

The Journey from Endoscopic Submucosal Dissection to Third Space Endoscopy



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KEYWORDS

• Submucosal endoscopy • Third space endoscopy • POEM

KEY POINTS

- Endoscopic submucosal dissection pushed forward development of peroral endoscopic myotomy (POEM).
- POEM opened the door of submucosal endoscopy.
- Treatment with submucosal endoscopy covers various muscle layer-related diseases.

BACKGROUND

Until the development of endoscopic submucosal dissection (ESD),^{1–4} therapeutic endoscopy of the gastrointestinal tract was referred to as endoscopic mucosal resection (EMR). EMR was an extension of polypectomy, in which a snare was used to strangle and remove mucosal lesions.⁵ There are several methods, including direct strangulation of the mucosa with a snare and EMR using a cap.^{6,7} EMR using a ligature device has been established as a simple and safe method of mucosal resection.⁸ However, EMR using a snare device is limited to resecting a 1 to 2 cm specimen in a single strangulation. In practice, resection of large mucosal lesions is ultimately limited to piecemeal resection. Fragmented resection has the potential risk of leaving a small amount of epithelial component at the resection margin; this was thought to lead to a risk of recurrence if cancer developed. Therefore, pioneers attempted to resect extensive mucosal lesions in one piece.⁹

Endoscopic Submucosal Dissection

In ESD, the mucosa is incised circumferentially, and the submucosa is detached. Although ESD seems simple at first glance, it is actually a technically difficult and

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time-consuming procedure. Reasons for the technical difficulty of ESD include the complex 3-dimensional structure and soft walls of the gastrointestinal tract, respiratory movement, heartbeat, peristalsis, and effect of insufflation and suction of the endoscope. In addition, the digestive endoscope has only 1 or 2 channels for instruments compared with laparoscopy that allows 4 to 5 trocars to be used. In the early days of ESD due to these constrained platforms, the following measures were naturally developed.

Knives

Initially, the only knife that existed was a simple needle scalpel. However, pushing the needle scalpel forward into the gastrointestinal wall often resulted in full-layer puncture. Therefore, the insulated tip knife (Olympus Medical, PA, USA) was designed, in which an insulator was attached to the tip of the needle scalpel to prevent puncture.¹ Many knives have since appeared, but the Dual Knife (Olympus Medical, PA, USA) is probably the most widely used today. It is an excellent knife because the outer sheath of the knife applies tension to the tissue to be incised.

Transparent hood

A transparent hood is an essential tool for ESD because it maintains a certain distance between the scope lens and the mucosa to prevent contact. Tapered hoods such as ST hoods (Fujifilm, Tokyo, Japan), short ST hoods (Fujifilm, Tokyo, Japan), and space adjusters (soft and flexible hood, Top) have been developed.^{2,7,10}

Carbon dioxide insufflation system

Insufflation of air was originally used in gastrointestinal endoscopy. A carbon dioxide (CO₂) insufflation system was developed to relieve discomfort caused by large amounts of air accumulation after colonoscopy. This CO₂ insufflation system can prevent gas retention in the small intestine even after prolonged ESD. It is also critical in preventing disruptive pressures in the case of perforation or breach of the muscle layer and the resulting pneumoperitoneum.

Electrosurgical devices

Originally, hot biopsy forceps were used for hemostasis and now have been switched to coagulation forceps. The establishment of a soft coagulation mode on the high-frequency power supply enabled effective control of bleeding. Subsequently, the introduction of the spray coagulation mode effectively contributed to tissue dissection with adequate hemostasis.

Development of the clip

Clips were originally developed for hemostasis of peptic ulcers.¹¹ Today, the primary role of clips has shifted to closure of tissue defects. Clips are often used with end loops to close large defects. To make it simple, several methods including clip closure with a line or “loop (thin slip knot tying to fix clips on the edge of defect)” method were developed.^{12,13} The over-the-scope clip (OTSC, Ovesco Endoscopic AG, Tübingen, Germany) was also used for tight closure of full-layer defect.¹⁴

Evolution of local injection

Initially, epinephrine was added to saline to reduce a risk of bleeding. However, the use of epinephrine has declined in order to avoid vasoconstriction of cardiac disease cases. On the other hand, the use of high-viscosity solution such as hyaluronic acid has made it possible to maintain the mucosal layer elevation for a longer period of time, which helps prevent muscle injury, especially in duodenal and colorectal

ESD.^{2,15} Later, with the advent of knives with a water delivery function, the local injection solution again returned to simple saline solution.¹⁶

Traction method

The traction method was very effective in reducing ESD procedure time.¹⁷ By retracting the specimen, the submucosal layer can be opened widely. Traction particularly makes the procedure easier when the specimen becomes floppy after mobilization of most of the lesion.

