the injection fluid is inserted toward the proximal side, followed by the incision. However, this can vary depending on the location of the lesion. The angle of the injection needle should be approximately 45 to 70° in the stomach and 30 to 45° in the colon. If the submucosal layer does not swell up well, it is usually because the injection needle is inserted too deeply. In this case, it is effective to pull the needle slightly toward the mucosal layer and inject the solution. Injections are usually made in multiple locations, with 1 to 5 cc injection in each location.

5. Circumferential incision and dissection

Understanding the anatomic structure of the GI tract is important for maintaining appropriate incision depth during mucosal incision and submucosal dissection. Most patients maintain a left lateral decubitus position during endoscopic procedures, so it is crucial to understand the direction of gravity and perform the incision and dissection in a direction that exposes the submucosal layer easily.

During submucosal dissection, a series of short, straight lines should be used to follow the overall curvature of the GI wall. The dissection plane of the submucosal layer should be kept as close as possible to the endoscopic view using CO_2 control, pushing and pulling, and torque rotation. The depth of dissection should be at the lower one-third of the submucosal layer or at the boundary between the submucosal layer and the muscularis propria, which helps reduce bleeding in ESD. This boundary can only be confirmed during close-up, direct-view dissection. Attaching a transparent cap to the endoscope tip helps with visibility during close dissection and helps induce countertraction when the tip enters the submucosal layer, aiding in dissection. If a vessel likely to bleed is encountered during dissection, coagulation is performed in advance using a coagulation forceps.

6. Tissue fixation and pathology

Accurate confirmation of the final pathology results in ER is important, as it determines whether complete resection has been achieved or additional surgery is needed. Generally, the dissected tissue is fixed and sent for pathology examination. To prevent the tissue margins from curling inward, the tissue is stretched and flattened as much as possible, pinned to a flat Styrofoam piece, and placed in formalin. However, individual differences in stretching technique may affect the results. Overcoming this issue has been the subject of research, but unifying the method through communication between physicians and pathologists at each center is crucial.

Pathologic criteria for endoscopically resected tissue may vary by country, but generally follow the World Health Organization (WHO) guidelines. Early GI cancer ER pathology diagnosis includes the presence or absence of tumor

invasion in the resection margins, determining complete resection, and histologic type, invasion depth, tumor size, ulcer, lymphatic, and vascular invasion, which are known risk factors for lymph node and distant metastasis. The results, except for histologic type, are usually indicated by agreed on terms, numbers, or presence/absence, making it easy to standardize among hospitals and medical centers. However, there may be confusion regarding histologic type and histologic differentiation. In this regard, ongoing communication between the endoscopist and the pathologist is necessary.

Endoscopic Full-Thickness Resection

EFTR is a method of resecting the entire layer of the GI wall surrounding the tumor. Initially developed and mainly used to remove GI subepithelial tumors (SETs), it has also been applied in cases of GI luminal/mucosal cancers where the indication for ESD is unclear. This technique is particularly useful for early-stage cancers, SETs, and benign tumors that have not yet penetrated the GI wall or metastasized to other parts of the body. EFTR can be a valuable option for patients who are not suitable candidates for surgery due to age or comorbidities. EFTR is a minimally invasive technique used to remove GI luminal tumors, such as those in the stomach, small intestine, and colon (**Fig. 10**).

1. Exposed EFTR

   This method involves cutting the entire gastric wall layer around the tumor and removing it, resulting in an artificial perforation that connects the abdominal cavity to the gastric space. To resolve this issue, the procedure is completed

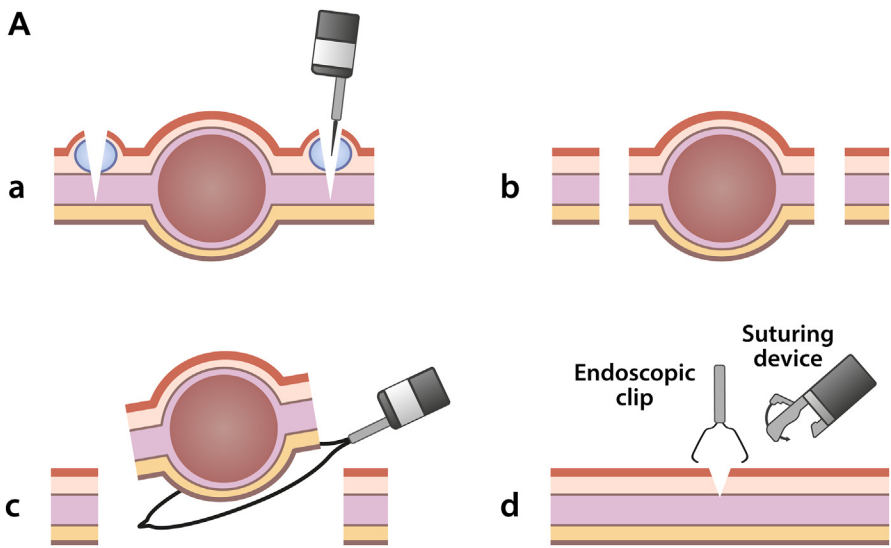

Fig. 10. Endoscopic full-thickness resection (EFTR). (*A*) Exposed EFTR. (*a*) Circumferential incision to the depth of the muscularis propria. (*b*) Intentional perforation to serosal layer. (*c*) Retrieving of resected entire wall including tumor with endoscope. (*d*) Suturing or clipping. (*B*) Nonexposed EFTR (band ligation). (*a*) Lesion confirmation. (*b*) Suction with forceps. (*c*) Band ligation deployed. (*d*) Cutting with snaring. (*C*) Laparoscopic endoscopic cooperative surgery (LECS). (*a*) Circumferential incision to the depth of the muscularis propria. (*b*) Intentional perforation to serosal layer. (*c*) Retrieving of resected entire wall including tumor with laparoscope. (*d*) Suturing with laparoscopic stapler.

