Endoscopic Submucosal Dissection for Colorectal Tumors

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Abstract
Endoscopic submucosal dissection (ESD) is a resection technique for superficial neoplastic lesions of the gastrointestinal tract without the use of snaring. It was developed for en bloc resection of large superficial mucosal tumors and initially used in the stomach, then later in the esophagus and colon and rectum as well. ESD provides a reliable en bloc resection of the lesions with a high complete resection rate and a low recurrence rate. However, it can be curative only when the tumors are localized without metastases. Staging of the tumor with precise endoscopic examination is important to select tumors appropriate for ESD. Moreover, a complete curative resection should be confirmed by detailed pathological examination of the resected tissue. The techniques of ESD for colorectal tumors are described in detail here.

Basic Principles

Endoscopic resection is less invasive than surgical resection. However, it has limited applications. Lymph node dissection cannot be performed with the currently available endoscopic techniques, including ESD. Therefore, endoscopic therapy for gastrointestinal neoplasms can be curative only when the tumors are localized and without metastases.
The risk of lymph node metastases strongly correlates with the depth of invasion of the tumor, the histopathologic type of the lesion and the presence of lymphatic or vascular involvement. Therefore, precise examination of the tumor for staging with pit pattern diagnosis using a magnifying endoscope is important to select tumors appropriate for endoscopic resection. Moreover, detailed pathological examination of the resected tissue is also important because it provides precise information regarding whether the neoplasms have been completely resected, allowing appropriate decisions regarding the need for additional surgery. Endoscopic resection can be considered curative by confirmation of negative resection margins, differentiated histopathologic type, depth of submucosal invasion to be <1,000 μm and no lymphatic or vascular involvement. For the accurate histopathologic assessment of the resected specimen, en bloc resection of the entire lesion is required.

ESD is superior to EMR for a more reliable en bloc resection of a targeted area of the mucosa. It also provides a higher complete resection rate with a lower recurrence rate compared with piecemeal EMR [7].

The drawbacks of ESD include the fact that it is a time-consuming procedure, has greater technical demands, and a higher rate of perforation.

**Technique**

ESD for colorectal tumors is considered more technically demanding than ESD in the stomach for a variety of reasons including: (1) the colonic wall is thinner and softer than the gastric wall; (2) endoscopic control is difficult in some parts of the colon because of paradoxical movement; (3) there are limitations in the retroflex approach due to the narrow lumen of the colon, and tumors can be located on or behind a prominent fold of the colon, and (4) moreover, perforation of the colon has a higher risk of diffuse peritonitis necessitating surgical repair compared with perforation of the stomach.

In order to overcome the above-mentioned difficulties, several devices have been applied to ESD in the colon and rectum. For ESD in the colon, it is important to use a dissecting technique that allows direct visualization of the submucosal tissue, and to use a long-lasting injecting fluid [8].

**Determination of TumorExtent**

Mucosal neoplasms in the colon and rectum typically have clear margins which become even clearer after submucosal injection. Therefore, placing marks around the tumor is not necessary in most cases. Chromoendoscopy with indigo carmine spray is useful to enhance the borders of the tumors. New imaging techniques, such as narrow band imaging and flexible spectral imaging color enhancement, are also useful to determine the borders of these tumors.

**Submucosal Injection**

Creation and maintenance of sufficient mucosal elevation with submucosal injection is essential for safe mucosal incisions and submucosal dissection. As long as thickening of the submucosal layer is maintained throughout the ESD procedure, one of the difficulties associated with ESD in the colon, namely the thin colonic wall, can be overcome. For these purposes, 0.4% sodium hyaluronate solution (MucoUp; Seikagaku Corp, Tokyo, Japan) is the best injection fluid for ESD. Submucosal injection of sodium hyaluronate creates a long-lasting mucosal protrusion that usually lasts more than 1 h [9–11].
Strategy and Technique for Mucosal Incisions and Submucosal Dissection

