

Colorectal Endoscopic Submucosal Dissection

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ABSTRACT

Colorectal endoscopic submucosal dissection (ESD) is a complex endoscopic technique that allows the en-bloc resection of large lesions. With ESD, the submucosa is dissected under the lesion with a specialized knife. This enables removal of larger and potentially deeper lesions with a curative intent than cannot be accomplished with endoscopic mucosal resection (EMR), especially non-granular laterally spreading tumors and lesions with submucosal fibrosis. It is vital to estimate depth of invasion through magnifying chromoendoscopy before attempting resection, and lesions showing invasive pattern should be directly submitted to surgery. The invasive pattern consists in macroscopic findings that suggest deep submucosal invasion and has been shown to have a high diagnostic accuracy (98.8%). The endoscopist has to be familiarized with a wide variety of materials available, like the appropriate endoscope, the electrosurgical unit and the coagulation forceps and should select the best suited knife depending on the lesion characteristics and location. This technique has a well-documented efficacy with an en-bloc resection rate around 96% and a low complication rate (3-4%) that has been shown similar to other surgical techniques with an even shorter in-hospital stay.

INTRODUCTION

Endoscopy is living a revolution. In the last decade many keystone-techniques have been widely spread such as therapeutic endoscopic ultrasonography, peroral endoscopic myotomy and ESD. The latter was developed in Japan for the en-bloc endoscopic resection of early gastric cancer [1] and in Asia is actually considered as a first line treatment [2]. Subsequently the indications have expanded to other locations of the gastrointestinal tract such as pharynx, esophagus, duodenum and colorectum. In recent years procedural techniques and equipment for ESD have evolved significantly allowing a rapid expansion through western countries. Nonetheless this is arguably considered the most complex endoscopic technique that requires a long training curve with mixed results in Europe and United States. Successful endoscopic resection with ESD in the colon remains a hard to reach goal due to anatomical features such as a thin colon wall and poor endoscope maneuverability. We will try to shed some light about the actual knowledge and results about ESD in the colon and rectum.

INDICATIONS

Standard EMR is a safe and effective treatment of lesions smaller than 20mm in diameter but is usually unable to achieve en bloc resection of larger tumors. Large adenomas can be treated by piecemeal EMR but it is well known that this approach reduces the reliability of the histopathologic analysis. Hence, ESD in the colon has generally been used for laterally spreading tumors (LST) larger than 2cm since larger lesions exceeding have a higher risk of submucosal invasion. LST granular type lesions have a low risk of submucosal (SM) invasion that typically lies within the largest nodule, therefore piecemeal EMR remains in these cases the treatment of choice. On the other hand LST nongranular type (LST-NG) poses a higher risk of SM invasion and approximately 30% harbor difficult to predict multifocal invasion [3,4] hence ESD could be the treatment of choice to allow en bloc resections of large LST-NG.

Recently the European Society of Gastrointestinal Endoscopy (ESGE) and the Japan Gastroenterological Endoscopy Society (JGES) have issued recent clinical guidelines in ESD. Indications for colorectal ESD are shown in the Figure 1.

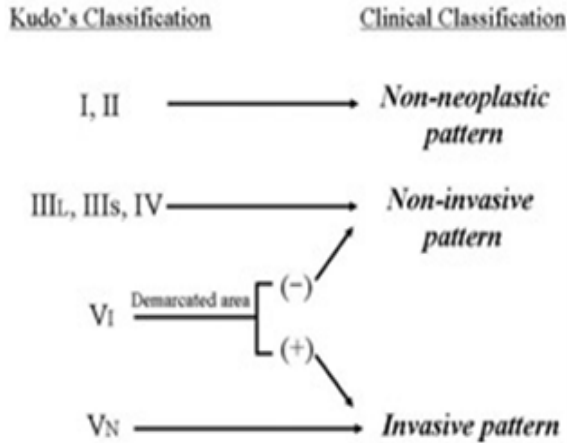


Figure 1: Courtesy of Prof. T Matsuda. Invasive vs non-invasive pattern.

Table 1: Indications for Colorectal ESD.