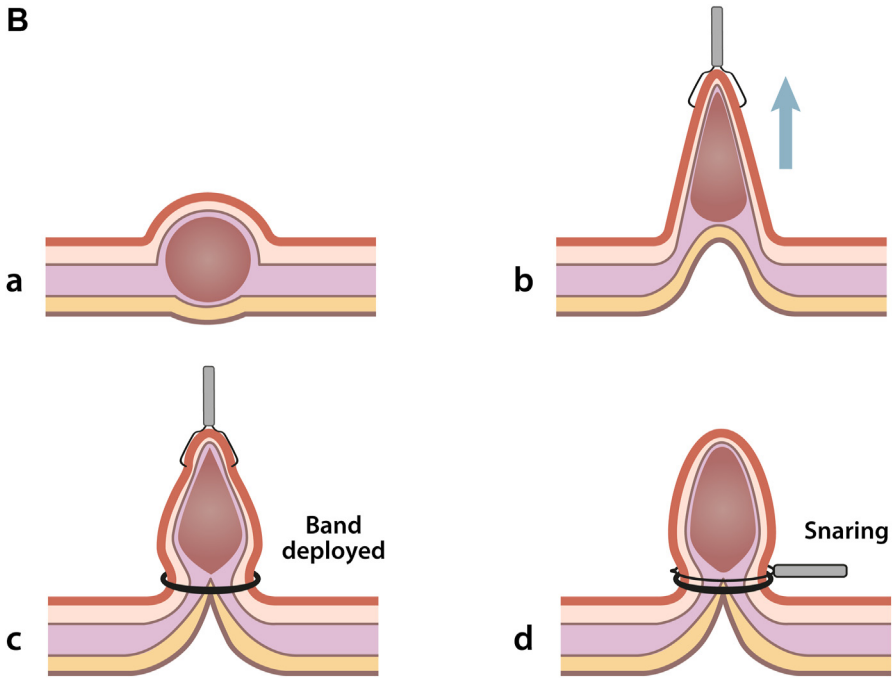

Fig. 10. (*continued*).

by closing the perforation using clips, loops, or endoscopic suturing devices. One consideration during the procedure is that the resected tumor may fall into the abdominal cavity; to prevent this, a grasping forceps can be inserted through a two-channel endoscope to hold the tumor tissue during the resection process. Hybrid methods such as laparoscopic-assisted EFTR (laparoscopic endoscopic cooperative surgery) are also being attempted. In these cases, the possibility of peritoneal infection and tumor cell dissemination due to artificial perforation can be a concern.[14]

2. Nonexposed EFTR (pure EFTR)

This is a surgical method where the tumor is resected without exposing the gastric space to the abdominal cavity. To achieve this, a plication process is included to grasp the folds of the GI wall surrounding the tumor before resection. After the tumor is removed, the resection site must be sutured using an endoscopic suturing device. Theoretically, nonexposed EFTR has many advantages; however, when using a flexible endoscope, there is a limitation to the size of the tumor that can be resected. Moreover, currently, there are no commercially available devices specifically designed for this technique in GI tumors.

The nonexposed EFTR technique involves the creation of a "double-layer" or "pseudo-cavity" to avoid exposing the resected area to the GI lumen. A solution is injected into the submucosal layer to lift the tumor away from the deeper layers, and then a circumferential mucosal incision is made around the tumor. Afterward, the seromuscular layer is incised, completing the full-thickness resection. The defect is closed using endoscopic sutures, clips, or other specialized devices without ever exposing the resected area to the GI lumen.

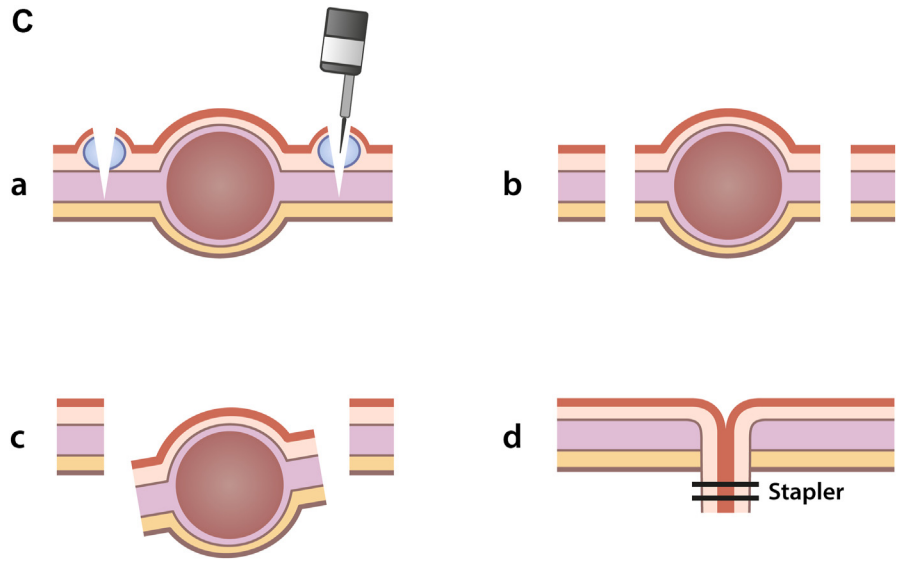

Fig. 10. (*continued*).

