Endoscopic Submucosal Dissection in the Colon and Rectum

Indications, Techniques, and Outcomes

Amyn Haji, MA, MBBChir, MSc, MD, FRCS

KEYWORDS

• Endoscopic submucosal dissection (ESD) • Colorectal polyps

KEY POINTS

- Accurate endoscopic diagnosis using magnification endoscopy is the key for decision-making on treatment of colorectal polyps.
- Endoscopic submucosal dissection (ESD) for colorectal lesions should be offered to polyps that have higher risk of submucosal invasion.
- Successful training in colorectal ESD requires knowledge of endoscopic diagnosis, colorectal endoscopic anatomy, strategy for resection, and awareness of management of complications.

INTRODUCTION

Endoscopic submucosal dissection (ESD) is a procedure, which is accepted worldwide for resection of colorectal lesions, and its presence is increasing in western practice. The complexity of the procedure requires a robust training program in order to minimize complications, notably perforation and bleeding. Recently, the position statement from the European Society of Gastrointestinal Endoscopy (ESGE)[1] addressed many of these training issues and produced guidelines to support the uptake of ESD in western practice. It is of paramount importance that accurate assessment of colorectal polyps is undertaken with careful endoscopic diagnosis in order to identify those lesions that are suitable for en bloc resection by ESD. This article addresses endoscopic diagnosis using advanced endoscopic imaging, indications, and decision-making for ESD, its technical aspects and surgical planning with appropriate strategy, and finally reviewing current outcomes in the literature.

Department of Colorectal Surgery, King's College Hospital, Denmark Hill, London SE5 9RS, United Kingdom
E-mail address: amynhaji@nhs.net

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ENDOSCOPIC DIAGNOSIS

It is imperative that an accurate endoscopic diagnosis is undertaken in order to identify lesions that are suitable for ESD. Guidelines have been introduced from both the Japanese Gastrointestinal Endoscopy Society (JGES)[2] and ESGE[3] indicating the importance of identifying high-risk lesions that would benefit from en bloc resection. An initial endoscopic examination with good technique is needed in order to detect lesions by using appropriate inflation and deflation during examination, changing the position of the patient and performing appropriate J maneuvers (retroflexion) in the right colon and in the rectum to identify subtle flat lesions and areas of faint redness that may indicate potential polyps with submucosal invasion.

Multimodal endoscopic examination has been shown to be superior for detection of high-grade dysplasia and early cancer than other cross-sectional imaging such as computerized tomography or MRI for rectal polyps.[4] Indeed, this is more useful than biopsy as the latter needs to be targeted accurately from the precise areas of suspected early invasive cancer in order to make an accurate judgment. In addition, this process creates submucosal fibrosis, which can make subsequent en bloc resection and submucosal dissection more challenging. In our institution, the following measures are undertaken for detailed assessment of colorectal polyps before decision-making regarding of whether techniques of endoscopic mucosal resection (EMR) or ESD or indeed full thickness resection and laparoscopic surgery are appropriate.

Steps for detailed endoscopic assessment.

1. Gentle irrigation of the surface of the lesion in order to wash all areas of fecal debris and mucous plugs. Ideally, an irrigation pump is used with reduced pressure so that there is limited surface trauma to the colorectal polyp in order to minimize bleeding.
2. Morphology of the polyp according to Paris classification[5] is carefully assessed and this is outlined in **Fig. 1**. Most lesions referred for ESD are lateral spreading tumors (LST) that can be subdivided into granular (G) or nongranular (NG). LST-G can be further subdivided into homogeneous (H) and multinodular (MN) types. In addition, LST-NG is also subdivided into a flat type (F) and a pseudo-depressed (PD) type. This morphologic classification is important because the risk of submucosal invasion increases as polyps progress from G to NG, and indeed, there are more occurrences of multifocal invasion and submucosal fibrosis with LST-NG. **Table 1** shows our institutional data regarding the risk of submucosal invasion for the different subtypes and this is compared with the Japanese literature.[6]
3. Magnification endoscopy (×80–130 zoom) and super magnification with endocytoscopy (EC; ×500 zoom) have been used for careful assessment of pit pattern and vascular pattern in order to make an accurate endoscopic diagnosis without biopsy. In our practice, we would use magnification narrow band imaging (NBI) to assess the vascular pattern initially according to the Japanese NBI expert team classification (JNET[7]; **Fig. 2**). JNET type 2A has a regular vascular pattern suggestive of benign adenomas. JNET type 2B has an irregular vascular pattern, and this should be evaluated further with chromoendoscopy with either indigo carmine (0.4%) or crystal violet 0.05% to give an accurate Kudo pit pattern diagnosis.[8] **Fig. 3** shows the different pit patterns along with their predicted histologic diagnosis. Vi pit pattern indicates either of high-grade dysplasia (intramucosal cancer) or the presence of early submucosal invasion, whereas Vn pit identifies lesions that require surgical resection in most cases due to deep submucosal invasive cancer. Furthermore, Vi is subdivided into Vi low-grade with well-defined regular borders and Vi high grade with irregular margins (**Fig. 4**) corresponding to an endoscopic diagnosis of high-grade dysplasia and early submucosal invasion, respectively.