1.	Large lesions (>20mm in diameter) where en bloc resection is required:
a.	LST-NG (particularly flat-depressed type)
b.	Lesions showing Kudo's Vi Pit Pattern
c.	Carcinoma with predicted shallow submucosal invasion
2.	Flat dysplastic lesions associated with Ulcerative Colitis non resectable by EMR.
3.	Lesions with submucosal fibrosis and/or non-lifting sign without predicted deep submucosal invasion

When NOT to Perform ESD in the Colorectum: Estimating Depth of Invasion

By using image-enhanced endoscopy such as NBI or BLI, specific dyes and optical magnification, the endoscopist has to evaluate the lesion through its macro- and microscopic appearance to assess the presence of deep submucosal invasion, thus rendering the ESD pointless. To distinguish between adenoma and adenocarcinoma, lesion color, surface unevenness, presence of depression, and fold convergence must be confirmed by ordinary observation and chromoendoscopic observation. The accuracy to discriminate neoplastic from non-neoplastic lesions was reported to be approximately 80% for standard observation, including magnifying chromoendoscopic observation, 96–98% for pit pattern observation, and 95% for magnifying observation using NBI and BLI. [5] Furthermore Matsuda et al. [6] published a relatively simple method to distinguish between adenoma or submucosal deep invasive adenocarcinoma. A total of 4215 neoplastic lesions (excluding advanced colorectal cancer) were evaluated using magnifying chromoendoscopy and the lesions were labeled as invasive or non-invasive pattern depending on the presence of regular or irregular pit pattern as well as the coexistence of a demarcated area. The classification is shown in Figure 1. The study found an overall sensitivity, specificity and

a diagnostic accuracy of 85.6%, 99.4% and 98.8% respectively. Thus, lesions showing invasive pattern should not be endoscopically resected and be evaluated for a surgical treatment. Examples are shown in Figure 2.

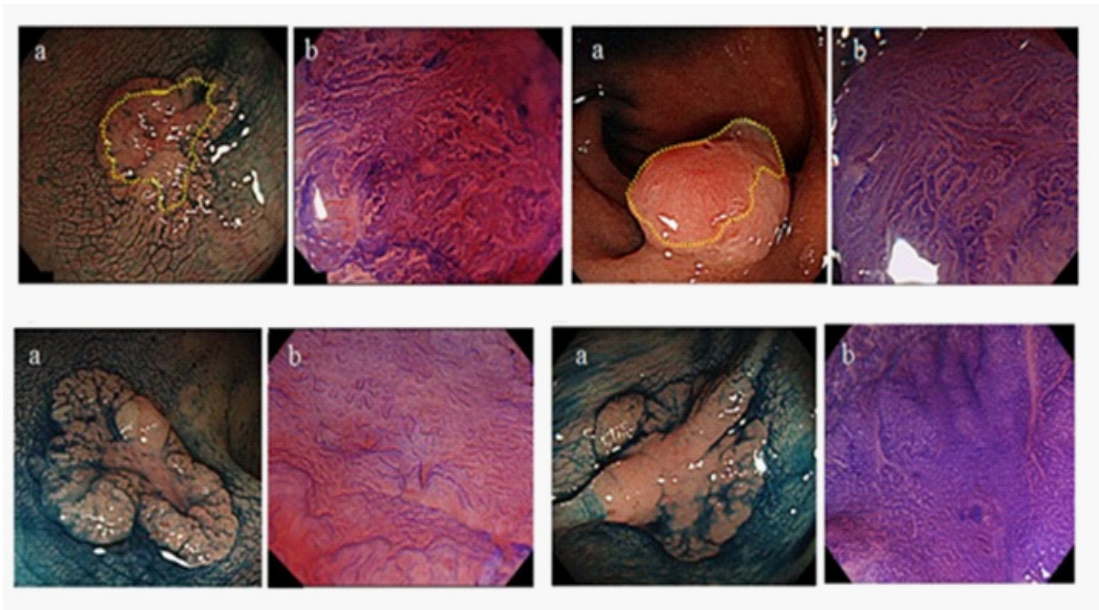


Figure 2: Courtesy of Prof. T. Matsuda. (A and B) invasive pattern: irregular or distorted pit with demarcated area. (C and D) Noninvasive pattern: regular pit with or without demarcated area or irregular pits without a demarcated area [7].

Furthermore, the same author published another study [7] showing several endoscopic findings that may harbor deep submucosal invasion such as the presence of: deep depression, fold convergence, irregular bottom depression surface, chicken skin appearing mucosa, redness, expansive appearance, firm consistency, irregular surface, loss of lobulation and a thick polyp stalk. Examples are shown in the Figure 3.