EFTR is a promising technique for the management of early-stage GI luminal cancers, providing a minimally invasive alternative to traditional surgery. However, patient selection and endoscopic expertise are crucial factors in determining the success of the procedure.

Submucosal Tunneling Endoscopic Resection/Endoscopic Submucosal Tunneling Dissection

STER was initially developed to resect SETs in the esophagus and gastroesophageal junction.[15] Subsequently, the technique was attempted for tumors in other parts of the GI tract, such as the rectum.[16] Compared with other ER techniques, the advantages of STER include preserving the mucosa, accelerating wound healing, and reducing the risk of infection. Several studies have already demonstrated the safety and efficacy of STER in the treatment of gastric submucosal tumors.[17]

However, there are limitations when using STER in stomach, such as difficulty in accessing lesions in the upper and lower parts of the stomach, and the challenge of removing tumors larger than 4 cm through the mouth. Recently, there have been reports of cases where the STER/endoscopic submucosal tunnel dissection method was used to remove lesions such as EGC and other mucosa cancers when fibrosis was severe or the deep margin was uncertain. In these cases, performing a sufficiently deep dissection during the procedure can enable *en bloc* resection of lesions that may be incompletely resected using the conventional ESD method.[18] The STER procedure for stomach tumors offers several advantages, including minimal invasiveness, preservation of the mucosal layer, and reduced risk of complications (**Fig. 11**).

CHARACTERISTICS OF ENDOSCOPIC RESECTION PROCEDURES BY ORGAN

Esophagus

The esophageal procedure can be carried out following the sequence of the EMR or ESD methods mentioned above. In the case of ESD, the procedure progresses in the order of marking, submucosal injection, circumferential incision, and dissection.

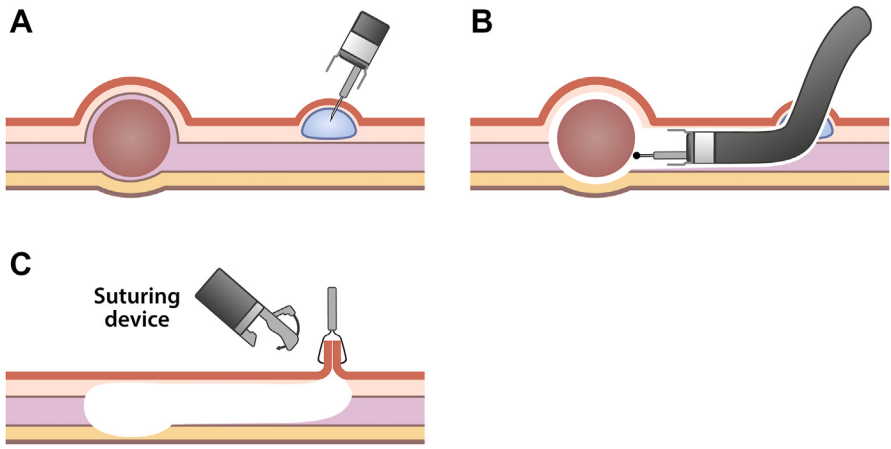

Fig. 11. Submucosal tunneling endoscopic resection (STER). (*A*) Marking and submucosal injection. (*B*) Mucosal incision and tunnel creation. (*C*) Tumor dissection and closure of mucosal incision.

For the esophagus, the esophageal wall is thin, and postoperative stricture may occur, so the procedure should be carried out considering these factors.

The esophagus, a tubular structure, is known to have a high incidence of stricture after ulcer healing in more than 75% of cases with ESD-induced ulcers. One way to prevent stricture is to mark and perform a circumferential incision as close as possible to the lesion. Because squamous cell carcinoma (SCC) esophageal lesions can be clearly observed with Lugol's solution or image-enhancing endoscopy/electronic chromoendoscopy, marking 5 mm outside the lesion and making a circular incision 5 mm outside the marking can bring both sides of the lesion very close, so the range of marking and circumferential incision should be determined with this in mind. If a postoperative stricture is expected, steroid injections can be given during or after the procedure, and/or oral steroids can be prescribed. If a stricture occurs despite these measures, it can be treated with endoscopic balloon dilation, preventive temporary stent insertion, or endoscopic incision (stricturoplasty).

The JGES guidelines reported that the stricture rate when using post-ER stricture prevention strategies was 76% in 45 patients receiving steroid injection therapy, 55% in 44 patients receiving oral steroid therapy, and 71% in 14 patients receiving both steroid injection and oral steroid therapy.[9]

Stomach

For beginners performing ESD for the first time, it is usually recommended to remove small tumors located in the anterior wall of the antrum. Depending on the location of the lesion within the stomach, there are various considerations when performing ESD (Fig. 12).