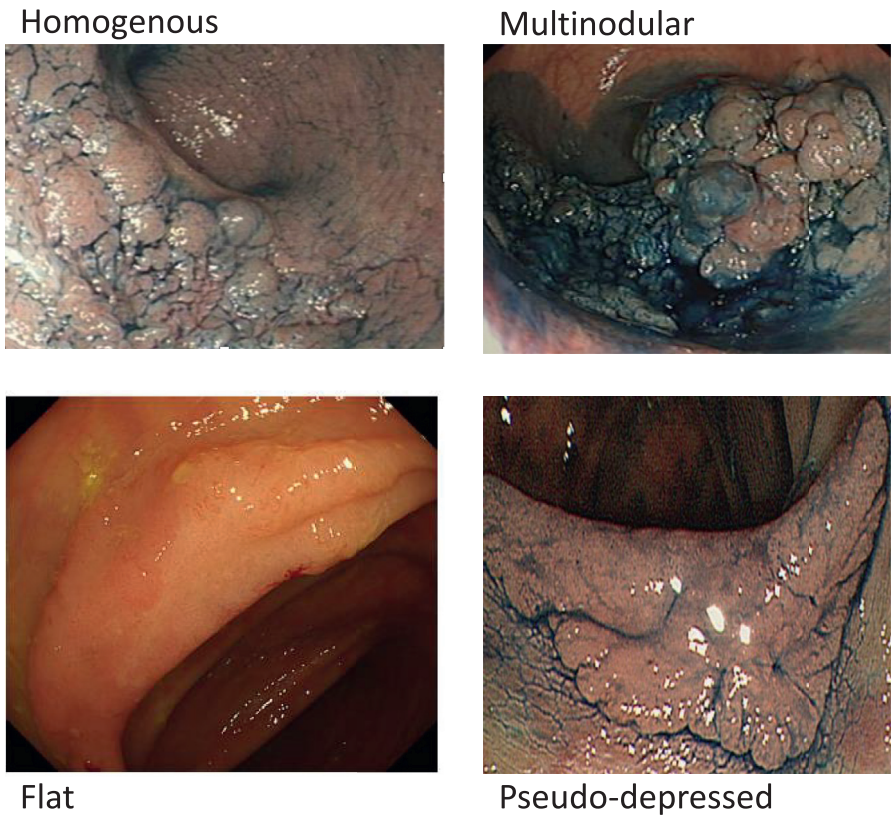


Fig. 1. LSTs.

This detailed examination of type V pit pattern is clearer with crystal violet rather than indigo carmine.

There are cases where the endoscopic diagnosis is difficult, and there is uncertainty regarding the histologic prediction. In such cases, super magnification with EC can be used. This requires staining with both 0.1% methylene blue and 0.05% crystal violet in order to stain both the nuclei and the cytoplasm. **Fig. 4** shows the EC classification

Table 1
Risk of submucosal invasive cancer within lateral spreading tumors

LST	King's Data (%)	Kobayashi et al (%)[a]
G—Homogenous	0.8	3
G—MN	8	11
NG—Flat type	12	14
NG—PD type	18	36

[a] Predictors of invasive cancer of large laterally spreading colorectal tumors: A multicenter study in Japan. Open JGH 2020 (4): 83-89.

	Type 1	Type 2A	Type 2B	Type 3
Vessel pattern	Invisible	Regular calibre and distribution	Irregular calibre and distribution	Loose areas
Surface pattern	Similar to surrounding mucosa	Regular	Irregular	Amorphous areas
Predicted histology	Hyperplastic / sessile serrated lesion	Low grade dysplasia	High grade dysplasia / early submucosal invasion	Deeply invasive cancer

Fig. 2. JNET classification.

developed by Professor Kudo at Showa University, Yokohama with the images being very similar to that seen on true histologic examination[9] (**Fig. 5**). Utilization of optical biopsy techniques are favored because this provides real-time endoscopic diagnosis without biopsy and subsequent fibrosis of the lesion. Further adjuncts to the endoscopic assessment include high-frequency mini probe ultrasound[10] introduced during the index colonoscopy through the working channel of the colonoscope in order to evaluate the depth of the colorectal polyps. The different layers of the colonic wall are imaged, and one can ensure that there is no deeper invasion into the muscularis propria before embarking on a trial ESD (**Fig. 6**). This can be particularly useful for colonic lesions in order to ensure that the lesion is favorable with no adverse features or deeper submucosal invasion thereby avoiding a long complex ESD procedure.

