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## Efficacy and safety of endoscopic submucosal dissection for submucosal tumors of the colon and rectum

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**Background and Aims:** Endoscopic submucosal dissection (ESD) of colorectal submucosal tumors (SMTs) is becoming increasingly common; however, there have been few large consecutive studies analyzing its therapeutic efficacy and safety. The aim of this study was to evaluate the efficacy, safety, and long-term outcomes of ESD for colorectal SMTs.

**Methods:** This retrospective study included 412 consecutive patients with colorectal SMTs who underwent ESD at the Zhongshan Hospital of Fudan University from January 2008 to July 2014. Tumor histopathology, completeness of resection, adverse events, tumor recurrence, and distant metastasis were analyzed.

**Results:** Complete resection was achieved for 358 lesions (86.9%). Thirteen patients had serious adverse events (3.2%) including bleeding and perforation, and 28 patients (6.8%) had post-ESD electrocoagulation syndrome (PEECS). Because more ESDs for colorectal SMTs were performed by endoscopists, the rate of complete resection increased (78.5% vs 88.5%), and the rate of serious adverse events decreased (9.2% vs 2.0%). SMTs in the colon increased the risk of incomplete resection (19.6% vs 11.3%), serious adverse events (8.7% vs 1.6%), and PEECS (16.3% vs 4.1%). SMTs originating from the muscularis propria and sized  $\geq 20$  mm increased the rate of PEECS (22.7% vs 5.9% and 31.3% vs 5.8%, respectively).

**Conclusion:** ESD is effective for resection of colorectal SMTs and rarely causes serious adverse events. Tumor location and the experience of endoscopists influence the complete resection rate and the development of serious adverse events. ESD is feasible for large tumors and tumors in the muscularis propria, but this is associated with relatively high risks of adverse events. (Gastrointest Endosc 2018;87:540-8.)

Recently, an increasing number of small and asymptomatic GI submucosal tumors (SMTs) have been diagnosed via the widespread use of digestive endoscopy and advances in EUS. In general, the management of SMTs includes 2 unsatisfactory options, namely, watchful waiting for SMTs <2.0

cm or highly invasive surgical resection for large lesions.<sup>1</sup> However, some SMTs, such as neuroendocrine tumors (NETs), GI stromal tumors, and granular cell tumors, have malignant potential.<sup>2-4</sup> Furthermore, when the tumor grows, patients may lose the opportunity to receive

*Abbreviations:* ESD, endoscopic submucosal dissection; NET, neuroendocrine tumor; PEECS, post-ESD electrocoagulation syndrome; SMT, submucosal tumor.

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minimally invasive treatment.<sup>5</sup> Therefore, the minimally invasive resection of these SMTs is crucial.

Endoscopic submucosal dissection (ESD) is a technique for endoscopic tissue resection that enables endoscopists to control the depth and direction of diathermic knife incisions. This technique has made it possible to resect even large mucosal or submucosal lesions en bloc. Recently, the number of reports in which ESD has been used to successfully treat colorectal SMTs has increased.<sup>4,6</sup> However, large consecutive studies analyzing the long-term outcomes of using this technique for SMTs have not been reported. In this study, we investigated the efficacy and safety of ESD for colorectal SMTs in a large series of patients and examined its long-term outcomes.

## METHODS

### Patients

We studied 412 cases of colorectal SMTs that were treated at 1 center, Zhongshan Hospital of Fudan University, from January 2008 to July 2014. All tumors were evaluated by using EUS (20 MHz miniprobe EUS for SMTs <10 mm, 12 MHz miniprobe EUS for SMTs  $\geq$ 10 mm) and CT before ESD for detecting the origin of the tumor and metastasis. The inclusion criteria for ESD of colorectal SMTs were (1) the tumor originated predominantly from the mucosa and/or submucosa and muscularis propria layer without restriction of extraluminal growth, (2) SMTs were detected without metastasis by using EUS and CT, (3) the diameter of the tumor was <20 mm if the SMT was predicted to be potentially malignant by EUS or biopsy, (4) any SMT that could not be diagnosed conclusively by EUS and/or EUS guided FNA and required histopathological examination, (5) patients with colorectal symptoms, and (6) patients who became stressed when recommended periodic follow-up and were specifically referred for endoscopic resection or aggressive treatment. Exclusion criteria were (1) disagreement regarding resection, (2) tumor diameter >50 mm, and (3) coagulation disorders. This project was approved by the institutional review board (No. 2009-135), and informed consent was obtained for all of the procedures and interventions described.

### Procedures

All ESD procedures were performed by 4 operators (Y.L.Q., Z.P.H., X.M.D., and Z.Y.S.) who are ESD specialists. Patients were treated under intravenous anesthesia while the parameters of cardiorespiratory function such as heart rate, blood pressure, and oxygen saturation were continuously monitored. Standard endoscopy (GIT-H260; Olympus, Tokyo, Japan) was used during the procedures. A short, transparent cap (ND-201-11802; Olympus) was attached to the front of the endoscope to provide a constant endoscopic view and to apply tension to the connective tissues during dissection. An insulation-tipped knife

and/or a hook-knife (KD-611 and KD-620LR; Olympus) was used to dissect the submucosal layer and to peel the tumor. The high-frequency generator used was the 200D system (ERBE, Shanghai, China). Other equipment included injection needles (NM-4L-1), snares (SD-230U-20), hot biopsy forceps (FD-410LR), and clips (HX-610-135) (all from Olympus).

ESD was performed as follows: (1) Marker dots were made about 5 mm from the lesion. (2) Several milliliters of solution (100 mL saline solution, 5 mL 0.8% indigo carmine, and 1 mL epinephrine) were injected around the lesion by using a 23-gauge disposable needle to lift the lesion off the muscularis propria layer. If the tumor originated from the muscularis propria, only the mucosa was lifted and not the tumor. (3) The mucosa was incised outside the marker dots by using the needle-knife. (4) The submucosal connective tissue beneath the lesion was gradually dissected with the aid of the transparent cap; the afore-mentioned solution was injected repeatedly during the dissection when necessary, and direct dissection of the submucosal layer was carried out until complete removal was achieved. (5) If the tumor originated from the muscularis propria, the insulation-tipped knife was used to peel the muscularis propria layer along the capsule of the lesions. The solution was injected repeatedly during dissection if necessary. Finally, (6) the lesion was resected completely from the muscularis propria layer with the needle-knife. As described in previous reports,<sup>7,8</sup> after ESD exposed vessels on the artificial ulcer were treated with argon plasma coagulation to prevent delayed bleeding (Fig. 1).

### Pathology examination

Tissue specimens were fixed by using 10% formalin solution embedded with paraffin and sectioned for histopathologic evaluation of the resected specimens. En bloc resection was defined as excision of a tumor in 1 piece without fragmentation. Complete resection was defined as en bloc resection of a lesion, with a tumor removed in a single piece, with the capsule intact.<sup>9</sup> In addition, the World Health Organization classification of tumors of the digestive system was used for histopathologic evaluation.<sup>10</sup> When the organization of a tumor was difficult to determine, immunohistochemistry was performed.<sup>11,12</sup>

### Adverse events

Postoperative bleeding was defined as hematochezia or melena requiring an endoscopic hemostatic procedure any time between 0 and 14 days after completion of ESD (Fig. 2A). Perforation was defined as colorectal wall penetration observed during or detected after the endoscopic procedure via radiologic examination by using a technique such as abdominal plain radiography or CT (Fig. 2B and C). All perforations that received a positive therapeutic intervention were defined as serious adverse events. Post-ESD electrocoagulation syndrome

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