1. Cardia and upper body: The cardia can be a challenging location for beginners, as it may be difficult for the endoscope tip (lens) to get close to the lesion. In addition, the cardia and upper body have a rich vascular supply and thinner gastric walls, making bleeding and perforation more likely, which makes ESD traditionally more difficult. Careful dissection is essential in the cardia and pyloric region, as the gastric wall is concave and may be challenging to operate on. Because it is

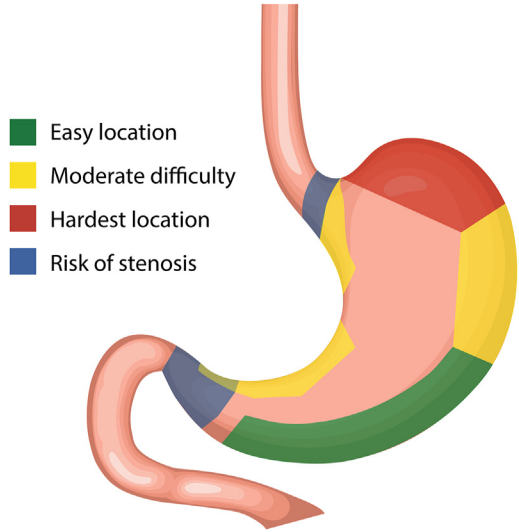

Fig. 12. Difficulty of performing endoscopic submucosal dissection (ESD) by location in the stomach.

difficult to observe the lesion directly, it is important to consider the direction of blood flow during dissection and to keep the lesion as close to the operator as possible in an inverted state. The amount of submucosal injection should be adjusted as needed, as bleeding can occur even with the injection alone. In addition to these location-specific considerations, using both the up-down and left-right levers of the endoscope simultaneously can help access the lesion more effectively.

2. Body: The body presents a higher degree of difficulty for ESD due to the anatomic features, such as abundant blood vessels and fibers, and the difficulty of maneuvering the endoscope. Proper dissection depth and sequence are crucial for successful ESD, and CO_2 insufflation and suctioning should be adjusted during the inverted state to avoid excessive flattening of the lesion and making it difficult to cut and dissect.

   The medial longitudinal oblique muscle in the stomach, along with the transverse vasoganglion, forms a fascia-like layer with a network of large blood vessels in the submucosal layer. This structure can cause significant bleeding and difficulty during ESD procedures in the anterior, posterior walls, and the greater curvature of the gastric body. To minimize bleeding and facilitate dissection, it is advised to maintain a dissection depth in the deep submucosal layer, which has fewer fibers and blood vessels. During dissection, thick perforating vessels should be carefully precoagulated using coagulation forceps.

3. Pyloric region: The pyloric region can be particularly challenging due to the proximity of the duodenal bulb. Special attention should be paid to the lesion's location and the submucosal injection to minimize the lesion from bending backward during cutting. Following an ESD procedure in the pylorus area, there is a risk of developing stenosis. Pyloric stenosis can occur due to scarring or fibrosis of the mucosal layer after the resection and healing process. This constriction can lead to difficulty in the passage of food through the pylorus, causing obstructive symptoms such as

vomiting, abdominal pain, and weight loss. To minimize the risk of stenosis, endoscopists should ensure a proper technique during the ESD procedure, focusing on preserving the muscular layer and avoiding excessive tissue removal. In some cases, endoscopic balloon dilation or other interventions may be required to treat stenosis that develops post-ESD.

Colon

Colon ESD poses several challenges depending on the location of the lesion within the colon. Some of the challenges associated with colon ESD based on lesion location include.

1. Cecum: The cecum is a relatively difficult area for ESD due to its thin wall and the presence of the ileocecal valve. Care must be taken to avoid damaging the valve and the risk of perforation is higher in this area.
2. Ascending colon: The ascending colon has a thicker wall compared with other parts of the colon, which can make dissection more challenging. Moreover, the proximity to the hepatic flexure may limit the maneuverability of the endoscope.
3. Transverse colon: The transverse colon can be difficult to access due to its length and mobility. It may be challenging to maintain stable positioning of the endoscope during ESD, and the risk of looping may be higher.
4. Descending colon: The descending colon can be challenging due to its proximity to the splenic flexure, which may limit endoscope maneuverability. In addition, the narrow lumen may make it difficult to maintain adequate visualization during the procedure.
5. Sigmoid colon: The sigmoid colon is highly mobile and has a narrow lumen, which can make ESD more challenging. The risk of looping is higher in this area, and it may be difficult to maintain stable positioning of the endoscope during the procedure.
6. Rectum: The rectum has a thicker wall and a more rigid structure, which can make dissection more challenging. The rectum is easily accessible with a standard colonoscope or upper scope. The risk of perforation during rectal ESD is generally lower than in other parts of the colon due to the thicker wall. However, rectal lesions are more prone to submucosal fibrosis due to prior inflammation or interventions. Fibrosis can make it more difficult to create a proper submucosal cushion and can increase the risk of complications during ESD.

To overcome these challenges, endoscopists must be skilled in maneuvering the endoscope, have a thorough understanding of the colon anatomy, and be able to choose the appropriate ESD technique based on the lesion location. In addition, new overtubes have been developed specifically to assist in stabilization and retraction for colon ESD procedures.

