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TECHNICAL NOTE

Experience with a new device for pathological assessment of colonic endoscopic submucosal dissection

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Abstract Endoscopic submucosal dissection (ESD) is gaining popularity worldwide in the treatment of neoplastic lesions of the gastrointestinal tract. However, the experience in Western countries is quite limited and restricted to large or academic centers. Besides, this approach requires an optimal pathological assessment. The aim of this study was to report our experience with colonic ESD using a new device that allows complete handling of the resected specimens and especially of lateral margins, for pathological analysis. In a 1-year period, 14 patients (6 men, 8 women, age range 50–82 years) underwent colonic ESD in a non-academic hospital. The endoscopic procedure was carried out successfully *en bloc* in more than 90 % of cases. Perforation requiring surgery occurred in one patient (7 %). Pathological assessment with the new device allowed entire and complete examination of both the deep and lateral margins of the excised specimens. Colonic ESD is a viable option for non-surgical treatment of large bowel lesions even in relatively small centers and in non-academic settings. The new device allows good handling of the specimens, and it seems to be useful for the entire examination of the resection margins.

Keywords Colon · Endoscopic submucosal dissection · Histology · Pathology

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Introduction

In recent years, improvement in the quality of endoscopic imaging and better awareness of the early signs, and symptoms of gastrointestinal tract neoplasms have led to increased recognition and detection of these forms [1]. This, in turn, has stimulated researchers and clinicians to find alternative approaches to surgery, approaches that introduced in clinical practice (after extensive investigation) both endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD). The latter in particular has been used, in the upper and lower gastrointestinal tract, to treat relatively large mucosal cancers [2] and minimally invasive submucosal cancers which have a very low metastatic potential, i.e. those best suited for an endoscopic therapeutic approach [3].

Although ESD is technically more demanding than EMR [4], it became very popular in the East, and results of large series from Asian countries are available [5], whereas the experience in Western countries is much more limited [6]. A recent review highlighted the effectiveness of ESD in treating large colorectal lesions, with good results and relatively low complication rates [7].

Compared with gastric ESD, colorectal procedures are less frequently performed, owing to the greater technical

difficulties due to anatomic factors (narrower lumen, thinner wall), longer procedure time, and increased risk of perforation [8]. The use of colorectal ESD still limited, and surgeons require specific training [9, 10], which is a challenging problem in the West due to the relative paucity of the early lesions [11].

An important point is the appropriate handling of the excised specimens, substantially larger than the common endoscopic biopsies, for a proper pathological evaluation. According to specific guidelines, the specimens should be stretched and pinned on a board in order to be immersed in formalin for fixation [12, 13]. However, such handling may be time-consuming and in addition leads to suboptimal flattening of specimens and alterations in the evaluation of margins due to the multiple pins needed to keep the specimen firmly stretched.

There are only a few articles from Italy describing large bowel (mainly rectal) ESD [14–18]. Here, we report our experience with colorectal ESD and the use of a new device that avoids the use of pins and allows good flattening, to prepare the specimens for pathologic examination.

Materials and methods

Data from all patients undergoing colonic ESD in a single center (Department of Operative Endoscopy, USI Group, Rome) in the period December 2012–December 2013 were retrospectively retrieved and analyzed. Patients were referred for the procedure after having colonic polyps demonstrated in a previous colonoscopy and chose this approach over surgical excision.

Endoscopic procedure

After careful explanation of the procedure, all patients gave written informed consent, and endoscopy was carried out after standard bowel preparation (polyethylene glycol, 4 L). The procedures were performed under general anesthesia in an operative theater; no patient was on anticoagulation therapy.

One of the authors (AT) with more than 15 years of experience in therapeutic colonic procedures underwent ESD training as follows: A first 2-week period at the Endoscopic Division of the National Cancer Center Hospital, Tokyo, Japan, observing and discussing gastric and colonic ESD, in March 2008, followed by ESD procedures performed on humans and supervised by an expert, in May 2008. This author carried out all the ESD procedures.