ASSESSMENT OF COLORECTAL ANATOMY

The strategy for endoscopic resection during ESD requires precise planning in order to maximize efficiency and minimize complications. During the initial assessment, it is important to view the polyp in all patient positions. This would mean that the patient needs to be turned from left lateral to supine to right lateral and indeed prone

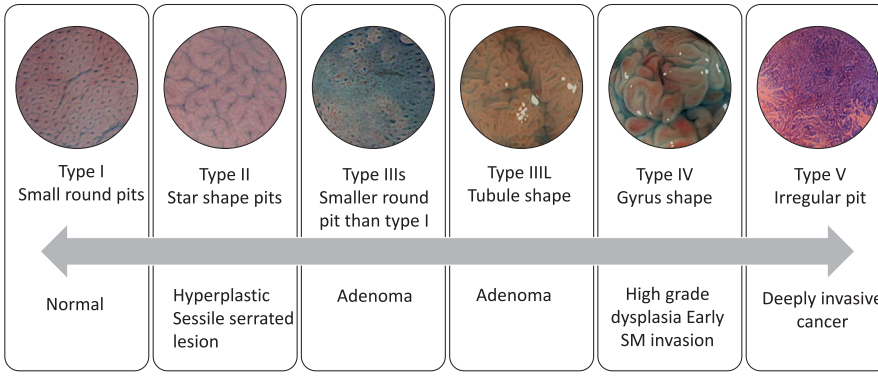


Fig. 3. Pit pattern classification.

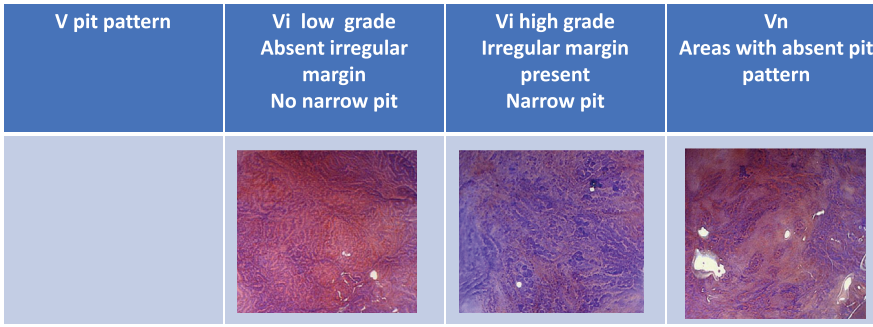


Fig. 4. V pit pattern.

positioning in order to identify the most favorable approach. Fluid is irrigated during such assessment so that we can identify the areas of the colon and rectum that are retroperitoneal and those that are antimesenteric. For example, in evaluating rectal lesions, if patients are in the supine position and the lesion is in the pool of fluid, then we know this is a posterior lesion and, therefore, on the mesorectal side. However, if the lesion is on the opposite side to the pool of fluid (antigravity), then it is an anterior lesion. A perforation during such a procedure may be intraperitoneal particularly in women as the pouch of Douglas often descends lower anteriorly. This assessment using fluid to identify the gravity side of the lesion, and the antigravity part helps in the decision-making for the steps of the dissection. The antigravity section is often easier because the submucosal plane is more open when compared with the gravity side. Therefore, if the gravity position is not easily accessible by the scope when turning the patient, it is important to dissect this area first because this will get increasingly difficult with ongoing dissection of the easier antigravity side. In addition, because the length of the procedure increases, there is worsening colorectal spasm that often makes the oral side of the lesion more difficult to access. One should therefore contemplate making the oral incision earlier in these circumstances.

The assessment report should not only contain a detailed description of the polyp including morphology, JNET and pit pattern diagnosis but also the relevant colorectal anatomy and the strategy for endoscopic resection. In this manner, more appropriate scheduling of patience can occur with a limited number of unexpected events.