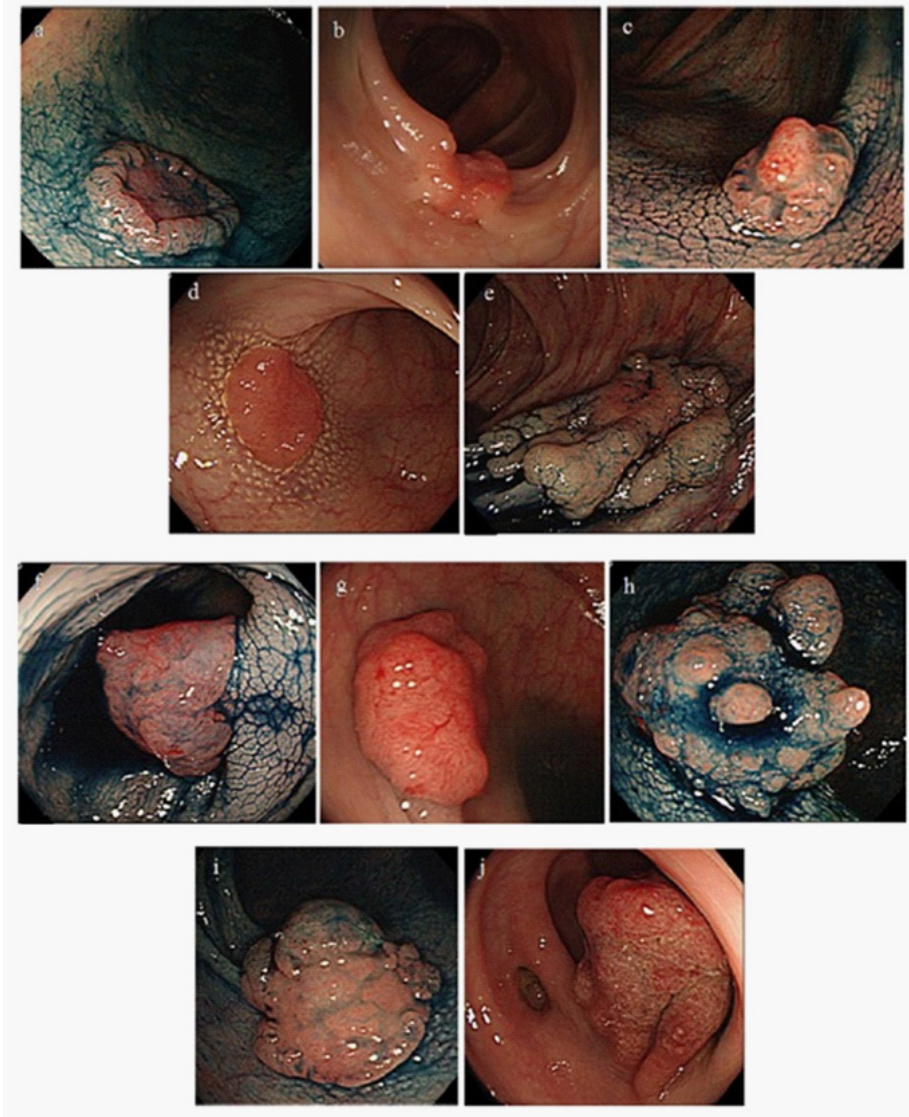
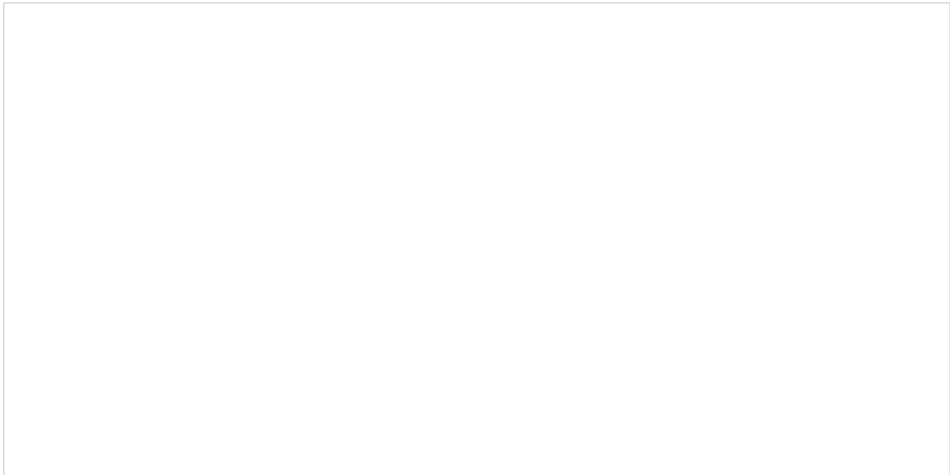