Endoscopically visualized lesions were classified according to standard criteria (type 0, divided into three categories: protruding (0-I), non-protruding and non-excavated (0-II), and excavated (0-III). Type 0-II lesions are then subdivided into slightly elevated (IIa), flat (IIb), or depressed (IIc). [19, 20]. Olympus colonoscopes (CFQ-165L, Olympus Optical Co, Tokyo, Japan) were used. A single-use distal attachment (short type hood, D-201-11802, Olympus Optical Co, Tokyo, Japan) was placed at the tip of the scope during all the procedures, in order to better visualize the submucosal layer and to provide adequate counter-traction during the resection. The margins of the lesion were evaluated using narrow-band imaging and 0.4 % indigo carmine dye spray. Submucosal injection was carried out with a solution of a mixture of hydroxyethyl starch (Voluven; Fresenius Kabi, Isola Della Scala, Italy), indigo carmine, and epinephrine (1:250.000). This dilution was chosen because in our experience, it was safe to obtain long-lasting vasoconstrictive effect. Additional submucosal injection with the same solution was performed in order to maintain an adequate dissection plane from the muscularis propria and to avoid perforation during the procedure.

After an initial incision in the mucosa, a submucosal circumferential incision was made using Dual Knife (KD-650U, Olympus) or Flush Knife (DK2818J, Fujinon Europe GmbH, Düsseldorf, Germany) with an electrosurgical current applied in endocut mode (50 W), VIO200 (ERBE, Tubingen, Germany). In case of lesions with a larger diameter, the submucosal incision was started on the proximal side of the lesion, and the submucosal dissection was first performed from that side and then completed from the distal side. For all procedures, the submucosal dissection was completed with the same devices, except in one case in which a Hook Knife (KD-620QR, Olympus) was used to complete submucosal dissection. The patient's position was changed as needed to better visualize the dissection plane and to complete the procedure.

Hemostasis of visible vessels to prevent further bleeding was achieved during the procedure with both Dual Knife or Flush Knife and Coagrasper (FD-411UR, Olympus) with coagulation mode (25 W). At the end of the procedure, an attempt was always made to close the defect using endoclips (Resolution Clip, Boston Scientific, Milan, Italy) (Fig. 1a–f).

Tissue processing

The specimen was handled according to the biospecimen reporting for improved study quality (BRISQ) recommendations, with the pathologist receiving a report with the known and applicable specific items (e.g., specimen type, collection site, disease status, clinical characteristics of patients, collection mechanisms, type of preservation, constitution and concentration of fixative/preservation solution) [21]. After excision, the specimen was gently placed on a board which was put into a special fenestrated