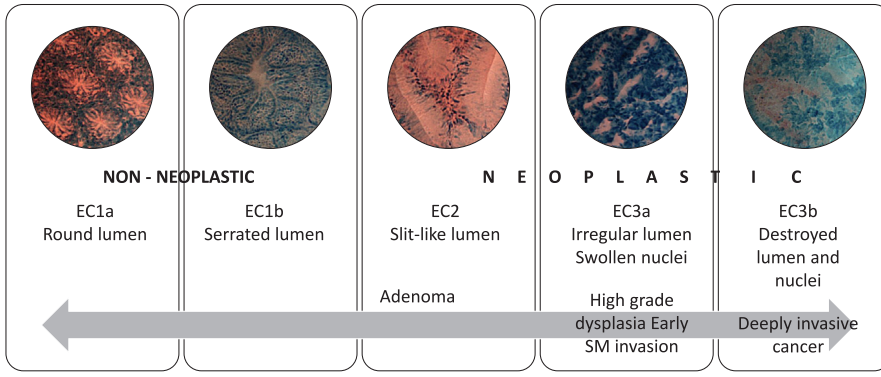
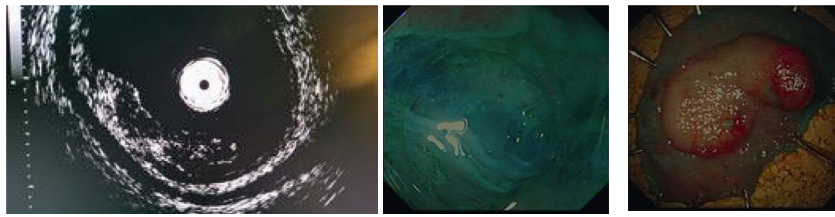


Fig. 5. EC classification. (*Courtesy* of Yuichi Mori, MD, PhD.)



T1 tumour – 20 MHz mini probe

T1 tumour – during ESD
Submucosal invasion but
clear plane

En bloc resection, R0
1200 micrometres submucosal
Invasion

Fig. 6. Miniprobe ultrasound during colorectal ESD.

INDICATIONS FOR ENDOSCOPIC SUBMUCOSAL DISSECTION

The Kings' algorithm for decision-making and treatment of colorectal polyps is outlined in Fig. 7. Patients with polyps that have a Vi pit pattern or LST-NG are absolute indications for colorectal ESD. LST-G (MN) has a higher risk of submucosal invasion and should also be treated by en bloc resection. In addition, lesions that have significant fibrosis either due to previous manipulation by biopsy or attempted snare resection, lesions in patients with inflammatory bowel disease or previous radiotherapy, all

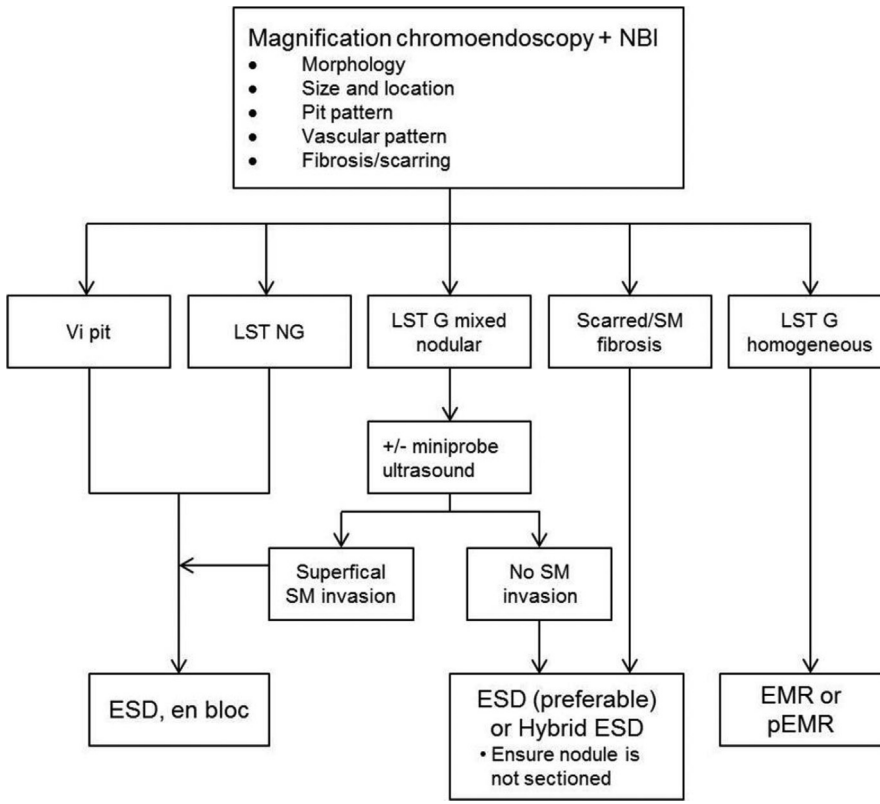


Fig. 7. King's decision-making for endoscopic resection.

require treatment with ESD if technically feasible. This is similar to the guidance produced by the JGES.[2]

There is some debate regarding patients that have LST-G (H) because the risk of submucosal invasion is less than 1%.[6] Therefore, in western practice, many of these patients are treated with piecemeal EMR techniques particularly if patients have existing comorbidities.

