Gut and Liver
https://doi.org/10.5009/gnl210454
pISSN 1976-2283 eISSN 2005-1212

Original Article

Clinical Efficacy and Safety of Endoscopic Treatment of Gastrointestinal Stromal Tumors in the Stomach

Moon Kyung Joo[1], Jong-Jae Park[1], Yeon Ho Lee[1], Beom Jae Lee[1], Seong Min Kim[1], Won Shik Kim[1], Ah Young Yoo[1], Hoon Jai Chun[2], and Sang Woo Lee[3]

[1]Division of Gastroenterology, Department of Internal Medicine, Korea University Guro Hospital, Korea University College of Medicine, [2]Division of Gastroenterology, Department of Internal Medicine, Korea University Anam Hospital, Korea University College of Medicine, Seoul, and [3]Division of Gastroenterology, Department of Internal Medicine, Korea University Ansan Hospital, Korea University College of Medicine, Ansan, Korea

Article Info

Received October 1, 2021
Revised February 4, 2022
Accepted March 15, 2022
Published online February 15, 2023

Corresponding Author

Jong-Jae Park
ORCID https://orcid.org/0000-0002-4642-5405
E-mail gi7pjj@korea.ac.kr

Background/Aims: Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors in the stomach. We evaluated the clinical outcomes of endoscopic treatment for gastric GISTs.

Methods: This is a single center, retrospective study that enrolled 135 cases of gastric subepithelial tumors (SETs) resected by endoscopic procedures and confirmed as GISTs by histopathology from March 2005 to July 2019. The immediate and long-term clinical outcomes were analyzed retrospectively.

Results: The mean patient age was 57.9 years, and the mean tumor size was 2.1 cm. Of the tumors, 43.0% were located in the body, followed by the fundus (26.7%) and cardia (17.0%). Most tumors (85.2%) were resected by endoscopic submucosal dissection, followed by endoscopic mucosal resection (6.7%), submucosal tunneling endoscopic resection (5.9%), and endoscopic full-thickness resection (2.2%). Macroperforation occurred in 4.4% and microperforation in 6.7% of the cases. The R0 resection rate was 15.6%. However, the rate of complete resection by the endoscopic view was 90.4%, of which 54.8% of cases were in the very-low-risk group, followed by the low-risk group (28.1%), intermediate-risk group (11.9%), and high-risk group (5.2%). During 36.5 months of follow-up, recurrence was found in four (3.4%) of the 118 patients who were monitored for more than 6 months (low-risk group, 1/37 [2.7%]; intermediate-risk group, 2/11 [18.2%]; high-risk group, 1/6 [16.7%]).

Conclusions: Endoscopic treatment of a GIST appears to be a feasible procedure in selected cases. However, additional surgery should be considered if the pathologic results correspond to intermediate- or high-risk groups. **(Gut Liver 2023;17:217-225)**

Key Words: Gastrointestinal stromal tumors; Endoscopy; Recurrence

INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors and originate from the interstitial cells of Cajal in the gastrointestinal (GI) tract. In several studies, the endoscopic ultrasonography (EUS) characteristics that could predict the malignant potential of GISTs included large size (>3 cm), heterogeneous echogenicity, irregular extraluminal borders, cystic changes, calcification, exogastric growth, echogenic foci, lobulation, and ulceration.[1-3] It is generally known that gastric GISTs show better prognosis than those of the small intestine, if the mitotic count is identical, and recent guidelines recommend surveillance monitoring rather than resection if gastric GIST is smaller than 2.0 cm and has no suggestive features of malignancy such as presence of symptoms, increase in size or high risk findings of EUS.[4-8] However, even small gastric GIST may have high mitotic count >5/high power field (HPF), and repeated surveillance without resection may lead to patient's anxiety and poor compli-

ance to examination. Thus, several researchers suggest earlier resection of small GIST less than 2.0 cm.

To date, surgical resection is considered the main treatment modality of GISTs.[9] However, as endoscopic techniques have advanced rapidly, *en bloc* resection of GISTs by endoscopic procedures has been available. In particular, several endoscopists have suggested that endoscopic treatment would be useful for tumors in areas where a laparoscopic approach is thought to be difficult such as in the cardia or esophagogastric junction.[10] Moreover, previous studies showed that major complications such as macroperforation, major bleeding, pneumoperitoneum or intra-abdominal infection were generally managed by conservative medical treatment, and oncologic outcomes such as recurrence rate was relatively favorable, which was reported around 5%.[11-14] Nonetheless, there is still some debate on the role of endoscopic treatment mainly because long-term follow-up data are insufficient.

