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## Long-Term Outcomes after Endoscopic Treatment of Gastric Gastrointestinal Stromal Tumor

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Endoscopic resection of gastric subepithelial tumors (SETs) has several advantages over biopsy techniques, such as superior diagnostic yield and definite diagnosis. Removal of gastric SETs and histopathologic confirmation should be considered whenever gastric SETs are highly suspected to have malignant potential such as gastrointestinal stromal tumor (GIST) or neuroendocrine tumor. According to our clinical experience, we suggest that endoscopic resection of gastric SETs is feasible for GISTs less than 3.0 cm without positive endoscopic ultrasonography findings or for hypoechoic SETs less than 3.0 cm. However, serious complications such as macroperforation may occur during endoscopic resection, and this procedure is highly dependent on endoscopists' skills. We recently reported the long-term clinical outcomes of endoscopic resection of gastric GIST, which showed a relatively low recurrence rate (2.2%) during long-term follow-up (46.0±28.5 months) despite the low R0 resection rate (25.0%). We suggest that endoscopic surveillance might be possible without additional surgical resection in completely resected GISTs without residual tumor confirmed to be lower risk, even if they show an R1 resection margin. **Clin Endosc 2016;49:232-234**

**Key Words:** Subepithelial tumor; Gastrointestinal stromal tumors; Endoscopy

### INTRODUCTION

Subepithelial tumors (SETs) in the stomach are usually found incidentally during endoscopic examinations.<sup>1</sup> Most gastric SETs do not cause symptoms and were formerly considered to have a benign nature, such as lipomas, inflammatory fibroid polyps, or several neural origin tumors (i.e., schwannomas).<sup>2</sup> However, several gastric SETs have malignant potential, especially when they originate from the muscularis propria (MP) layer, such as gastrointestinal stromal tumors (GISTs), neuroendocrine tumors (NETs), glomus tumors, and even metastatic tumors.<sup>3</sup> Thus, removal of gastric SETs and histopathologic confirmation are required when GIST or NET

is highly suspected.

In this review, we summarize the critical points when planning endoscopic resection of gastric SETs as well as the long-term clinical outcomes of endoscopic resection of gastric GIST.

### CONSIDERATIONS FOR ENDOSCOPIC RESECTION OF GASTRIC SETs

Endoscopic resection of gastric SETs has several advantages over biopsy techniques. First, diagnostic yield can be improved by obtaining whole SET tissue; thus, endoscopists can avoid frequent re-examination. Second, physicians are able to confidently provide a therapeutic plan to patients according to definite diagnosis; thus, reassuring patients and reducing their anxiety. Third, insurance-related conflicts can be avoided. Unfortunately, neither strict guidelines nor widespread acceptance for endoscopic resection as the treatment for gastric SETs have yet been established. We cautiously suggest indications for endoscopic resection based on our clinical ex-

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**Table 1.** Results of Endoscopic Treatment of Subepithelial Tumor in the Upper Gastrointestinal Tract

Study	Method	No. of case, total (E/S/D)	Layer of origin, mm/sm/mp	Dx., GIST/ other	Complete resection, n (%)	Perforation, n (%)
Li et al. (2013) <sup>6</sup>	ESD	11 (0/11/0)	0/0/11	8/3	10/11 (91)	3/11 (27)
Chun et al. (2013) <sup>7</sup>	ESD	35 (0/35/0)	0/0/35	10/25	26/35 (74)	2/35 (5.7)
Lee et al. (2006) <sup>8</sup>	ESD/EMD	12 (0/12/0)	0/0/12	8/4	9/12 (75)	0/12 (0)
Park et al. (2004) <sup>9</sup>	EE-I	15 (5/10/0)	1/2/11	4/11	14/15 (93)	1/15 (7)
Goessl et al. (2007) <sup>10</sup>	EE-I	3 (0/3/0)	0/0/3	3/0	3/3 (100)	0/3 (0)
Sun et al. (2004) <sup>11</sup>	Band ligation	64 (50/12/2)	0/0/64	0/64	61/64 (95)	0/64 (0)
Hoteya et al. (2009) <sup>12</sup>	ESD	9 (0/9/0)	mm or sm only	1/8	9/9 (100)	0/9 (0)
Bialek et al. (2012) <sup>13</sup>	ESD	37 (0/37/0)	0/15/22	17/20	30/37 (81)	2/37 (5.4)
Catalano et al. (2013) <sup>14</sup>	ESD	20 (0/20/0)	0/17/3	10/10	18/20 (90)	3/20 (15.0)
He et al. (2013) <sup>16</sup>	ESD	144 (0/144/0)	0/0/144	89/55	134/144 (92)	21/144 (14)
Zhang et al. (2013) <sup>17</sup>	ESD	18 (0/18/0)	0/0/18	13/5	17/18 (94)	2/18 (11)