Figure 3: Courtesy of Prof. T. Matsuda. Findings suggestive of submucosal invasive cancer: (A) Deep depression, (B) fold convergence, (C) irregular bottom of depression surface, (D) chicken skin appearance, (E) redness, (F) expansive appearance, (G) firm consistency, (H) irregular surface, (I) loss of lobulation, and (J) thick stalk [7].

TECHNIQUE

The steps of this complex technique are explained in Video1 and Figure 4.



Video:

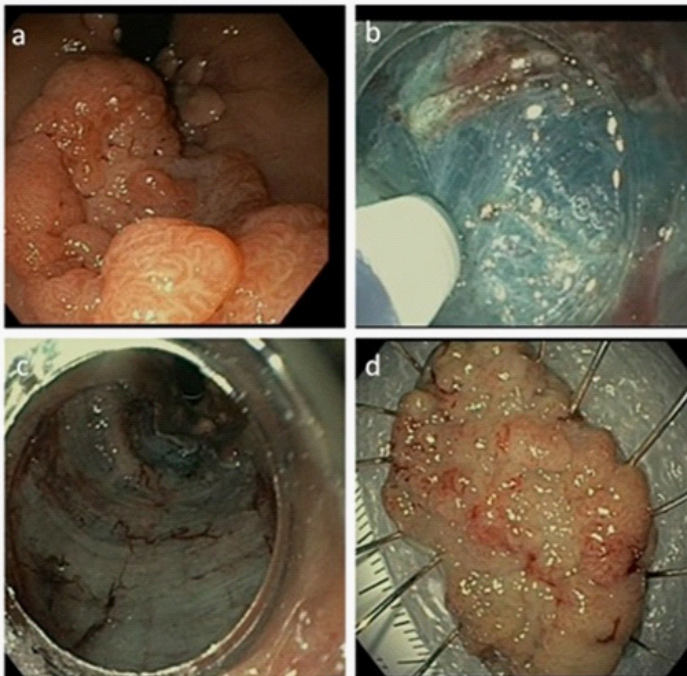


Figure 4: Rectal ESD procedure: (a) Rectal 4cm lesion Paris 0-IIa+IIc LST-Granular type. (b) Submucosal dissection. (c) Resection bed. (d) Excised lesion.

MATERIALS

Another important issue to bear in mind is the need to fulfill a series of equipment requirements before starting to perform ESD.

CO₂ Insufflation

Even though ESD can be performed with standard air insufflation, the importance of performing under CO₂ insufflation cannot be overemphasized. CO₂ is known to be absorbed 160 times more rapidly than nitrogen and 13 times than oxygen [8]. Since this procedure frequently requires hours to complete, the luminal distension caused by air insufflation can lead to complications and patient discomfort. Furthermore, in the likely event of a perforation that one has to eventually face when performing this technique, the risk of causing tension pneumoperitoneum may be reduced with the use of CO₂. (Figure 5)



Figure 5: UCR, Olympus medical systems co.

Electrosurgical Units

ESD requires different monopolar or bipolar instruments that function more efficiently under the appropriate current delivered by the electrosurgical unit (ESU). Newer ESUs have the ability to sense the impedance of the tissue. The impedance may vary due to multiple circumstances such as tissue carbonization or submucosal fat infiltration. Therefore these modern ESUs adjust to changing impedances to deliver a constant voltage. Furthermore there are a variety of current modes available to successfully perform the different phases of ESD: marking, circumferential incision, vessel coagulation using hemostatic forceps and submucosal dissection. Even though there is a wide variety of ESUs available to safely perform ESD, the one that has largely been utilized

and has gathered more experiences is ERBE VIO 300® D(ERBE). This ESU has the advantage of a high level of customization, one being able to change settings such as the cut effect (more effect meaning more hemostasis), cut depth (cut duration) and cut interval (Figure 6).



Figure 6: VIO 300® D Electrosurgical Unit. ERBE.

Furthermore the VIO 300D provides a few proprietary and classic modes that are suited for ESD. Recommended settings are summarized in the figure.