There are several considerations when adopting a piecemeal EMR. In Japanese practice, ESD is used to treat polyps that cannot be treated with en bloc EMR and these are often those with lesion size greater than 2 to 3 cm. There is some evidence that risk of submucosal invasion increases with size and recurrence after piecemeal EMR and has been shown to be between 10% and 30% in the literature.[11] The Australian data[12] suggests that the use of snare tip coagulation to treat the edges reduces recurrence significantly in good quality wide field EMR and should be adopted. We have also shown that there is 13% residual adenoma at the edges when sampled using the EndoRotor device (Interscope, Interscope, Inc, USA) after piecemeal EMR.[13] This provides some histologic evidence and a rationale for using ablative techniques on the margins of the EMR scar. The second consideration is in relation to surveillance after endoscopic resection. It should be noted that patients after piecemeal EMR potentially require more visits for follow-up colonoscopy due to the higher recurrence rate.[14] Therefore, the decision between EMR and ESD for patients with LST-G H type needs to be considered carefully in conjunction with the patient's comorbidities and the expertise of the endoscopist, and discussed with the patients so that they are suitably counseled before making a decision regarding the procedure.

ENDOSCOPIC SUBMUCOSAL DISSECTION TECHNIQUE

The usual practice in our institution is to initially perform a colonoscopy without a distal attachment before embarking on commencing the ESD procedure. This allows for appropriate irrigation and cleansing of the proximal colon as well as washing the lesion appropriately to minimize the fecal debris and mucus before the resection. Once this has been established, a distal attachment is placed (Fuji ST hood) on the end of the endoscope. The conical shape of the attachment allows for easier access to the submucosal space, whereas the straight type distal attachments allow for wider views (**Fig. 8**). The steps of the procedure, particularly for training, have been subdivided into appropriate subsections so that they allow for a standardized robust approach

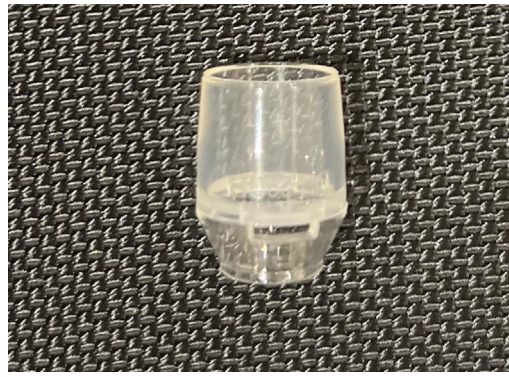


Fig. 8. Fujifilm ST Hood DH-29CR.

to the majority of cases and also allow for endoscopists at different stages of the training to perform different sections of the dissection. This process is outlined in Fig. 9 and the steps are detailed below.

1. Injection using a 23-gauge needle using gelofuscine or volpex (colloid) mixed with indigocarmine solution to ensure that this is a light blue color that is not too dark so that a newspaper print can be read through the transparency. This shade of solution allows for easy visualization of the muscle layer and vessels in the submucosal layer, and the fluid is injected on the anal side of the lesion.
2. The rate of injection by the assistant needs to be slow initially until there is an increase in the submucosa and then can increase in speed ensuring that the assistant counts the number of millilitres introduced, and the rate of lifting of the submucosal space is at the same speed as the counting. This also avoids a submucosal hematoma forming with an initial forceful injection.
3. ESD knives are manufactured either as needle type or with a ball/wider tip and endoscopists often choose one that supports their technique. In our institution, we use a 1.5 to 2-mm knife that can be irrigated through (flush knife). The flushing solution is normal saline with indigocarmine at the same concentration as the injection solution.
4. Mucosal incision (Effect 2, cut interval 2, cut duration 2-ERBE Vio 300D [ERBE Vio 300D, ERBE Elektromedizin, Gemany]) and trimming is undertaken using the flush knife on the anal side of the lesion starting one cap distance away from the margin of the polyp. This is increased to 2 cap distances if there are areas of fibrosis in patients that have recurrent polyps or previous treatment. The submucosal space is entered and submucosal tunneling is undertaken through to the central part of the lesion until arriving at a distance beyond the oral edge of the lesion. If vessels are encountered during the dissection, they are treated with the following algorithm: (1) all arterial vessels are coagulated with a bipolar grasper before division with the knife and (2) venous structures are divided using the knife as follows. If the vein is larger than the diameter of the knife, then a low effect on low wattage (Effect