MANAGEMENT FOR ADVERSE EVENTS OF ENDOSCOPIC RESECTION

ER complications such as perforation and bleeding during ER can occur not only in beginners but also in experienced practitioners. Therefore, it is crucial to become familiar with the management of possible complications in ESD. This is because, in addition to complete resection, patient safety should always be considered during the ESD process.

1. Bleeding

   Endoscopic treatment for bleeding is essential during the resection process, as the occurrence of bleeding can worsen visibility and make the procedure very difficult. Even a small amount of bleeding can accumulate from multiple points,

making it difficult to secure a clear view or perform delicate hemostasis due to bloody staining of the submucosal layer. Therefore, it is advisable to perform hemostasis with hemostatic devices as much as possible whenever bleeding occurs and then proceed to the next step.

During the procedure, it is good to perform preventive hemostasis on the visible blood vessels before cutting them. When encountering thinner blood vessels during submucosal dissection, coagulation of vessels can be performed using the ESD knife by applying coagulation current at a lower current density than used for dissection. This can be achieved by placing more of the surface area of the knife on the vessel or decreasing the power setting on the ESU. However, for thicker, pulsating blood vessels, it is important to use coagulation graspers, using a pure coagulation current, to perform safe preventive coagulation. Occasionally, large pulsatile bleeding may occur during the cutting and submucosal dissection process, which should also be treated with coagulation graspers. Coagulation graspers are effective because they mechanically stop the flow of blood in vessels (preventing a heat sink effect by active blood flow) and by lowering the current density to effectively coagulate the blood vessel. If the use of coagulation graspers fails, consider using a hemostatic clip. Hemostatic clips can physically obstruct the cutting plane during ESD, so it is better to consider them as a last resort for massive bleeding that cannot be stopped by other methods. Careful treatment of exposed blood vessels after dissection completion can help prevent delayed bleeding. However, excessive coagulation during hemostasis should be avoided, as it can increase the risk of delayed perforation by damaging the muscle layer. Delayed Bleeding can occur after the ESD procedure, typically within the first few days. It can often be managed with endoscopic hemostasis or supportive care, such as blood transfusion if necessary.

2. Perforation

To prevent perforation, it is important to secure an adequate submucosal fluid cushion and to only cut or dissect when the knife tip can be visualized. Perforation can occur when operating blindly with an electronic knife, when making long continuous incisions, or when using a tip-shaped knife such as a needle knife or dual knife and the cutting direction is mistakenly directed toward the deeper layers. When using a knife, it is necessary to adhere to the principle of cutting while directly observing the knife tip, and when using a non-insulated cutting knife, it is important to operate the knife in a direction away from the muscle layer to prevent perforation. Performing the procedure while observing the cutting surface being dissected allows for a relatively safe dissection.

If a perforation occurs, in most cases, recovery is possible with endoscopic closure and conservative treatment. If a perforation occurs, minimize insufflation of gas to avoid expanding the perforation site and apply a clip to close the defect. It is preferable to quickly add dissection around the perforation site to secure space so that dissection can continue after closure of the perforation. If the perforation site is difficult to close with a clip, it is recommended to suture using a suture device such as an overstitch/T-tag. This procedure must be performed while thoroughly monitoring for signs of tension pneumoperitoneum, as excessive leakage of gas into the abdominal cavity due to perforation can compress the diaphragm upward, leading to respiratory distress. If the patient exhibits decreased oxygen saturation, it is necessary to quickly decompress by inserting an 18-gauge angiocatheter or Veress needle into the abdomen to decompress the peritoneum. Because gas rises to the right side of the abdomen in the left lateral position,

puncturing the right 9 to 10 or 10 to 11 intercostal space and the intersection with the right midaxillary line can safely release the accumulated air above the liver. In the supine position, air can be released by puncturing the site where abdominal paracentesis is performed in the left lower abdomen.

3. Incomplete resection
   In some cases, ESD may not completely remove the lesion, leading to the possibility of residual or recurrent disease. Incomplete resection may be due to technical challenges, submucosal fibrosis, or a poorly delineated margin. If incomplete resection is identified during the procedure, additional dissection or a second resection attempt may be performed to ensure complete removal of the lesion. In some cases, close surveillance or additional treatment modalities, such as ablation or surgery, may be necessary.
4. Infection
   Infection is a rare but potential complication after ESD, which can manifest as fever, abdominal pain, and/or leukocytosis. Infection after ESD can be caused by factors such as perforation, contamination, poor wound healing, immunosuppression, and bacterial translocation. In some cases, prophylactic antibiotics may be administered to reduce the risk of infection. For example, in the case of ER procedure for dialysis patients, including those on hemodialysis and peritoneal dialysis, the use of prophylactic antibiotics may be recommended to reduce the risk of infection.
5. Stricture formation
   Strictures or stenosis may develop after ESD, particularly in cases where a large portion of the circumference of the GI tract (specially, esophagus, cardia, pylorus, ileocecal [IC] valve, anus, and so forth) is resected. Endoscopic balloon dilation or stent placement can be used to manage strictures.
6. Deep vein thrombosis (DVT) or pulmonary embolism (PE)
   Prolonged immobilization during or after the procedure may increase the risk of DVT or PE. Prophylactic anticoagulation and early mobilization may help reduce this risk in high-risk patients.