1. **ENDOCUT:** This type output mode alternates a pure cut current with soft coagulation. ENDOCUT Q (the “Q” resembles a closing snare) is suited for EMR and standard polypectomy. ENDOCUT I (the “I” imitates a papylotome) will be used for ERCP and the precut and circumferential incision phases in ESD.
2. **DRY CUT:** A pulsed cut with intense hemostasis frequently used as well in the precut and circumferential incision phase.
3. **FORCED COAG:** This classic mode delivers a high voltage coagulation current that generates spark to induce effective hemostasis during the submucosal dissection phase.
4. **SWIFT COAG:** This new type of current delivers a lower Voltage than FORCED COAG and achieves a faster coagulation with less tissue penetration and better-cut profile that is ideal for a safe submucosal dissection.
5. **SOFT COAG:** Pure coagulation with a low voltage that dissects the tissue with low carbonization. It is usually recommended to perform long coagulation periods with a low effect setting to “dry out” large vessels with hemostatic forceps.

Endoscopes

The choice of the appropriate endoscope varies greatly depending on the characteristics of the lesion and the instruments used. When planning to perform ESD, one has to consider acquiring

a high definition endoscope with optical magnification. This technology features optical zoom to obtain images magnified up to 150 times that in association with specific dyes, will enable to accurately determine, as previously exposed, the presence of signs of deep submucosal invasion. In the colon is vital to obtain a stable position, which can be hard to achieve in the cecum or ascending colon. A very important tip to stabilize the scope is to perform ESD in retroflexion, hence the need to use thin pediatric colonoscopes. During the dissection and most importantly in the rectum, significant bleeding may occur, therefore it is always very useful to use endoscopes with an auxiliary water jet.

Devices for ESD

Knives

There exist a wide variety of devices needed to perform ESD in the colorectum. The most essential component in ESD is the knife. Not every knife is suited for all stages of ESD. For example, insulated-tip **IT-KNIFE NANO**[®] (Olympus Medical Systems Co.) cannot be used for initial incision and will require the use of another non-insulated tip knife at the beginning of the technique. Also, newer devices such as **HYBRID KNIFE**[®] (ERBE), **FLUSHKNIFE**[®] (Fujifilm) and **DUALKNIFEJ**[®] (Olympus Medical Systems Co.) include a fluid injection function that can be used to inject fluid into the submucosal layer as often as needed without the need to swap devices. This function can also be used as a frontal wash jet to improve visualization of bleeding vessels. We recommend trying different kinds of devices on animal models and select the one the endoscopist feels most comfortable with. These devices are designed to fit a regular endoscope channel of 2.8mm and available in different knife lengths (the recommended knife length in the colon is 1.5mm) and catheter lengths (to fit a gastroscope or a colonoscope).

HOOK KNIFE[®] (Olympus Medical Systems Co.): The tip of the **HOOK KNIFE**[®] (Figure 7A) is bent at a right angle creating an L shape. The knife extends to 4.5mm in length with a 1.3mm hook⁹, and the orientation of the tip and the knife length are adjustable at the instrument handle. This device is suitable through all the stages in ESD and the technique consists in grasping the target tissue, retracting the knife and performing the cut (“catch and cut technique”). This allows a slow but safe procedure especially in areas of fibrosis or lesions located perpendicular to the endoscope such as the cecum.

TRIANGLE TIP KNIFE[®] (Olympus Medical Systems Co.): The **TRIANGLE TIP KNIFE**[®] (Figure 7B) has a non-insulated triangular electrode at the tip of a 4.5mm-long cutting knife. The triangle at the tip measures 1.6mm on each side and maximally extends 0.7mm away from the central cutting knife [9], therefore one has to bear in mind the risk of extending the cut deeper than expected and causing a perforation. Hence, this device is virtually not used in the colon anymore.

DUALKNIFE[®] and **DUALKNIFEJ**[®] (Olympus Medical Systems Co.): Both, the **DUALKNIFE**[®] and **DUALKNIFEJ**[®] (Figure 7C and G) have a very similar design. They can be used at all stages in

ESD. Available in 1.5 and 2mm knife lengths that incorporate a 0.3mm non-insulated door knob-like tip designed to allow an effective grasp of the tissue and a lower current density at the tip for better hemostasis. The knife can also be used when retracted where the knife will protrude 0.3mm. This is useful both at the marking stage and at inducing hemostasis. The **DUALKNIFE**[®] will be commercialized in Europe probably on the first semester 2016 and adds, as previously mentioned, a fluid jet function.