In our retrospective study, we evaluated the feasibility, long-term efficacy, and safety of the endoscopic treatment of gastric GISTs.

MATERIALS AND METHODS

1. Patients' characteristics

Between March 2005 and July 2019, 296 cases of subepithelial tumors (SETs) were resected by endoscopic procedures such as endoscopic submucosal dissection (ESD), endoscopic full-thickness resection (EFTR), submucosal tunneling endoscopic resection (STER), endoscopic mucosal resection, and polypectomy at Korea University Guro Hospital. Patient who had SET in upper GI tract initially underwent esophagogastroduodenoscopy (EGD) and EUS before the procedure. If patients agreed to undergo endoscopic resection for pathologic confirmation and therapeutic purpose, we performed the procedure under informed contents.

Patients underwent EGD and EUS before the procedure. We analyzed the size, location, and layer of the tumor by EUS. After excluding esophageal or duodenal SETs, a total of 135 patients were diagnosed as GIST, and 107 patients were diagnosed as non-GIST (leiomyoma 57, ectopic pancreas 27, neuroendocrine tumor 10, schwannoma 5, gastritis cystica profunda 4, duplication cyst 3, and lipoma 1). If SETs were diagnosed as GIST after the procedure, surveillance EGD and abdominal computed tomography (CT) were performed during the follow-up periods. We previously reported that recurrence rate of endoscopic treatment of GISTs in the upper GI tract was not significantly different with that of surgical resection, comparing 90 cases of endoscopic resection and 40 cases of surgical resection.[14] In this study, we further followed up 84 of 90 patients and their clinical outcomes focusing on recurrence, and additionally enrolled 51 patients who underwent endoscopic resection for treatment of gastric GIST. Thus, we retrospectively analyzed the 135 cases of gastric GIST including immediate clinical outcomes such as the procedure type, complete resection rate, R0 resection rate, complications, and long-term clinical outcomes such as the recurrence rate were also included. This study was approved by the Institutional Review Board of Korea University Guro Hospital (IRB number: 2020GR0027).

2. Endoscopic procedures

An experienced endoscopist (J.J.P.) who experienced more than 2,000 ESD cases for lesions in the upper GI tract performed all procedures. In ESD, the endoscopist's preferred technique, which was different from the standard ESD, was used. At first, peeling the mucosa off of the overlying peripheral margin was performed using a snare and grasping forceps. After injection into the submucosal layer, the SET was dissected using an insulated tip or a needle knife (Fig. 1). In the STER procedure, a submucosal entry was made by a mucosal incision 5 cm proximal to the SET, and a submucosal tunnel was created until the tumor was noted by endoscopic view. After exposure of the SET, the tumor was dissected completely. Finally, closure of the submucosal entry was performed using hemostatic clips. For the EFTR procedure, we made a circumferential incision around the tumor as deep as the muscularis propria layer, then a perforation hole to allow an incision into the serosal layer. We resected the tumor with the muscularis propria and serosal layer together using a snare. Finally, we completely closed the iatrogenic perforation using hemostatic clips.[14] All procedures were performed with written informed consent from the patient and guidance.

3. Histopathology

The pathologic diagnosis was made by hematoxylin and eosin staining and immunochemical findings. The mitotic count was measured in 50 HPFs, and we classified the risk of malignancy into four categories of very low, low, intermediate, and high-risk groups by evaluating the mitotic counts and measuring the largest tumor size, based on the National Institutes of Health Consensus.[15]

4. Definitions

R0 resection was defined as a resection with a clear margin microscopically. R1 resection was defined as the state where resection of the tumor was achieved macroscopically, but the tumor margins were positive microscopically.