To minimize the risk of adverse events during ESD, it is crucial to ensure proper patient selection, have a well-trained and experienced endoscopist, and follow meticulous procedural techniques. Moreover, close postoperative monitoring and prompt management of complications are essential for a successful outcome.

CLINICAL MANAGEMENT AFTER ENDOSCOPIC RESECTION

Post-Endoscopic Submucosal Dissection Care for the Upper Gastrointestinal Tract

Following ESD for the esophagus, stomach, and duodenum, patients are recommended to fast for a certain amount of time to check for any potential complications before gradually introducing clear liquids and progressing to a soft diet as tolerated. Acid suppression therapy, such as proton-pump inhibitors (PPIs) or histamine H2-receptor antagonists, is essential for these areas. Stricture prevention measures, such as balloon dilation or steroid injection, may be needed for the esophagus, whereas prophylactic antibiotics can be considered for the stomach and duodenum when the risk of infection is high. Regular follow-up endoscopies are necessary to monitor for complications and recurrence.

Following gastric ESD, acid suppression therapy is essential for promoting the healing of artificial ulcers and preventing complications such as bleeding, stricture formation, and perforation. PPIs are the preferred choice for acid suppression therapy following ESD for esophageal and gastric lesions due to their superior efficacy in

promoting ulcer healing and preventing complications. However, H2 blockers may be considered in cases where PPIs are contraindicated or not tolerated.

The recommended usage of PPI varies depending on the individual patient and the extent of the procedure. A general guideline is as follows:

- Initiate PPI therapy immediately after ESD.
- Administer PPIs once or twice daily at standard or double the standard dose, depending on the severity of the lesion and the risk of complications.
- Continue PPI treatment for 4 to 8 weeks, depending on the ulcer size and the patient's response to therapy.

H pylori infection is a known risk factor for gastric cancer, and eradication of the bacteria is essential for preventing recurrence and improving long-term outcomes post-ESD. The treatment should be tailored to the individual patient, considering local antibiotic resistance patterns and the patient's prior exposure to antibiotics. A general approach is as follows.

- Test for *H pylori* infection before ESD or during the post-ESD follow-up period, using methods such as histology, rapid urease test, urea breath test, or stool antigen test.
- If *H pylori* infection is confirmed, initiate eradication therapy. The choice of regimen depends on local antibiotic resistance patterns and patient factors. A common first-line treatment is a 10 to 14 day course of triple therapy, including a PPI, clarithromycin, and amoxicillin or metronidazole.
- After completing eradication therapy, confirm the success of treatment with a noninvasive test, such as the urea breath test or stool antigen test, typically 4 to 6 weeks after therapy.

Post-Endoscopic Submucosal Dissection Care for the Colon

After ESD for the colon, patients should fast for a certain amount time, and then gradually introduce clear liquids and transition to a low-residue diet once tolerated. Prophylactic antibiotics can be considered in cases with a high risk of infection.

ENDOSCOPIC RESECTION OUTCOMES

Esophagus

ER has become a standard treatment for early esophageal cancer, including early-stage squamous cell carcinoma and Barrett's esophagus-associated neoplasia, with ESD providing better outcomes for larger lesions and reduced recurrence rates compared with EMR.

1. Efficacy: ESD has demonstrated *en bloc* resection rates of 95.1% to 100% and curative resection rates of 88% to 89.4% for early esophageal cancer.[19–21]
2. Safety: The overall complication rate for esophageal ESD ranges between 5% and 15%, with bleeding (2.1%), perforation (5.0%), and stricture formation (11.6%) being the most common adverse events.[20,21]
3. Long-term outcomes: Studies have reported 5-year overall survival rates of 86.4% and disease-specific survival rates of 97.5% for early esophageal cancer treated with ESD.[22]

Stomach

ER has emerged as a standard treatment for EGC without lymph node metastasis, providing comparable survival rates and reduced morbidity compared with surgery.

ESD has been reported to achieve higher *en bloc* and curative resection rates than EMR, especially for larger lesions.[23]

1. Efficacy: ESD has demonstrated *en bloc* resection rates of 85% to 97% and curative resection rates of 71% to 82%.[24]
2. Safety: The overall complication rate for ESD/EMR ranges between 5% and 10%, with bleeding(9.3%/8.6%, including delayed bleeding) and perforation(4%/0.8%) being the most common adverse events.[23]
3. Long-term outcomes: Studies have reported 5-year overall survival rates of 96% and disease-specific survival rates of 99.4% for EGC treated with ESD.[25]

Colon

ER, particularly ESD, has gained recognition as a viable treatment option for early-stage colorectal cancer and large premalignant lesions, offering high curative resection rates and lower recurrence rates compared to EMR.[26]

1. Efficacy: ESD has achieved *en bloc* resection rates of 65% to 100% and R0 resection rates of 53% to 100% for early colorectal cancer and large adenomas.[27]
2. Safety: The complication rate for colorectal ESD varies, with the most common adverse events being bleeding (occurring in approximately 2.4%–5% of cases), perforation (found in around 4%–8% of cases), and recurrence rate (ranging between 1% and 3%).[28]
3. Long-term outcomes: Research has shown that early colorectal cancer treated with ESD has a 5-year overall survival rate of 92.3% and a disease-free survival rate of 99.6%.[29]