FLEXKNIFE[®] (Olympus Medical Systems Co.): The **FLEXKNIFE**[®] (Figure 7D) comprises a 0.8mm flexible stranded wire with a looped tip that can be adjusted to different lengths depending on the electrosurgical phase in ESD. This device may be used in all the stages in ESD.

CLUTCH CUTTER[®] (Fujifilm): The **CLUTCH CUTTER**[®] (Figure 7E) is grasping-type rotatable scissor knife. The outer edge of the knife is insulated to avoid unwanted tissue damage. This tool is effective in some difficult situations in ESD, such as paradoxical movements of the scope, submucosal fibrosis and unstable position in the colon due to respiratory movements [10].

ITKNIFE NANO[®] (Olympus Medical Systems Co.): The **ITKNIFE NANO**[®] (Figure 7F) comprises an isolated ceramic ball tip mounted at the tip of the knife. The main applications of this device are for circumferential incision and submucosal dissection phases. Due to the characteristics of this device, a second needle knife will be needed for the initial incision.

HYBRIDKNIFE[®] (ERBE): The **HYBRIDKNIFE**[®] (Figure 7H) has a unique feature. Through the cutting knife runs a central capillary that serves as an ultrafine 120µm water jet [9]. When coupled with a dedicated water surgical unit the ERBEJET 2 provides a high-pressure water jet that can deliver a pressure up to 80 bar. This high-pressure jet can be injected through the mucosa into the submucosa in a needle-less fashion. The knife can be adjusted to the desired length depending on the lesion location. There are three types of knives available: the I-type, which features a straight tip; the T-type with a 1.6mm diameter disk-shaped electrode at the tip; and the O-type with an insulated domelike tip. [9]

FLUSHKNIFE[®] (Fujifilm): As the previous knife, the **FLUSHKNIFE**[®] (Figure 7I) also has a waterjet system incorporated that runs parallel to the knife. Nevertheless this system features a low-pressure jet that can only be injected directly into the submucosa and not through the mucosa as the previous device. The **FLUSHKNIFE**[®] is available in two tip versions: the standard version, **FLUSHKNIFE**, with a straight tip; and the **FLUSHKNIFE BT**[®] which features a ball tip that enables better hemostasis due to reduced current density.



Figure 7: ESD Knives: (A) Hook Knife, (B) Triangle-Tip Knife, (C) Dual Knife, (D) Flex-Knife, (E) Clutch Cutter, (F) IT Knife Nano, (G) Dual Knife J, (H) Hybrid Knife, (I) Flush Knife.

Hemostatic forceps

There are monopolar and bipolar hemostatic forceps that have been designed to treat bleeding as well as prophylactic treatment of thick submucosal vessels. The **COAGRASPER**[®] (Olympus Medical Systems Co.) is a rotating monopolar forceps available in 165cm and 230cm to fit a gastroscope and a colonoscope. The gastric configuration features a 5mm opening diameter jaw and the colonic forceps has a smaller 4mm opening. The **CLUTCH CUTTER**[®], as previously mentioned, can also be used as a coagulation forceps. Some groups in Europe routinely use instead regular hot biopsy forceps as hemostatic devices in endoscopic submucosal dissection.

Caps

Caps are transparent, opaque, or colored hollow cylinders that can be attached to the distal tip of the endoscope. They are available in a variety of sizes and forms and are made by different commercial brands. The proximal part of the cap fits the outer aspect of the distal end of the endoscope. To prevent displacement or even dislodgement of the cap, the cap can be secured to the endoscope by using waterproof adhesive tape. The distal part of the cap is its working part. It

can be conic, straight, or funnel-shaped with a horizontal or oblique end, which, in turn, may be rounded or internally beveled. Some caps have one or more side holes designed to prevent fluid accumulation within the cap. The depth of the cap is important for its diagnostic and therapeutic applications. The depth of the cap may be classified as short (1-2 mm), medium (3-4 mm), and long (>4 mm).[11]

This devices are essential in ESD by many ways: endoscope stabilization, optimum focal distance to ensure a correct magnification visualization, tissue retraction and finally by maintaining adequate separation from the lens during submucosal dissection to avoid “red outs”.