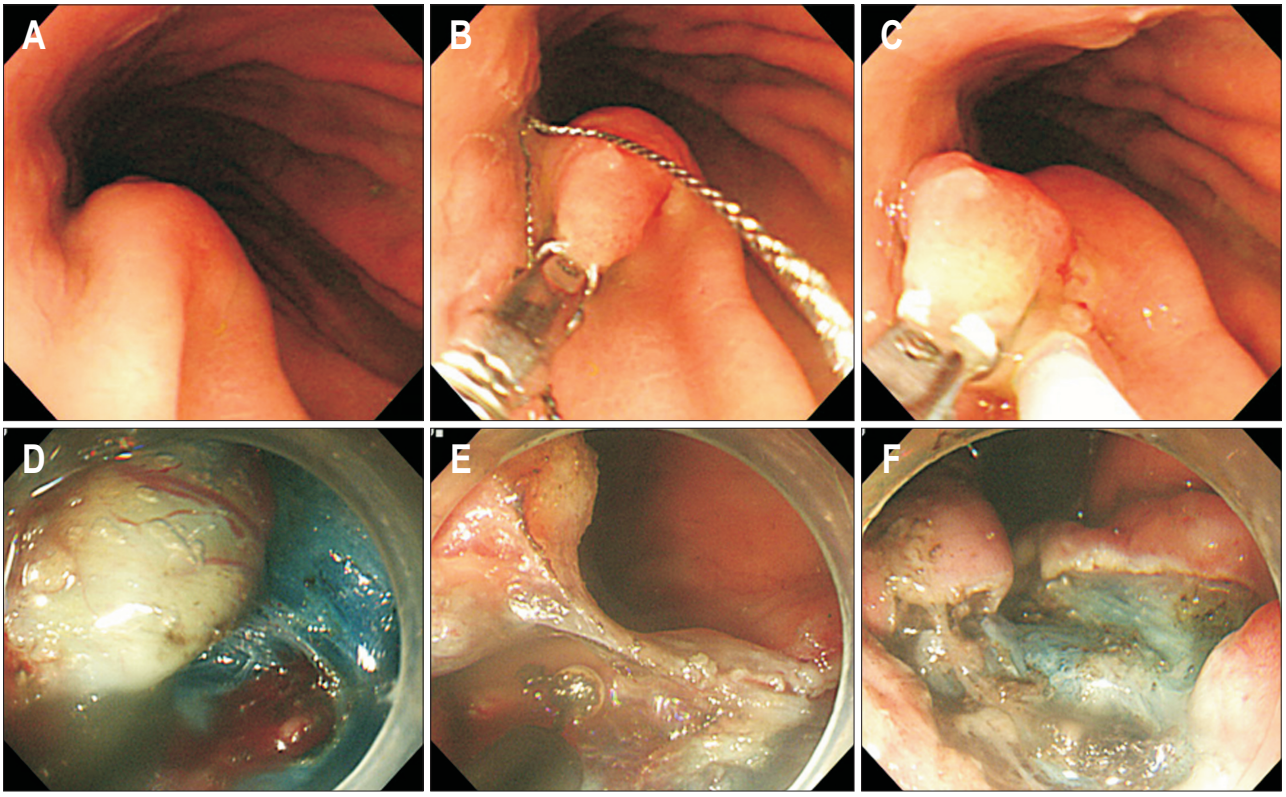

Fig. 1. A gastric subepithelial tumor (SET) was resected by the endoscopist's preferred submucosal dissection technique. (A) Esophagogastroduodenoscopy showed a large SET at the lesser curvature side of the antrum in the stomach. (B, C) Peeling the mucosa from the overlying peripheral margin rather than the whole overlying mucosa was performed using a snare and grasping forceps. (D, E) The SET was dissected using an insulated-tip knife. (F) After resection of the tumor, no adverse events occurred.

R2 resection was defined as the state in which the tumor remained grossly.[4] We defined complete resection as the removal of the entire tumor, which was judged by the endoscopic view, including R0 and R1 resections. Macroperforation was defined when mesenteric tissue was identified in an endoscopy. Microperforation was defined as perforation that was not identified during the procedure, but free air was identified on radiologic findings after the procedure.[14] Major bleeding was defined as massive bleeding requiring surgery or transfusion. The procedure time was defined as the time from marking to complete removal, including the time required for hemostasis.[16] The follow-up period was defined as the duration from the time of the procedure to the last EGD or CT. Recurrence was defined if at least one of the following is found during surveillance: (1) gross tumor or SET-like bulging of mucosa is noted by EGD; (2) definite tumor is noted by CT scan; or (3) if the biopsy result from resection site suggests GIST (i.e., spindle cell), even post-procedure scar is clean by endoscopic view.

5. Follow-up

After endoscopic removal of the tumor, an endoscopic evaluation was performed the next day to identify whether there was bleeding and to examine ulcer formation. To evaluate healing of the tumor resection site, a follow-up endoscopy was performed 4 and 12 weeks after the resection. After that, the patients underwent an endoscopy every year for surveillance and CT scans were also performed.