ER techniques, such as EMR and ESD, have shown promising results in treating early-stage stomach, colon, and esophageal cancers. Although outcomes may vary slightly between countries and institutions, these techniques continue to demonstrate significant potential. Furthermore, as endoscopic techniques and skills continue to advance, recent studies and analyses are revealing even better outcomes in the field, showcasing the ongoing progress in this area. High *en bloc* and curative resection rates, manageable complication rates, and favorable long-term survival rates showcase the potential of these minimally invasive approaches in the management of GI cancers. As ER techniques continue to advance and become more refined, they are expected to play an increasingly important role in the management of these malignancies. Ongoing research and development of novel endoscopic tools, as well as improvements in training and standardization of ER procedures, will be crucial in further optimizing patient outcomes and expanding the indications for ER in the treatment of GI malignancies.

THE FUTURE OF ENDOSCOPIC RESECTION FOR EARLY LUMINAL CANCER

As endoscopy continues to evolve, technological advancements in robotic assistance and innovative endoscopic tools are being developed, holding the potential to revolutionize ER by enhancing the accuracy, safety, and efficiency of these procedures, ultimately improving patient outcomes and expanding the range of treatable lesions.

Robotic assistance in ER can potentially improve the precision and safety of procedures by offering enhanced dexterity, improved visualization, and increased stability. For instance, the robotic-assisted ESD system enables the precise resection of lesions located in challenging anatomic sites, such as the colon or the esophagus, while minimizing the risk of complications. This technology can also reduce the physical strain on

endoscopists, allowing for longer and more complex procedures. Innovative endoscopic tools, such as electrocautery knives, submucosal injection solutions, and endoscopic suturing, and closure devices, can also significantly impact the efficacy and safety of ER. For instance, novel electrocautery knives can improve cutting efficiency and reduce thermal damage to surrounding tissues, whereas advanced endoscopic suturing and closure devices can promote faster healing and minimize the risk of postprocedure complications. Moreover, the development of artificial intelligence (AI) and machine learning (ML) algorithms holds promise in enhancing the accuracy and efficiency of endoscopic procedures. For instance, AI-aided detection and characterization of colorectal polyps have shown high accuracy and could potentially reduce the need for unnecessary biopsies or surgeries.

In conclusion, the continuous development of technology in endoscopy offers the potential to revolutionize ER by improving accuracy, safety, and efficiency, leading to better patient outcomes and expanding the range of treatable lesions.

SUMMARY

"The Endoscopic Oncologist" refers to a medical professional who specializes in the ER of early luminal cancer. ER is a minimally invasive technique that involves the removal of early-stage tumors from the lining of the digestive tract.

ER is an effective and safe treatment option for early luminal cancer, which is cancer that is confined to the inner lining of the digestive tract. ER procedures can be performed using various techniques such as EMR or ESD. These techniques enable the removal of cancerous tissues while preserving the underlying layers of the digestive tract, thereby reducing the risk of complications such as bleeding, perforation, and stenosis.

The endoscopic oncologist is a highly skilled and specialized medical professional who is trained in the use of advanced endoscopic tools and techniques for the resection of early luminal cancer. The endoscopic oncologist works closely with a multidisciplinary team of health care professionals to ensure that patients receive comprehensive and personalized care.

Overall, the endoscopic oncologist plays a crucial role in the management of early luminal cancer, providing patients with a minimally invasive treatment option that offers excellent outcomes and a faster recovery time compared with traditional surgery.

DISCLOSURE

J.H. Hwang is a consultant for Boston Scientific, Olympus, Medtronic, FujiFILM, Lumendi, Neptune, and Micro-Tech. H.S. Choi has no disclosures.

CLINICS CARE POINTS

- Prior to performing endoscopic resection, the lesion should be evaluated carefully to confirm that the lesion is amenable to endoscopic resection. If there is any concern for advanced pathology, the case should be presented in a multidiciplinary conference prior to performing endoscopic resection.
- Patients undergoing endoscopic resection should be followed closely to monitor for any delayed complications such a bleeding or perforation.
- Following endoscopic resection, surveillance should be performed based on pathologic findings and established guidelines.