Chromoendoscopy and injection agents

Chromoendoscopy consists in the topical instillation of dyes through an endoscope channel to highlight small details of the mucosa. The two most commonly used dye types are vital or absorptive dyes that are taken up by intestinal cells, such as methylene blue and crystal violet, and contrast dyes such as indigo carmine, which are deposited in the mucosal grooves and enhance subtle mucosal unevenness and lesion demarcation. [12] The dyes can be applied using a spray catheter or directly injected through the working channel.

Different injection agents have been successfully used during ESD. Submucosal injection plays a critical role in providing a sufficiently high submucosal elevation to perform a safe submucosal dissection during ESD. These solutions can be mixed with indigo carmine or methylene blue in order to help demarcate the submucosal tissue from the muscular layer.

Normal saline (NS) has been commonly used for this purpose but, because of its rapid absorption, requires frequent reinjection in order to maintain an adequate fluid cushion. In general hypertonic and viscous solutions create a higher and longer lasting mucosal elevation than NS. **Glycerol** (GLYCEOL, Chugai Pharmaceutical Co, Tokyo, Japan) is a hypertonic solution consisting of 10% glycerin and 5% fructose in an NS solution. An in vitro study [13] was conducted to compare the submucosal elevation caused by Glycerol vs. NS. Glycerol maintained a significantly longer-lasting submucosal elevation than the NS group. Randomized controlled trials comparing NS with alternative solutions have shown that a colloidal solution, **succinylated gelatin** (GELOFUSINE [B.Braun], an inexpensive plasma volume expander), results in fewer injections and improved procedure time in lesions >20 mm. Finally, **Hyaluronic acid** (HA) is a type of glycosaminoglycan found in connective tissue. It has a high viscosity and water retention capability without being antigenic or toxic to humans. Approved indications for its use in clinical practice in many countries are for intra-articular injections for osteoarthritis and eye surgery. A 0.4% solution of HA has been approved for commercial use as a submucosal solution (MUCOUP, Johnson and Johnson Medical Co., Tokyo, Japan) in Japan. HA has provided the longest-lasting fluid, and a higher successful en-bloc resection and lower perforation complication rates have been reported using HA in colorectal agent for submucosal injections¹⁴; however, its disadvantages are mainly high cost (US \$49.50–128.00/mL in the United States) and unavailability [13].

RESULTS

Efficacy

Technical success in ESD is considered as the removal of the target lesion in a single piece (en bloc). Resection is considered complete (defined as R0) when the tumor is removed en bloc with tumor-free horizontal and vertical margins. Resection is considered incomplete when tumors are removed piecemeal, margins are positive for tumor invasion or when the margins are not evaluable because of tissue carbonization (R1), and finally resection success is unknown (Rx) when reconstruction is not possible due to multiple piecemeal fragments.

In the colorectum intramucosal carcinomas have virtually no risk of lymph node metastasis hence an en bloc R0 resection is considered a curative resection. Therefore, in these cases, positive lateral margins are not an indication for surgical treatment and should be endoscopically surveilled. In sessile and flat lesions the depth of invasion plays a critical role since the risk of lymph node metastasis appears significant in lesions with $>1000\mu\text{m}$ ($>1\text{mm}$) submucosal invasion [15]. Also, presence of lymphovascular invasion or poor differentiation are associated with increased risk of lymph node metastasis, independently of the depth or morphology of the tumor and are an indication for surgical treatment [15].

The efficacy of ESD in the colon and the rectum has been well documented in many studies (Table 2). A systematic review published in 2012 by Repici et al. [16] including 2841 lesions, reported a complete resection rate of 96% (95%CI 91%-98%), R0 resection rate of 88% (95 %CI 82 % – 92 %) and a negligible local recurrence rate ($<0.1\%$). Another report by Lee et al. [17] that gathered 1000 cases showed similar results.

Nevertheless western endoscopists have also published results that differ from those reported by more experienced centers, like the multicenter study published by Rahmi et al¹⁸ that gathered 45 cases with an en bloc resection rate of 64%, R0 resection rate of 53% and a local recurrence rate of 7% [18].

Safety

The previously mentioned systematic review published in 2012 showed an adequate safety profile for colorectal ESD [16]. It is well known that this technique poses a low yet significant perforation rate with published results that usually range 2-10% but in some studies up to 18% [18]. Nevertheless nearly all perforations can be managed endoscopically with a reported a post-ESD complication-related surgery of 1%. Delayed bleeding rate in the colon is reported to be low, usually ranging 1-2%, and should be managed endoscopically. Prophylactic coagulation of visible vessels preferable with coagulation forceps has been shown to reduce post-procedural bleeding up to 60% [19].