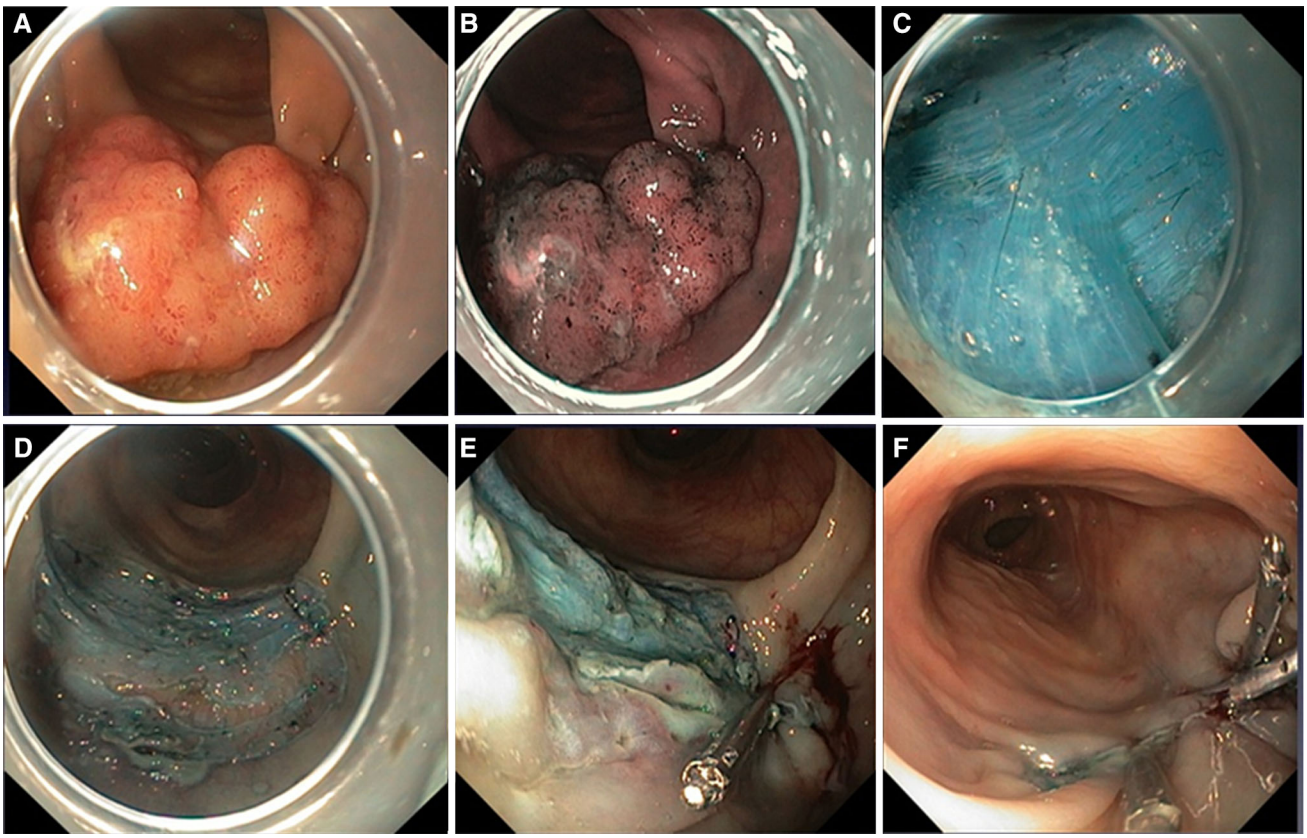

Fig. 1 Large sigmoid polyp, visualized with white light (**a**) and narrow-band imaging (**b**). **c**, **d** Results after endoscopic excision. **e**, **f** Clipping up to closure of the excision margins

box (Biocassette for mucosectomy, Bioptica, Milano, Italy) (Fig. 2a, b), covered with a thin sponge (Fig. 2c), and immersed in neutral buffered formalin 10 % for fixation. The box cover provides gentle pressure on the specimen, allowing flat fixation without distortion, and avoids the use of pins that may alter a correct evaluation of the margins (Fig. 2d). Therefore, the specimens were photographed, sectioned thinly along the minor axis (Fig. 2e), and paraffin embedded. After a first section of the internal part of the specimen, lateral parts (resection margins) were re-inclosed after a rotation of 180° and then cut again (Fig. 2f), in order to better visualize the margins and improve the diagnostic yield, according to a previously described method [22]. Histology slides were prepared using conventional hematoxylin & eosin staining, and immunohistochemistry was performed when needed.

Ethical considerations

Since this was a retrospective study, no individual patient identification was involved, and no study-driven clinical intervention was performed; moreover, the study was an extension of existing procedures; therefore, the institutional review board waived formal review and approval.

Results

In the study period, 14 patients (6 men, 8 women, age range 50–82 years) underwent colonic ESD. Tables 1, 2 show the demographic, anatomic, endoscopic, and pathologic results obtained in this group of patients. The mean diameter of the lesions was 3 ± 0.3 cm (range 1.5–5.5 cm), and the mean operative time was 123 ± 47 min (range 60–240 min). All lesions but one (93 %) were resected *en bloc*, and the resection was complete in 12 (86 %) cases. In two lesions both with positive lateral margins, one located in the ileocecal valve and the other in the sigmoid, we still obtained curative resections because one was an adenoma with high-grade dysplasia and the other sigmoid lesion with only slight submucosal invasion [<1,000 μm (SM1)], with no lymphatic and vascular involvement and no poorly differentiated components.