6. Statistical analysis

We used SPSS 20.0 (IBM Corp., Armonk, NY, USA) for statistical analysis. Discontinuous data were assessed by using the chi-square test. Recurrence-free survival rate was assessed by using the Kaplan-Meier survival analysis and log-rank test. A p-value less than 0.05 was considered statistically significant.

RESULTS

1. Patient characteristics

The mean patient age was 57.9±12.2 years. Females represented 57.8% of the patients. Most patients were asymptomatic (120 patients, 88.9%), with epigastric discomfort (11 patients, 8.1%), GI bleeding (3 patients, 2.2%), and jaundice (1 patient, 0.8%). The most frequent tumor

location was the body (58 patients, 43.0%), followed by the fundus (36 patients, 26.7%), cardia (23 patients, 17.0%), and antrum (18 patients, 13.3%). On the pre-procedure EUS, the tumor layer was the muscularis propria in 84 patients (62.2%), submucosa in 49 patients (36.3%), and muscularis mucosa in one patient (0.7%) (Table 1).

Table 1. Baseline Characteristics of Gastric Gastrointestinal Stromal Tumors

Variable	Data (n=135)
Age, mean±SD, yr	57.9±12.2
Sex, No. (%)	
Male	57(42.2)
Female	78(57.8)
Symptoms, No. (%)	
No symptom	120 (88.9)
Epigastric discomfort	11 (8.1)
Bleeding	3 (2.2)
Jaundice	1 (0.8)
Tumor location, No. (%)	
Fundus	36 (26.7)
Cardia	23 (17.0)
Body	58 (43.0)
Antrum	18 (13.3)
Layer, No. (%)*	
Muscularis mucosa	1 (0.7)
Submucosa	49 (36.3)
Muscularis propria	84 (62.2)

*Evaluated in 134 patients.

Table 2. Pathologic and Clinical Outcomes of Endoscopic Resection of Gastric Gastrointestinal Stromal Tumor

Variable	Data
Size, mean±SD, cm	2.1±1.1
Resection, No. (%)	
R0	21 (15.6)
Complete resection	122 (90.4)
NIH risk group, No. (%)	
Very low	74 (54.8)
Low	38 (28.1)
Intermediate	16 (11.9)
High	7 (5.2)
Procedure type, No. (%)	
ESD	115 (85.2)
STER	8 (5.9)
EFTR	3 (2.2)
EMR	9 (6.7)
Procedure time, mean±SD, min	44.9±33.5
Complication, No. (%)	19 (14.1)
Macroperforation	6 (4.4)
Microperforation	9 (6.7)
Major bleeding	4 (3.0)

NIH, National Institutes of Health; ESD, endoscopic submucosal dissection; STER, submucosal tunneling endoscopic resection; EFTR, endoscopic full-thickness resection; EMR, endoscopic mucosal resection.

2. Pathologic outcomes

The mean tumor size was 2.1±1.1 cm. Most of the patients had complete resections (122 patients, 90.4%), which were judged by the endoscopic view, and 21 patients (15.6%) had R0 resections. More than 50% of the patients (74 patients, 54.8%) were classified in the very-low-risk group, followed by the low-risk (38 patients, 28.1%), intermediate-risk (16 patients, 11.9%), and high-risk groups (7 patients, 5.2%) (Table 2).

3. Procedure-related outcomes

Most patients were treated by ESD (115 patients, 85.2%), followed by endoscopic mucosal resection (9 patients, 6.7%), STER (8 patients, 5.9%), and EFTR (3 patients, 2.2%). The mean procedure time was 44.9±33.5 minutes. Nineteen patients (14.1%) had complications, with microperforation occurring in nine patients (6.7%), followed by macroperforation (6 patients, 4.4%) and major bleeding (4 patients, 3.0%) (Table 2). When comparing complication rates between GIST and non-GIST, no statistical significance was found (macroperforation 4.4% vs 2.8%, p=0.503; microperforation 6.7% vs 1.9%, p=0.075; major bleeding 3.0% vs 2.8%, p=0.941). To further analyze complication rates by tumor size, we classified the enrolled patients into three groups (<1 cm [n=16], 1 cm to ≤3 cm [n=101], >3 cm [n=18]), and found that complication rates among three groups were not significantly different (macroperforation 0% vs 4.0% vs 11.1%, p=0.253; microperforation 11.8% vs 5.0% vs 11.1%, p=0.412; major bleeding 0% vs 3.0% vs 5.6%, p=0.623). We also sub-analyzed the perforation rate by procedure type, and found that macroperforation was frequently found in STER (1/8, 12.5%) or ETFR (1/3, 33.3%) than ESD (4/115, 3.5%). Microperforation was found in eight cases (6.9%) by ESD, and one case by ESTD (12.5%). We consider that both complications