For successful ESD, it is mandatory to have a good strategy considering the angle of approach to the lesion, and the direction of gravity in relation to the location of the lesion. The position of the patient should be selected to locate the lesion at the top of the colonic lumen with regard to gravity. If the lesion is located at the top, the dissected part of the lesion is naturally pulled down by gravity, which allows sufficient opening of the incised wound with good visualization of the submucosal tissue during the procedure. In cases of unfavorable events such as bleeding and perforation, this positioning is beneficial to avoid or minimize further complications. In the case of bleeding, blood flows down from the bleeding point by gravity. If bleeding occurs at the bottom of the lumen with regard to gravity, the bleeding point is immediately covered by a pool of blood which hampers appropriate hemostatic procedures. Conversely, if the bleeding point is at the top of the lumen, hemostasis can be performed reliably with accurate identification of the bleeding point because blood flows away from the bleeding point by gravity. Even in cases of perforation, if the perforation occurs at the top of the lumen with regard to gravity, identification and closing of the perforation is easier, maintaining a good view of the site of perforation. Only air, not infected intestinal fluid, will flow out from the lumen to the abdominal cavity before closing the perforation, which is important to prevent diffuse peritonitis.

It is also important to maintain sufficient elevation of the mucosa from the muscle layer throughout the ESD procedure because the wall of the colon is so thin that it becomes very difficult to dissect if submucosal thickening disappears. The operator should elevate the mucosal area to be dissected by injecting a sufficient amount of sodium hyaluronate into the submucosa. The mucosal incision is made only in the area to be dissected and then dissection of the submucosa from the incised part is promptly started. If the operator performs a circumferential mucosal incision and postpones submucosal dissection, even viscous sodium hyaluronate will eventually drain from the incised wound, resulting in loss of submucosal thickening, which makes completion of the procedure difficult.

The mucosal incision is made with a short FlushKnife (1.5 mm; DK2618JN15; Fujifilm Corp., Tokyo, Japan) after sufficient protrusion of the mucosa is obtained. Only the needle part should be used for the incision, keeping the tip of the sheath touching the surface of the mucosa without pushing the sheath into the submucosal layer. The Endo Cut mode is used for the mucosal incision.

Submucosal dissection can be performed safely with a FlushKnife as long as adequate thickening of the submucosal layer, as a safety margin away from the muscle layer, is maintained. The dissection should be done parallel to the muscular layer, by sliding the knife from the center of the tumor toward the mucosal incision on the side, while hooking submucosal fibers with the knife.

Recently, we have often used a tunneling method to dissect the submucosal layer. With this method, after mucosal incision and submucosal dissection at the proximal edge of the colonic tumor, the mucosal incision and submucosal dissection are then performed from the distal edge of the tumor. Submucosal dissection is continued to make a tunnel in the submucosal layer by inserting the tip of the endoscope with a transparent hood under the mucosal tumor. The tunneling dissection is continued, to reach the mucosal incision at the proximal edge. After penetration of the tunnel from the distal edge to the proximal edge of the tumor, the tunnel is widened on both sides laterally. Finally, the mucosa on both sides of the tumor is incised laterally and then dissection of the submucosa on both sides is also performed to complete the resection (fig. 1). By making a submucosal tunnel, the endoscope tip is stabilized allowing precise control of the knife for dissection. It also opens the dissected wound with the hood at the endoscope tip providing...
a good safety margin for further dissection by stretching the submucosal tissue. Adjusting the approach angle of the knife to be tangential to the wall also is easy with this method because an adjusting force with the endoscope tip can be applied in either direction by pushing the mucosa up or pushing the muscle wall down with the tip of the hood. The tunneling method is particularly useful for large lesions, lesions with fibrosis, and lesions located on a curved wall.

**Endoscopes**

ESD procedures require precise control of the endoscope tip. Therefore, a thin endoscope is preferred over a robust therapeutic colonoscope. For this reason, some operators select a single-
channel upper endoscope for ESD in the distal colon or rectum. We use a specifically designed colonoscope (EC-450RD5; Fujifilm Corp., Tokyo, Japan; fig. 2) for ESD in the colon and rectum. This colonoscope is a single-channel scope with a thin upper endoscope tip size (9.8 mm) and a regular colonoscope shaft size (12.8 mm). The retroflex approach is available in any part of the colon and rectum using this scope because the bending section of the endoscope tip is thin and short with good angulation ability. A relatively large accessory channel of 3.2 mm and a water jet function with good targeting direction make this scope suitable for ESD.

When a lesion for ESD is located in an unstable part of the colon and paradoxical movements with a standard colonoscope hamper the reliable performance of the ESD procedure, we select a double-balloon colonoscope (EC-450Bi5, Fujifilm, Japan; fig. 3). The double-balloon colonoscope provides precise control of the endoscope tip, even in this situation (fig. 4).

**Accessories**

**Injection Needle**
For the injection of sodium hyaluronate solution, a high-flow injection needle with a large inner lumen should be used to minimize injecting resistance.

