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# Current Techniques for Treating Gastrointestinal Stromal Tumors in the Upper Gastrointestinal Tract

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Most gastrointestinal stromal tumors (GISTs) arise from the proper muscle layer of the upper gastrointestinal (GI) tract and have a low malignant potential. They are sometimes accompanied by symptoms, but in most cases are detected by chance. Endoscopic surgery of subepithelial tumors in the upper GI tract has been actively performed, and its merits include the need for fewer medical devices compared with other surgical procedures and post-resection organ preservation. However, because endoscopic procedures are still limited to small or pilot studies, a multidisciplinary approach combining laparoscopy and endoscopy is needed for more effective and pathologically acceptable management of GISTs. Many new endoscopic surgeries have been developed, and this review describes the current status of and the new approaches for endoscopic surgery of GISTs in the upper GI tract. **Clin Endosc 2016;49:226-228**

**Key Words:** Gastrointestinal stromal tumors; Endoscopic surgery; Endoscopic full-thickness resection

## INTRODUCTION

Most subepithelial tumors (SETs) are asymptomatic and found in only about 0.3% of all endoscopic examinations.<sup>1</sup> Owing to limited information about the natural course and malignant potential of SETs less than 2 cm in size and the difficulty in targeting and completely resecting such tumors, regular follow-ups rather than resection have been recommended.<sup>2-4</sup> However, according to previous reports, up to 3.7% of gastrointestinal stromal tumors (GISTs) less than 2 cm in size and benign-appearing on endoscopic ultrasonography have a high mitotic index<sup>5</sup> and rapidly increase in size, and hence have a high risk of malignancy.<sup>6</sup> Therefore, resection procedures that allow a definitive diagnosis as well as an evaluation of malignant potential are needed. Furthermore, complica-

tions resulting from repetitive endoscopic procedures that delay diagnosis may arise, and doctor-patient relationships may be influenced by indecisiveness on the part of the physician.

Surgical approaches for GISTs in the upper gastrointestinal (GI) tract include open surgery and laparoscopic surgery, both of which are more invasive than is endoscopic surgery and potentially lead to several complications.<sup>7</sup> On the other hand, most endoscopic methods, including endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD), are usually only applicable to the submucosal layer of the gastric wall. Complete resection often fails because GISTs are tightly connected to the underlying muscle. Therefore, many endoscopic surgeries have been developed and attempted. In this article, recent developments in the procedures for treating GISTs in the upper GI tract are discussed.

## EMR AND ESD

Endoscopic resection is indicated for GISTs in the upper GI tract that are located in the proper muscle (PM) layer and protrude into the endoluminal side. GISTs arising from the PM layer are not easily, completely, or safely resected via EMR or ESD alone. Owing to the high risk of perforation when resect-

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ing SETs deep in the GI wall, deep submucosal and muscular dissection around the tumor should be carefully performed. Perforation after dissection and margin involvement are frequently observed. Several studies reported high *en bloc* resection rates (64% to 94%) and low perforation rates (0% to 12%) for ESD of GISTs.<sup>8-10</sup>

## ENDOSCOPIC MUSCULARIS DISSECTION

Endoscopic muscularis dissection (EMD) involves pre-cutting the mucosa that covers the tumor via a longitudinal incision, endoscopically dissecting the tumor away from the submucosal and PM layers, and closing the wound with clips. Perforations occurring during dissection are closed by using only endoscopic devices, and a longitudinal incision is usually used during this procedure. EMD can be performed within a relatively short period of time, and injuries to the overlying mucosa are minimal, resulting in easier mucosal closure. In 2012, Liu et al.<sup>11</sup> reported that EMD completely removed 30 of the 31 tumors (96.8%; 14 esophagus, seven cardia, and 10 stomach tumors) in their study. The mean size of the SET was 22.1 mm, and the procedure required 76.8 minutes (range, 15 to 330). Perforation occurred in four patients (12.9%), all of whom were managed successfully by using endoscopic devices.

## ENDOSCOPIC SUBMUCOSAL TUNNEL DISSECTION

Endoscopic resection without laparoscopic assistance has recently come to be regarded as a minimally invasive method for treating SETs. However, it is not commonly used to resect tumors that have invaded the muscular layer because it requires advanced skill, and the need to suture intentionally perforated holes after resection increases the length of the procedure. In 2012, Inoue et al.<sup>12</sup> proposed an endoscopic submucosal tunnel dissection (ESTD) technique for SETs that consisted of five major procedures: (1) creation of a mucosal entrance 2 to 3 cm in size 5 cm above the tumor; (2) creation of a submucosal tunnel to provide endoscopic working space; (3) separation of the tumor from the covering submucosa; (4) dissection of the tumor away from the PM layer; and (5) closure of the mucosal entry after specimen retrieval. Gong et al.<sup>13</sup> successfully resected 10 of 12 SETs (83.3%; eight esophagus and four cardia tumors) by using ESTD with *en bloc* resection. The mean resected tumor size was 19.5 mm, and the mean operation time was 48.3 minutes (range, 30 to 60). All

complications were resolved by using only conservative medical management. The most important advantage of ESTD is the maintenance of the mucosal integrity of the GI tract.

## ENDOSCOPIC FULL-THICKNESS RESECTION

Endoscopic full-thickness resection (EFTR) was designed to resect gastric SETs located in the PM layer. It consists of four steps: (1) circumferential incision around the tumor; (2) an incision as far as the subserosal layer along the circumferential incision; (3) removal of the tumor including the surrounding PM layer and serosa by using a snare immediately after partial perforation; and (4) closure of digestive wall defects by using endoscopic closure devices. Zhou et al.<sup>14</sup> successfully used EFTR to remove 26 gastric SETs originating in the PM layer. The complete resection rate was 100%, the mean operation time was 105 minutes (range, 60 to 145), and the mean size of the resected lesions was 2.8 cm (range, 1.2 to 4.5). In the study by Ye et al.,<sup>15</sup> complete resection via EFTR was achieved in 50 cases (98.0%).

Advances in the over-the-scope clip (OTSC) system led to the use of OTSC devices for removal of SETs. Sarker et al.<sup>16</sup> was the first to perform a snare resection after clipping with an OTSC device, and Schmidt et al.<sup>17</sup> developed a device for full-thickness resection. Both methods involve suctioning the SET lesion into an endoscopic cap using grasping forceps. Once applied, the OTSC device captures the pathologic lesions, and the snare removes intentionally created pseudopolyps. The full-thickness resection device is an endoscopic suturing device that captures the muscularis layer below the pathologic lesion and resects the lesion after submucosal resection.<sup>17</sup>

## CONCLUSIONS

Owing to technical advances in endoscopic surgery and increases in the numbers of experienced endoscopists, various endoscopic technologies for resection of GISTs in the upper GI tract have been developed. The key to improving therapeutic outcomes following endoscopic enucleation of these tumors is to minimize the number of incomplete resections and maximize safety. However, perforations and pseudocapsule injuries, which can increase procedure time and peritoneal seeding, are possible. Furthermore, information regarding the use of endoscopy procedures is still limited to case reports and small or pilot series. In the future, large-scale studies in clinical practice are required to accurately assess the efficacy

and safety of these procedures.

### Conflicts of Interest

The authors have no financial conflicts of interest.

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