The new cassette device for pathologic examination allowed complete assessment of the whole specimens and of their deep and lateral margins (Table 2; Fig. 3a–h). Complete examination of the lateral margins was possible in 100 % of the specimens.

Concerning complications, there was a case of minor bleeding (managed only by clinical observation) and four

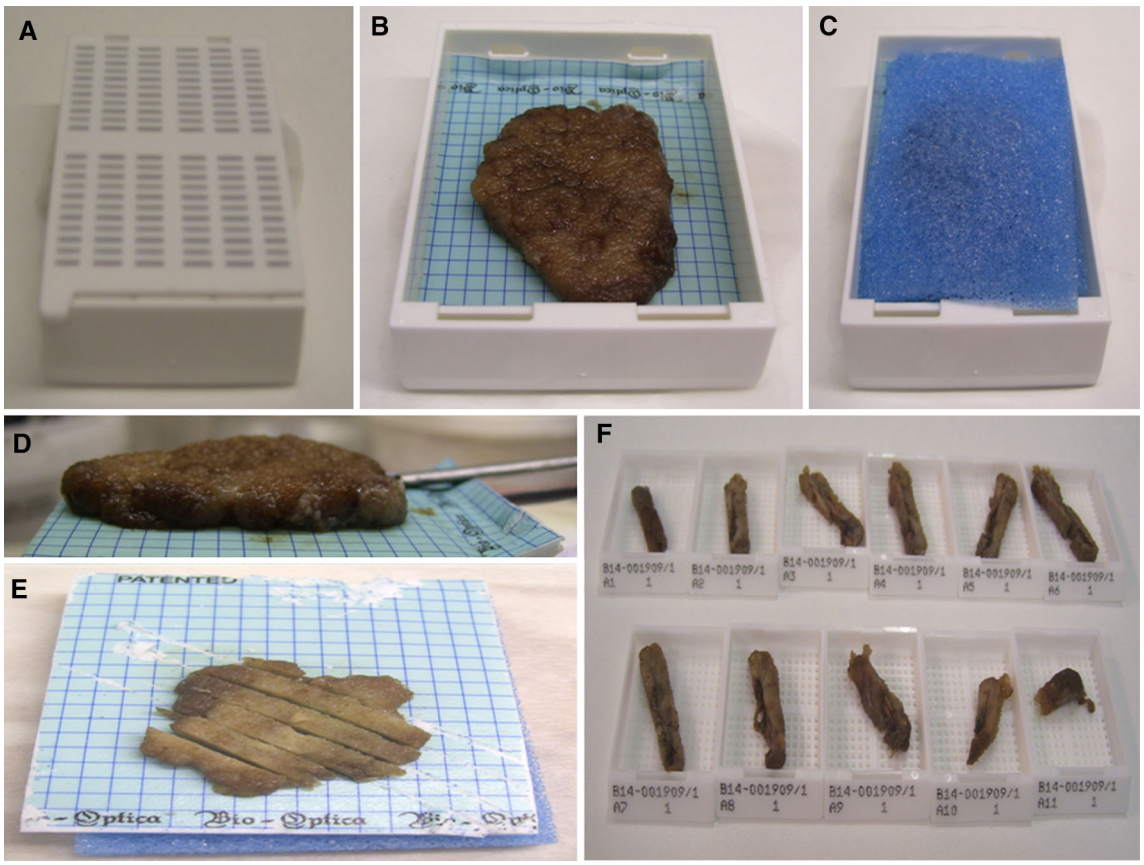

Fig. 2 **a** Picture of the fenestrated biocassette. **b** The specimen is put in the cassette and covered with a sponge (**c**). Once fixed, pictures are taken (**d**) and multiple sections made (**e**, **f**) for pathologic analysis