REFERENCES

1. Suzuki H, Oda I, Abe S, et al. High rate of 5-year survival among patients with early gastric cancer undergoing curative endoscopic submucosal dissection. Gastric Cancer 2016;19(1):198–205.
2. Moghimi-Dehkordi B, Safaee A. An overview of colorectal cancer survival rates and prognosis in Asia. World J Gastrointest Oncol 2012;4(4):71–5.
3. Gelberg HB. Comparative anatomy, physiology, and mechanisms of disease production of the esophagus, stomach, and small intestine. Toxicol Pathol 2014; 42(1):54–66.
4. Soybel DI. Anatomy and physiology of the stomach. Surg Clin North Am 2005; 85(5):875–94, v.
5. Sadalla S, Lisotti A, Fuccio L, et al. Colonoscopy-related colonic ischemia. World J Gastroenterol 2021;27(42):7299–310.
6. Torre LA, Siegel RL, Ward EM, et al. Global Cancer Incidence and Mortality Rates and Trends–An Update. Cancer Epidemiol Biomarkers Prev 2016;25(1):16–27.
7. Endoscopic Classification Review G. Update on the Paris classification of superficial neoplastic lesions in the digestive tract. Endoscopy 2005;37(6):570–8.
8. Draganov PV, Wang AY, Othman MO, et al. AGA Institute Clinical Practice Update: Endoscopic Submucosal Dissection in the United States. Clin Gastroenterol Hepatol 2019;17(1):16–25 e1.
9. Ishihara R, Arima M, Iizuka T, et al. Endoscopic submucosal dissection/endoscopic mucosal resection guidelines for esophageal cancer. Dig Endosc 2020; 32(4):452–93.
10. Gotoda T, Yanagisawa A, Sasako M, et al. Incidence of lymph node metastasis from early gastric cancer: estimation with a large number of cases at two large centers. Gastric Cancer 2000;3(4):219–25.
11. Shaukat A, Kaltenbach T, Dominitz JA, et al. Endoscopic Recognition and Management Strategies for Malignant Colorectal Polyps: Recommendations of the US Multi-Society Task Force on Colorectal Cancer. Gastrointest Endosc 2020; 92(5):997–1015 e1.
12. Committee AT, Maple JT, Abu Dayyeh BK, et al. Endoscopic submucosal dissection. Gastrointest Endosc 2015;81(6):1311–25.
13. Choi HS, Chun HJ. Accessory Devices Frequently Used for Endoscopic Submucosal Dissection. Clin Endosc 2017;50(3):224–33.
14. Maehata T, Goto O, Takeuchi H, et al. Cutting edge of endoscopic full-thickness resection for gastric tumor. World J Gastrointest Endosc 2015;7(16):1208–15.
15. Standards of Practice C, Faulx AL, Kothari S, et al. The role of endoscopy in subepithelial lesions of the GI tract. Gastrointest Endosc 2017;85(6):1117–32.
16. Hu JW, Zhang C, Chen T, et al. Submucosal tunneling endoscopic resection for the treatment of rectal submucosal tumors originating from the muscular propria layer. J Cancer Res Ther 2014;10(Suppl):281–6.
17. Cao B, Lu J, Tan Y, et al. Efficacy and safety of submucosal tunneling endoscopic resection for gastric submucosal tumors: a systematic review and meta-analysis. Rev Esp Enferm Dig 2021;113(1):52–9.
18. Choi HS, Chun HJ, Seo MH, et al. Endoscopic submucosal tunnel dissection salvage technique for ulcerative early gastric cancer. World J Gastroenterol 2014;20(27):9210–4.
19. Tsujii Y, Nishida T, Nishiyama O, et al. Clinical outcomes of endoscopic submucosal dissection for superficial esophageal neoplasms: a multicenter retrospective cohort study. Endoscopy 2015;47(9):775–83.

20. Ono S, Fujishiro M, Niimi K, et al. Long-term outcomes of endoscopic submucosal dissection for superficial esophageal squamous cell neoplasms. Gastrointest Endosc 2009;70(5):860–6.
21. Kim JS, Kim BW, Shin IS. Efficacy and safety of endoscopic submucosal dissection for superficial squamous esophageal neoplasia: a meta-analysis. Dig Dis Sci 2014;59(8):1862–9.
22. Yeh JH, Huang RY, Lee CT, et al. Long-term outcomes of endoscopic submucosal dissection and comparison to surgery for superficial esophageal squamous cancer: a systematic review and meta-analysis. Therap Adv Gastroenterol 2020;13. 1756284820964316.
23. Lian J, Chen S, Zhang Y, et al. A meta-analysis of endoscopic submucosal dissection and EMR for early gastric cancer. Gastrointest Endosc 2012;76(4): 763–70.
24. Daoud DC, Suter N, Durand M, et al. Comparing outcomes for endoscopic submucosal dissection between Eastern and Western countries: A systematic review and meta-analysis. World J Gastroenterol 2018;24(23):2518–36.
25. Abdelfatah MM, Barakat M, Ahmad D, et al. Long-term outcomes of endoscopic submucosal dissection versus surgery in early gastric cancer: a systematic review and meta-analysis. Eur J Gastroenterol Hepatol 2019;31(4):418–24.
26. Fujiya M, Tanaka K, Dokoshi T, et al. Efficacy and adverse events of EMR and endoscopic submucosal dissection for the treatment of colon neoplasms: a meta-analysis of studies comparing EMR and endoscopic submucosal dissection. Gastrointest Endosc 2015;81(3):583–95.
27. Repici A, Hassan C, De Paula Pessoa D, et al. Efficacy and safety of endoscopic submucosal dissection for colorectal neoplasia: a systematic review. Endoscopy 2012;44(2):137–50.
28. Lim XC, Nistala KRY, Ng CH, et al. Endoscopic submucosal dissection vs endoscopic mucosal resection for colorectal polyps: A meta-analysis and meta-regression with single arm analysis. World J Gastroenterol 2021;27(25):3925–39.
29. Boda K, Oka S, Tanaka S, et al. Clinical outcomes of endoscopic submucosal dissection for colorectal tumors: a large multicenter retrospective study from the Hiroshima GI Endoscopy Research Group. Gastrointest Endosc 2018;87(3): 714–22.