E/S/D, esophagus/stomach/duodenum; mm/sm/mp, muscularis mucosa/submucosa/muscularis propria; Dx., diagnosis; GIST, gastrointestinal stromal tumor; ESD, endoscopic submucosal dissection; EMD, endoscopic muscular dissection; EE-I, *en bloc* enucleation with IT-knife.

periences as follows: GISTs less than 3.0 cm without positive endoscopic ultrasonography (EUS) findings (i.e., irregular borders, cystic space, ulceration, echogenic foci, and heterogeneity) or hypoechoic SETs less than 3.0 cm. However, there are several limitations in applying these indications. First, the tumor should be smaller than 3.0 to 4.0 cm, even though the exact cut-off limit remains controversial. If the tumor is larger than this limit, endoscopic resection might be technically unavailable or cause serious complications including macroperforation. Second, the endoscopic procedure is operator-dependent, because the techniques mentioned above require highly advanced skills and sufficient clinical experience. Third, only limited studies including small numbers of patients and short-term follow-up periods have been published and are thus subject to selection biases. Table 1 summarizes procedure-related outcomes of endoscopic resection of SETs in the upper gastrointestinal tract (UGIT).

Another important issue concerning endoscopic resection is post-procedural use of imatinib. Recent guidelines from the National Comprehensive Cancer Network state that if GISTs are completely resected (including R1 resection), adjuvant therapy with imatinib can be considered, especially for patients with a significant high risk of recurrence (intermediate or high risk by recent World Health Organization classifications).<sup>4</sup> However, imatinib therapy followed by endoscopic resection is neither approved nor covered by the national health insurance system in Korea, and guidelines from the Korean GIST Study Group suggest that complete *en bloc* resection with negative margins should be performed regardless of tumor size; therefore, even if the tumor is small, endoscopic shell-out procedure or enucleation should be avoided if GIST

is suspected.<sup>5</sup> Further discussion and opinions should be based on clinical outcomes and long-term follow-up data of endoscopic procedures.

## LONG-TERM CLINICAL OUTCOMES OF ENDOSCOPIC TREATMENT OF GASTRIC GIST

As technical skills have advanced and novel endoscopic procedures have been developed, complete *en bloc* endoscopic resection of gastric SETs has been reported.<sup>6-17</sup> However, they included only a small number of gastric GISTs, and their long-term follow-up results have not yet been reported. Recent studies have reported no recurrence of gastric GISTs resected by endoscopic procedure; however, their follow-up periods were relatively short, ranging from 1 to 2 years.<sup>16,17</sup> Here, we show our clinical outcomes of endoscopic resection for gastric GISTs.<sup>18</sup> A total of 249 patients with SET in the UGIT underwent endoscopic resection in our hospital; among them, 89 cases were confirmed as gastric GIST by histopathologic examination. The most common site of the gastric GISTs was the gastric body (43.3%), followed by the cardia (22.2%) and fundus (21.1%). The mean tumor size was 2.3±1.2 cm, and most were considered to have originated from the MP layer (64.4%) based on pre-procedural EUS findings. Most of the tumors were resected by endoscopic submucosal dissection (80.0%), followed by submucosal tunneling endoscopic resection (8.9%), and two cases (2.2%) by endoscopic full-thickness resection. The complication rate was 14.4%, including micro- and macroperforation (5.6%/4.4%, respectively) and major

bleeding (2.2%). The recurrence rate was relatively low (2.2%) during the long-term follow-up period (46.0±28.5 months) despite the low R0 resection rate (25.0%) and did not differ significantly from that of surgically resected gastric GIST (5.0%). This comparable recurrence rate may be explained by the fact that most of the gastric GISTs in the endoscopic resection group had smaller sizes and low mitotic index counts (<5/high power field, 84.4%), which consequently corresponded to very low (50.0%) and low (31.1%) risk. Indeed, if a GIST is completely resected without residual tumor in an endoscopic view and is classified as lower risk by histopathological evaluation, the endoscopic procedure may be an alternative choice for optimal treatment of GIST in the UGIT, even with R1 resection margins. Further evaluation with large-scale prospective studies is needed to clarify this issue.

## CONCLUSIONS

Endoscopic resection of gastric GIST is increasingly used for tissue diagnosis and treatment, and is expected to be a substitute for surgical resection in selected cases. Endoscopic resection is a feasible and effective alternative therapeutic modality for lower risk gastric GIST with acceptable long-term follow-up results.

### Conflicts of Interest

The author has no financial conflicts of interest.

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