ESD vs. Surgery

Laparoscopic colorectal resection (LC) is currently a widely accepted treatment for colorectal neoplasms that are deemed not amenable to endoscopic removal. However, LC carries an inherent complication rate of over 15%. Also, for almost 30 years [20], transanal endoscopic microsurgery (TEM) has been the mainstay treatment for large rectal lesions [21]. Our group has also published [22] the utility of combining simultaneous flexible endoscopy with TEM. The endoscope can be introduced through one of the single-incision laparoscopic surgery ports. With the advent of ESD questions have risen regarding the appropriate treatment and, furthermore, few comparative studies have been published.

LC vs. ESD

The only comparative study between colorectal ESD and LC was first published in 2015 by Hon et al. [23] This retrospective cohort study that gathered 120 patients show that ESD could be accomplished with a shorter procedure time (113 ± 66 min vs. 153 ± 43 min, $P < 0.01$) for lesions of comparable size (3.0 ± 1.2 cm vs. 3.4 ± 1.4 cm, $P = 0.22$) and location (colon/rectum: 59/6 vs. colon/rectum: 52/3, $P = 0.43$). Also, ESD appeared to be associated with a lower short-term complication rate, but the difference did not reach statistical significance (10.8% vs. 23.6%, $P = 0.06$). It has to be noted that all perforations were successfully managed by endoscopic clipping without emergency surgical intervention. And finally patients in the ESD arm had a faster recovery than patients in the LC arm, which included shorter time to resume normal diet (2 d vs. 4 d, $P = 0.01$) and a shorter hospital stay (3 d vs. 6 d, $P < 0.01$).

TEM vs. ESD

A large systematic review was published in 2014 by Arezzo et al. [24] included a total of 11 ESD and 11 full-thickness TEM series of studies published between 1984 and 2010 with a total of 2077 patients. The en bloc resection rate was 87.8 % (95 % confidence interval [CI] 84.3-90.6) for the ESD patients versus 98.7 % (95 % CI 97.4-99.3 %) for the TEM patients ($P < 0.001$). The R0 resection rate was 74.6 % (95 % CI 70.4-78.4 %) for the ESD patients versus 88.5 % (95 % CI 85.9-90.6 %) for the TEM patients ($P < 0.001$). The postoperative complications rate was 8.0 % (95 %, CI 5.4-11.8 %) for the ESD patients versus 8.4 % (95 % CI 5.2-13.4 %) for the TEM patients ($P = 0.874$). The recurrence rate was 2.6 % (95 % CI 1.3-5.2 %) for the ESD patients versus 5.2 % (95 % CI 4.0-6.9 %) for the TEM patients ($P < 0.001$). Also, the rate for the overall need of further abdominal treatment, defined as any type of surgery performed through an abdominal access, including both complications and pathology indications, was 8.4 % (95 % CI 4.9-13.9 %) for the ESD patients versus 1.8 % (95 % CI 0.8-3.7 %) for the TEM patients ($P < 0.001$). Therefore, in this study, even though ESD appears a safe and effective technique appears to be less definitive than full-thickness TEM that has shown a higher R0 resection rate, reducing the need for further surgical treatment [25].

Table 2: Outcomes of colorectal ESD.

Study	Lesions included, n	En bloc resection rate, n/N (%)	Complete R0 resection rate, n/N (%)	Local recurrence rate, n/N (%)	Mortality ESD related	Procedure related bleeding, n/N (%)	Procedure related perforation, n/N (%)
Repici 2012 [16]	2841	2727/2841 (96)	2500/2841 (88)	1/1397 (<0.1)	0	47/2841 (2)	135/2841 (4)
Lee 2013 [17]	1000	973/100 (97)	911/1000 (91)	3/722 (<1)	-	4/1000 (<1)	53/1000 (5)
Rahmi 2014 [18]	45	29/45 (64)	24/45 (53)	3/45 (7)	0	6/45 (13)	8/45 (18)

CONCLUSIONS

ESD is an established effective treatment modality for premalignant and early-stage malignant lesions in the colorectum. Compared with EMR, ESD clearly achieves higher rates of en bloc, R0 and curative resections. And, furthermore, offers comparable efficacy and complication rate with surgical interventions having also shown shorter in-hospital stay.

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