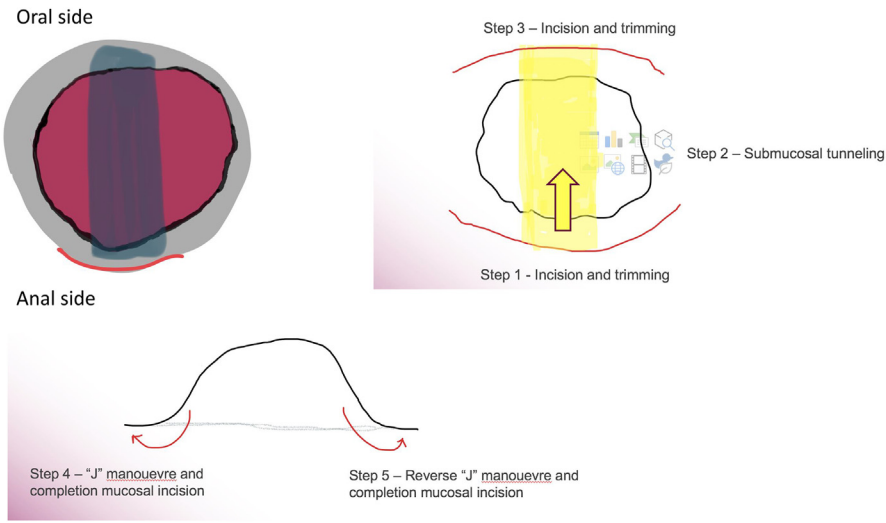


Fig. 9. Steps for ESD tunneling of colorectal lesion.

1, 10 W – ERBE Vio 300D) is applied, which allows for appropriate precoagulation as the blood-stained structure in which the color changes to white with a noticeable "boiling effect" of the current. The vein can then be divided with the knife. Smaller veins can be divided directly using forced coagulation (Effect 2, 40W – ERBE Vio 300D).

5. Incision and trimming on the oral side is now performed so that the submucosal central tunnel can meet from beneath the lesion to break through to the oral side. This creates a self-retracting polyp similar to a bridge over water.
6. The next stage is to dissect the 2 lateral margins. The mucosal incisions are initially created on the lateral edges of the polyp followed by dissection from the inside of the submucosal tunnel to the outside in order to dissect the 2 lateral pillars. This maneuver is termed the J maneuver on the left and the reverse J maneuver on the right.
7. Copious irrigation of the scar is undertaken with water to ensure that the base is clearly evaluated for visible vessels and muscular defects. In addition, this irrigation of the scar may help ensure that polyp seedlings are not present from the trauma of submucosal dissection.
8. Patients who are on antiplatelet or other anticoagulants usually have their mucosal defect closed either using clips or endoscopic suturing using the Apollo overstitch device (Apollo Overstitch device, Apollo Endosurgery Inc., USA). It is important to adhere to surgical principles and achieve a tension free repair and closure of the defect. On occasions, where this is not possible, a hemostatic agent can be applied to the base in order to reduce the risk of delayed bleeding (eg, Purastat, three-dimensional matrix). Nonetheless, it is important to identify the visible vessels on the scar and treat these prophylactically using the bipolar forceps (Haemostat, Pentax Medical [PENTAX Europe GmbH, Hamburg, Germany]).
9. Withdrawal of the specimen after procedure requires careful manipulation in order to minimize the risk of trauma or fragmentation during extraction. Smaller lesions can often be removed using an endoscopic net to capture the polyp and withdraw through the anal canal easily. Polyps larger than 5 cm often are removed using careful suction into the distal attachment and withdrawal into the low rectum followed by gentle assistance using a rectal digital examination alongside the scope in order to have some anal dilatation while carefully withdrawing the polyp alongside the inserted index finger. Alternatively, a proctoscope can be inserted into the anal canal and low rectum, which can provide assistance to evacuate the contents of the rectum and the dissected polyp.

"J" Maneuver and Traction

Access of the lesion during a J maneuver (retroflexed scope) should be assessed early on during the procedure. In many circumstances, particularly in the right colon, stability is improved in this position allowing access to the oral side, enabling earlier mucosal incision and trimming. If this position proves to provide good access, the submucosal dissection is continued until technically feasible.

In some scenarios, if access to the submucosal plane is challenging and the lesion continues to be on the gravity side due to the concavity of the colorectum and pooling of fluid, traction can be used to assist opening up the submucosal plane with better visualization. There are 2 techniques that we currently use in our institution. The first relates to a clip flap technique[15] (**Fig. 10**) where a clip is placed on the mucosal edge of the polyp on the anal side, and this allows the clip to be an extension of the polyp enabling the distal attachment to apply countertraction against the clip itself.