Table 1 Demographics and clinical characteristics of the resected lesions

No	Sex/age (years)	Location	Maximum diameter (cm)	Type (Paris)	En bloc	Complete	Complications	Management
1	F/50	Right colon	2.2	0-Is	Yes	Yes	No	–
2	F/51	Rectum	2.5	LST–G	Yes	Yes	No	–
3	F/56	Ileocecal valve	3.5	0-Is + IIa	Yes	No	No	–
4	F/55	Sigmoid colon	3	0-Is	Yes	Yes	P	CL
5	F/73	Sigmoid colon	1.5	LST–NG	Yes	Yes	P	CL + A
6	F/71	Descending colon	2	LST–NG	Yes	Yes	P	Surgery
7	M/70	Rectum	2.5	0-IIb	Yes	Yes	B	No
8	F/82	Sigmoid colon	4	0-Is	Yes	Yes	No	–
9	M/76	Descending colon	2	0-IIa + IIc	Yes	Yes	No	–
10	M/56	Sigmoid colon	5.5	0-Is	No	No	No	–
11	M/55	Rectum	2.5	LST–G	Yes	Yes	P	CL + A
12	M/77	Rectum	3	LST–G	Yes	Yes	No	–
13	M/81	Rectum	5	0-Is	Yes	Yes	No	–
14	F/72	Right colon (relapse of previous mucosectomy)	3	LST–G	Yes	Yes	No	–

A broad-spectrum antibiotic therapy, *B* bleeding, *CL* endoscopic clipping, *LST* laterally spreading tumor, *G* granular, *NG* non-granular, *P* perforation

Table 2 Pathological results of the resected lesions

No	Histology	Deep margin	Lateral margin
1	TVA + HGD	Negative	Negative
2	TVA + LGD	Negative	Negative
3	TVA + LGD + HGD	Negative	Positive (one margin)
4	TVA + LGD	Negative	Negative
5	TVA + LGD	Negative	Negative
6	TVA + LGD	Negative	Negative
7	TVA + LGD + HGD	Negative	Negative
8	TVA + LGD + HGD	Negative	Negative
9	TVA + LGD	Negative	Negative
10	Serrated adenoma + HGD + AC	Negative	Positive (both)
11	TVA + LGD	Negative	Negative
12	TVA + LGD	Negative	Negative
13	TVA + LGD + HGD	Negative	Negative
14	TA + LGD + HGD	Negative	Negative

AC Adenocarcinoma, *HGD* high-grade dysplasia, *LGD* low-grade dysplasia, *TA* tubular adenoma, *TVA* tubulovillous adenoma

perforations. Three of the perforations were treated conservatively with mucosal clipping and medical therapy, whereas the fourth (which occurred after excision of a laterally spreading tumor, non-granular type, located in the anterior wall of the left colon) required surgery (left hemicolectomy). There was no relationship between perforation and the size of the lesion. After an observation period of 2–4 days, all patients treated conservatively were sent home without further problems, whereas the surgical patient was discharged after 12 days.

Seven patients completed follow-up, which included colonoscopic examination at 3, 6, and 12 months. No disease recurrence was reported in the five patients in whom complete resection was achieved and in the two patients with histologically positive lateral margins.

Discussion

There is a growing interest in non-surgical approaches to gastrointestinal mucosal lesions detected at endoscopy. Because of this, ESD has gained popularity in the East