**Electrosurgical Knife**
Several kinds of electrosurgical knives have been developed for ESD. Among the currently available knives, we usually use a FlushKnife for ESD in the colon. A FlushKnife is a special needle knife featuring the water jet function through the knife sheath. This water jet function can be used to cleanse the surface of the mucosa and the needle itself. It can also be used for fluid injections directly into the submucosal layer through the FlushKnife after mucosal incision. Because a FlushKnife can be used for both injection and dissection, submucosal dissection can be performed immediately after the injection without changing the devices, which makes the procedure efficient. For this knife, the appropriate length of the needle can be selected from among 1, 1.5, 2, 2.5 and 3 mm sizes, based on the specific situation (fig. 5).

**Hood**
A transparent hood attached to the tip of the endoscope is useful to open the incised wound and to maintain a good endoscopic view during the procedure. It also allows precise control of the knife by stabilizing the target with its tip. Use of a hood is substituted for the triangulation used during surgical procedures, which is difficult to apply in endoscopic procedures. We mainly use a transparent hood with a small-caliber tip (ST hood; DH-15GR, DH-16CR; Fujifilm, Japan; fig. 6) for colonic ESD. The ST hood has an aperture small enough to make it easy to widen an incised wound using the edge of the hood, and to allow more accurate adjustment of the depth of incision by the knife point. Using the ST hood, it is easy to create a submucosal tunnel proceeding with submucosal dissection by inserting the tip of the hood into the submucosal layer, which is a useful strategy for effective ESD.

**Electrosurgical Current Generator**
It is important to select the appropriate high-frequency electrosurgical current generator and to set it appropriately for a reliable incision with effective control of bleeding and minimum tissue damage. We mainly use the ERBE VIO 300 D (Erbe, Tubingen, Germany). It is set to ‘Endo Cut
**Fig. 2.** Colonoscope for ESD (EC-450RD5; Fujifilm Corp.).  

*a* The bending section of the endoscope tip is thin and short with good angulation capability.  

*b* A large accessory channel and a water jet channel are situated close to each other.  

*c* Water jet function of the scope.  

*d* Good targeting direction of the water jet to the tip of an accessory device.

**Fig. 3.** Double-balloon colonoscope (EC-450BI5, Fujifilm Corp.).  

*a* Soft balloons are equipped at the tip of the endoscope and the tip of the overtube.  

*b* A balloon controller to inflate or deflate the balloons.
**Fig. 4.**  
**a** Paradoxical movements with a standard colonoscope.  
**b** Precise control of the endoscope tip provided by the double-balloon colonoscope.

**Fig. 5.**  
**a** Flush knife (DK2618JN10–30; Fujifilm Corp.).  
**b** The appropriate length of the needle can be selected from among 1, 1.5, 2, 2.5 and 3 mm sizes.  
**b** Water jet function through the knife sheath.

**Fig. 6.**  
**a** ST hood (DH-15GR, DH-16CR; Fujifilm Corp.).  
**b** Two sizes of the hood, DH-15GR for a thin endoscope tip and DH-16CR for a standard colonoscope tip) are available.  
**b** ST hood attached to the endoscope.

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I’ mode for mucosal incision, and to ‘swift coagulation’ or ‘dry cut’ mode for submucosal dissection. The output settings for the procedures are summarized in table 1.

**Hemostatic Forceps**
Effective control of bleeding during the procedure is a vital factor for successful ESD. Minor bleeding and small blood vessels can be managed using the knife. However, more reliable hemostasis for a larger vessel can be achieved using hemostatic forceps (HDB2422W; Pentax, Tokyo, Japan). The generator is set to soft coagulation mode for the hemostatic forceps.

**Outcomes**

In our experience of over 500 cases of colorectal ESD, en bloc resection has been successfully performed for lesions up to 164 mm in diameter with an en bloc resection rate of 92% and a perforation rate of 4%. A perforation made by the knife is usually tiny and recognized immediately; therefore, a perforation can be closed with endoscopic clip placement and managed non-operatively.

**Conclusions**

Tips and tricks for ESD for colorectal tumors have been described. ESD is a reliable method for the en bloc resection of large superficial mucosal tumors. En bloc resection is important for the accurate histopathologic examination of lesions to ensure curative resection by confirming complete local resection and assessing the risk of lymph node metastases. Complete resection can be achieved using en bloc resection and a minimum risk of recurrence.

**References**