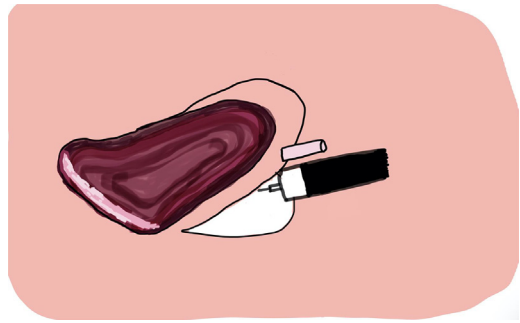


Fig. 10. Clip flap technique.

Furthermore, a clip and line technique[16](Fig. 11) can also be used in the distal colon, whereby countertraction is applied using either some dental floss or surgical suture. In the circumstances whereby the line is too long due to a proximal location of the lesion in the colon, one can use a loop on the clip, which is then used as a purchase for the second clip to apply countertraction to the opposing mucosal surface.

Dealing with Fibrosis

Prior biopsy, attempted endoscopic resection, or inflammatory conditions of the bowel can induce fibrosis in the submucosal layer. In addition, LST-NG lesions also naturally have fibrosis in the submucosal layer. Careful planning of the approach to the fibrosis is the key for successful resection of these lesions. Our practice is to start the mucosal incision 2 cap (distal attachment) distances away from the area of fibrosis and access the submucosal space in an area devoid of such fibrosis. This ensures that an adequate flap is created in normal tissue and allows easier traction with a sufficient tunnel in order to treat the fibrotic area. The technique of dissection is slightly different in that the tip of the knife is used for applying diathermy carefully so that vessels are not divided inadvertently with deeper penetration of the knife.

Regular injection using the flushing knife and appropriate traction is also used to tackle fibrosis. It may require multiple approaches in areas of relatively normal submucosa from all sides of the lesion before tackling a stubborn fibrotic region adherent to the muscular layer. In such circumstances, dealing with such an area at the end of the procedure is advantageous because this area offers a higher risk of perforation. If perforation were to occur then we know that the procedure is nearly complete and the perforation can be closed in a timely manner.

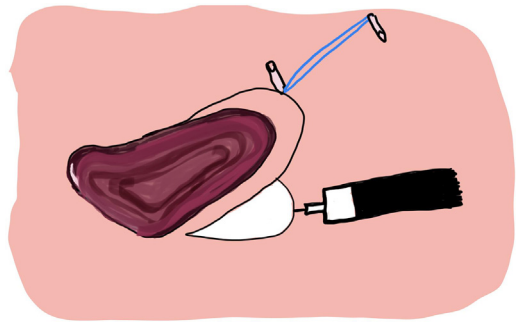


Fig. 11. Clip and line technique.

INTRAPROCEDURAL COMPLICATIONS

Bleeding

Bleeding during ESD often stains the submucosa causing a hematoma making subsequent dissection more difficult. Endocut current for dissection through the hematoma in the submucosa enables dissection without excessive charring and allows effective identification of the bleeding point. Massive hemorrhage during the procedure often obscures the view, and formation of clots in the lumen makes suction increasingly difficult. Change of position of the patient allows the bleeding vessel to be more accessible or placing the patient in a head down, or Trendelenburg position, with copious irrigation allows the blood flow into the proximal colon away from the endoscopic lens allowing quick and safe coagulation of the visible vessel. The evacuation of clots can be challenging and requires further suctioning often with the removal of the suction button to generate further power. In addition, a proctoscope or rigid sigmoidoscope can be inserted to evacuate any clots in the rectum quickly.

Perforation

Perforation is more likely if the knife is perpendicular to the muscular layer. In addition, errors in knife management can occur if there is undue tension in countertraction with the distal attachment, leading to the loss of endoscopic tip control. On occasion, the muscular fibers are split but perforation is not full thickness with no visible pericolic or perirectal fat. In these circumstances, it is prudent to continue with the dissection until the end of the procedure, and then evaluate the muscle layer carefully in order to identify areas that might require closure. In rare circumstances, the perforation is full thickness, and in this situation, the perforation should be closed with through the scope clips at a time when the polyp has been dissected away from the perforation site so that the clips do not interfere with subsequent submucosal dissection. In our experience, it is extremely rare for a procedure to be abandoned for such a complication.

Management of patients after procedure would depend on the institution guidelines and often can be managed as an outpatient if secure closure of the defect is achieved and appropriate prophylactic antibiotics are given. This would largely depend on the clinical status of the patient.

POSTOPERATIVE MANAGEMENT

In our practice, 90% of patients for colorectal ESD are treated as a day case (outpatient) procedure. In western practice, decisions regarding conscious sedation, propofol and general anesthesia are made after appropriate discussions with the patient and anesthesia colleagues. It is particularly advantageous for training, to perform procedures under general anesthesia because these are likely to be longer procedures; however, turning of the patient may be problematic if needed multiple times during the procedure. Therefore, appropriate planning and preoperative strategy as discussed earlier in this article are of paramount importance.