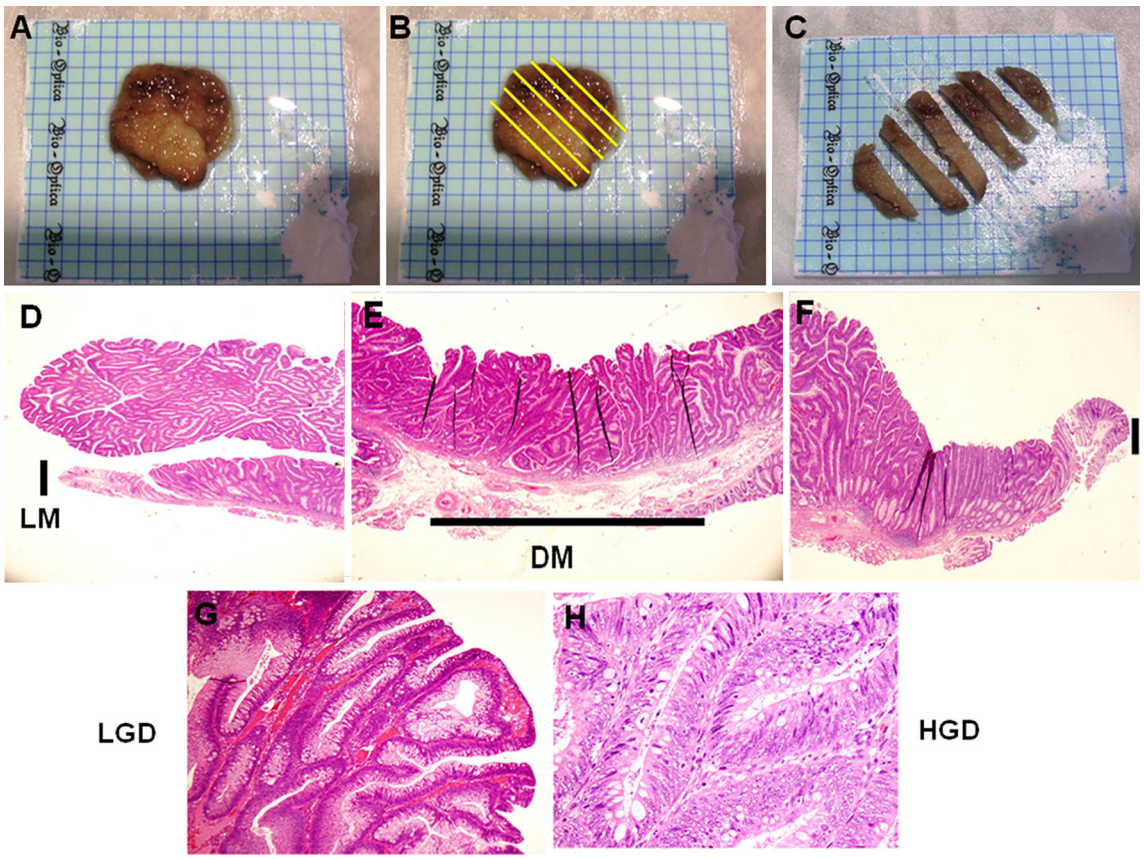

Fig. 3 a–h Representative results as provided from the pathology report. *DM* deep margin, *HGD* high-grade dysplasia, *LGD* low-grade dysplasia, *LM* lateral margin

[23], whereas experience in Western countries, especially for the large bowel, is still limited. Only a few studies are available from Western countries and only a handful from Italy, mostly on rectal lesions [14–18].

Here, we report our experience with colonic ESD in both proximal and distal colonic segments, with 64 % of the lesions located outside the rectum. Overall, this endoscopic approach was quite successful, allowing resection *en bloc* of more than 90 % of the lesions, and most of these were completely excised. All the complications that occurred during ESD were minor and treated conservatively, with only one patient requiring surgery. Complication rate observed in our series is very similar to those reported in other studies from Italy [15]. The new device we used to process the specimens, by simultaneously avoiding distortion by pins and providing optimal fixation through gentle flattening by the special cassette, allowed accurate sectioning of the resection margins and an optimal histological definition of the accuracy of ESD. This was increased by the rotation and re-inclusion of the lateral margins, according to a technique previously validated for esophageal mucosectomies [22]. Although not formally tested in this study, we feel that this handling of specimens may be faster, require less training, and improve tissue evaluation of the margins by better flattening and less distortion. In fact, it was possible to examine completely the lateral margins in all cases, whereas fixation and sectioning with conventional methods, in addition to pin-induced distortion, allow complete examination of the lateral margins in only about 50 % cases. This method allowed us to demonstrate histological tumor-free resection margins in 86 % of cases.

Conclusions

After a specific training, it is possible to carry out successfully colonic ESD in most endoscopic centers, even relatively small ones, or in non-academic settings. Optimal handling of the resected specimens offers a further chance of increasing the diagnostic yield and optimizing the results obtained after ESD. Further studies are needed, and close collaboration between clinicians, endoscopists, and pathologists is of paramount importance in determining the value of this treatment method in daily clinical practice.

Conflict of interest None.

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