Control of pneumoperitoneum

Pneumoperitoneum (or capnoperitoneum) may happen during submucosal endoscopy. Abdominal decompression with a needle is a simple, effective way to control the high pressure caused by pneumoperitoneum.

Development to Submucosal Endoscopy (Third Space Endoscopy)

Submucosal endoscopy and third space endoscopy can be considered synonyms.¹⁸ Submucosal endoscopy indicates the layers to be incised, whereas third space endoscopy is understood conceptually: the first space is the lumen of the digestive tract, second space is the abdominal cavity or thoracic cavity, and the third space is the artificially created submucosal space.

Development of peroral endoscopic myotomy

The natural orifice transluminal endoscopic surgery (NOTES) concept, as proposed by Dr A. Kalloo, attracted a great deal of attention as a minimally invasive procedure that would bridge the gap between gastrointestinal endoscopy and surgery.¹⁹ As background for the development of POEM, the mucosal flap safety valve concept by Sumiyama K and colleagues^{20,21} and the animal experiments of myotomy by Pasricha and colleagues were noted. In 2008, the first clinical case of POEM was performed.²² At our institution alone, we have treated more than 2500 cases in last 14 years. Now it became the standard care of achalasia in place of laparoscopic Heller-Dor surgery.²³

Peroral endoscopic tumor (submucosal tunnelling endoscopic reaction)

During POEM, we sometimes encountered small leiomyomas (originating from the muscularis propria). Removal of small leiomyomas through the submucosal tunnel was technically feasible,^{24,25} and this has led to development of the submucosal tunnelling endoscopic reaction procedure where a submucosal tunnel is specifically created in order to remove submucosal tumors less than 4 cm.²⁶

Diverticulum peroral endoscopic myotomy

Epiphrenic diverticulum sometimes appears in patients with achalasia. Originally, full-thickness septotomy (including the mucosa and the muscle layer) was performed to improve the symptom of dysphagia caused by the diverticulum. Diverticulum peroral endoscopic myotomy is when the POEM technique is used to perform muscular septotomy of the epiphrenic diverticulum.²⁷

Gastric peroral endoscopic myotomy

A pyloric sphincterotomy via the POEM procedure can be performed for gastroparesis.²⁸ It is a safe and effective procedure in expert hands.²⁹

From peroral endoscopic myotomy for Zenker diverticulum to peroral endoscopic septotomy

POEM for Zenker diverticulum has also been performed, and we now prefer to perform peroral endoscopic septotomy (POES), where the incision is performed along the edge of the septum.^{30,31}

Peroral endoscopic fundoplication

Post-POEM gastroesophageal reflux disease (GERD) was discussed from the beginning of the development of POEM. It has been shown to be preventable by adjusting the length of the gastric myotomy and preserving the collar-sling muscle.^{32,33} In order to reduce the risk of potential reflux disease, POEM with endoscopic fundoplication in a single session was successfully carried out.³⁴ Anti-reflux effect continues one year after POEM + F.³⁵ POEM + F is theoretically appropriate but it takes a longer procedure time. Now we perform POEF alone as a standard procedure. Just in case of refractory reflux POEF is independently performed.³⁶ In POEF, the transoral endoscope enters the abdominal cavity through the submucosal tunnel of the esophagus, thus providing a pure NOTES procedure.¹⁹

From Endoscopic Submucosal Dissection to Deeper Layer Dissection to Pure Natural Orifice Transluminal Endoscopic Surgery

From the early experience of perforation during ESD, it has been shown that even if perforation occurs in a clean gastrointestinal tract, there is no major problem if the gastrointestinal wall is closed tightly by clipping or other means. Therefore, we have developed the endoscopic muscle layer dissection, endoscopic subserosal dissection, endoscopic full-thickness resection, and pure NOTES.^{37–39} Pure NOTES is represented by POEF.³⁶

SUMMARY

With the advent of ESD, therapeutic endoscopy has greatly expanded from treatment using a snare to flexible endoscopic surgery and allowed endoscopists to potentially parallel laparoscopic surgery.

CLINICS CARE POINTS

- Check your endoscopy processor air insufflation is off even when CO2 insufflator is on.

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