There is no evidence regarding utilization of antibiotics routinely during colorectal ESD.[17] However, this is used in our institution if patients have muscle parting or perforation requiring closure and also routinely for rectal ESD particularly for larger lesions involving dissection times greater than 2 hours.

In our institution, there is currently no restriction to postoperative intake and patients increase their diet from free fluids through to normal diet depending on their appetite and desires. It should be noted that 8.6% to 14.2% of patients may develop abdominal pain, fever, and disturbances in bowel habit with some abdominal tenderness as part of the postpolypectomy coagulation syndrome.[18] Risk factors include right colonic

Table 2
Japanese Society of Colon and Rectal Cancer Guidelines 2019 for treatment of colorectal cancer

Endoscopic Surveillance	Lymph Node Harvest and Surgical Resection
R0 resection	R1 resection
No vascular or lymphatic invasion	Vascular or lymphatic invasion
No tumor budding	Tumor budding
Depth of invasion <1 mm	Depth of invasion >1 mm

lesions, procedural times greater than 90 minutes, and lesion size greater than 40 mm. Often, this is a minor concern and can be easily managed in the outpatient setting. Rarely, patients are admitted for inpatient management and often cross-sectional imaging is undertaken to exclude perforation. We should note with caution that often small amounts of free fluid and locules of air can be seen adjacent to the dissected area. This is not an indication for further surgical intervention and close observation is often needed for conservative management. Collaboration with colorectal surgeons to manage these patients jointly is currently best practice.

OUTCOMES FOLLOWING ESD

An audit of intraoperative and postoperative complications and quality of colorectal submucosal dissection is important in order to have insight into your practice. This will enable us to benchmark our unit figures with comparisons against national and international standards from expert centers. In our institution, we aim for outcomes of less than 1% risk of perforation and postoperative bleeding requiring admission to hospital. En bloc and complete (R0) resection should aim to be greater than 90%. The literature suggests that the rate of postoperative complications vary significantly among institutions depending on their experience. The incidence of intraprocedural perforations is 2.7% to 5.7%, whereas the incidence for delayed perforations is relatively rare at 0.2% to 1.4%.[19–24] Delayed bleeding often varies between 1.5% and 8.1%[25–28] and risk factors include rectal and cecal lesions, large polyp size greater than 30 mm and those patients on anticoagulants.

Vertical margin positivity has been a contentious issue in many units. For patients that have incidental early colorectal cancer, many institutions use the surgical clearance of 1 mm being the minimum in the submucosa. This would mean that although there is a clear histologic margin, if this is less than 1 mm, it is deemed an involved margin (R1) resection. Unfortunately, this has consequences for the patient, and the advice that the colorectal multidisciplinary team often gives is that of formal colorectal surgical resection and lymph node harvest due to involved margins. In our practice, R1 is only stated if there is involved cancer at the resection margin. Other histologic high-risk features for lymph node metastasis include vascular and lymphatic invasion, tumor budding, invasive cancer greater than 1000 μm and poorly differentiated adenocarcinoma.[6,29–31] The Japanese guidelines[32] are summarized in **Table 2** and recommends which patients should proceed to lymph node harvest and formal surgical resection after histologic evaluation. This is also similar to the European guidelines.[3] In practice, detailed discussion regarding risk of lymph-node metastases needs to be conducted with the patient preoperatively and postoperatively to understand their risk strategy. The location of the colorectal cancer resected by ESD is important because complications associated with rectal resection are very different to those for proximal colonic surgery.

Isolated deep submucosal invasion without any of the other risk factors has a low risk of lymph node metastasis, and this should be discussed with patients before decision-making regarding further treatment. Utilization of early colorectal cancer specialist nurses and a specialist multidisciplinary meeting is best practice in order to manage such patients and support their decision-making.

SUMMARY

Colorectal ESD requires detailed multimodal assessment of polyps to make an accurate endoscopic diagnosis in order to identify lesions suitable for en bloc resection. Knowledge of colorectal anatomy with careful planning ensures that a successful strategy is adopted to minimize complications.

CLINICS CARE POINTS

- Rectal polyps should be resected en bloc by ESD to ensure vertical margin clearance in those with incidental cancer, thereby avoid over treatment with surgery if piecemeal EMR is undertaken. MRI should be performed preoperatively for all lesions as artifact will be present if done after ESD leading to overstaging.
- When planning for ESD, identify the colorectal anatomy to understand the intraperitoneal and retroperitoneal side.
- Mucosal incision and trimming of the oral side of the lesion and the gravity side should be planned early if not accessible with turiing the patient to increase success of completion.

DISCLOSURE

The author has nothing to disclose.

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