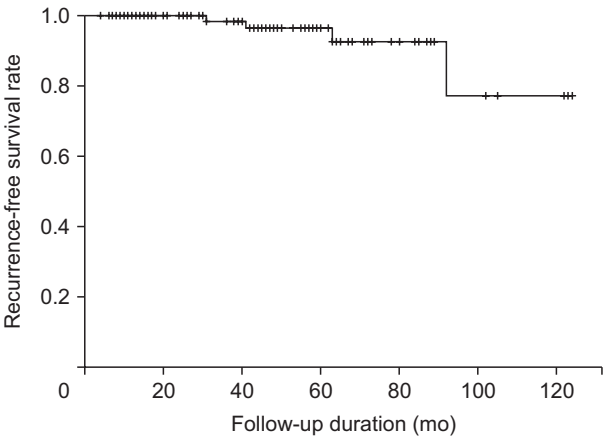

Fig. 2. Kaplan-Meier graph of the recurrence-free survival rate after endoscopic resection of gastric gastrointestinal stromal tumors.

would be inevitable during STER or EFTR.

4. Recurrence during follow-up

The recurrence rate was analyzed for 118 patients who were followed up more than 6 months by EGD and CT scans. Among them, the mean follow-up period was 36.5±30.1 months (range, 6 to 124 months) and a total of four patients (3.4%) had recurrences during the follow-up period. By Kaplan-Meier analysis, the 5-year and 10-year recurrence-free survival rates were 92.5% and 77.1%, respectively (Fig. 2). All the recurrent cases were larger than 2.0 cm, and the recurrence rate among subgroup of tumor size ≥2.0 cm and those who were followed up more ≥6 months was 6.8% (4/59). In terms of National Institutes of Health risk group, there was no recurrent case in very low-risk group (0/64, 0%), one in low-risk group (1/37, 2.7%), two in intermediate-risk group (2/11, 18.2%), and one in high-risk group (1/6, 16.7%) (Fig. 3).

Three recurrences were noted in patients with R1 resection and one in those with R2 resection. The first recurrent case was a 56-year-old female, who had a 2.4-cm GIST at the posterior wall of the high body that was resected by ESD and classified as low risk because of a low mitotic count (4/50 HPF). Recurrence was not found during 2.5 years of follow-up. However, the patient did not visit after 31 months from the procedure. The patient revisited our hospital after 33 months from the last follow-up because a newly developed SET was found at the previous ESD site in a local clinic. The tumor was re-resected by the ESD technique and confirmed as a GIST with high risk due to a high mitotic count (38/50 HPF). The second case was a 56-year-old male, who had a 3.1-cm GIST at the cardia that was resected by ESD method, and histopathologic evaluation showed high mitotic count (35/50 HPF) thus the tumor was classified as high-risk group. After 31 months of follow-up, surveillance EGD and CT found a recurrent tumor. The patient was transferred to another hospital at the patient's request. The third case was a 72-year-old female, who had a 4-cm GIST at the fundus that was resected by ESD and classified as an intermediate risk due to the relatively high mitotic count (9/50 HPF). After the procedure, the patient did not visit our hospital. After 92 months from the procedure time, the patient revisited and a recurrent tumor was noted by EGD and CT. The tumor was resected by laparoscopic wedge resection and confirmed as a GIST with high risk due to the high mitotic count (14/50 HPF). The fourth case was a 59-year-old male, who had a 2.5 cm, located at low body, anterior wall side and mitotic count was 7/50 HPF that was corresponding to intermediate risk. A gross recurrent SET was noted at 45 months after endoscopic resection. The patient underwent additional surgery, and its pathologic result was as follows; size: 2.5 cm, mitotic count: 5/50 HPF, very low-risk group.

DISCUSSION

In our study, the endoscopic resection of GISTs was technically feasible. The recurrence rate was relatively low, and the complete resection rate was high, even though the R0 resection rate was low. In previous studies where GISTs

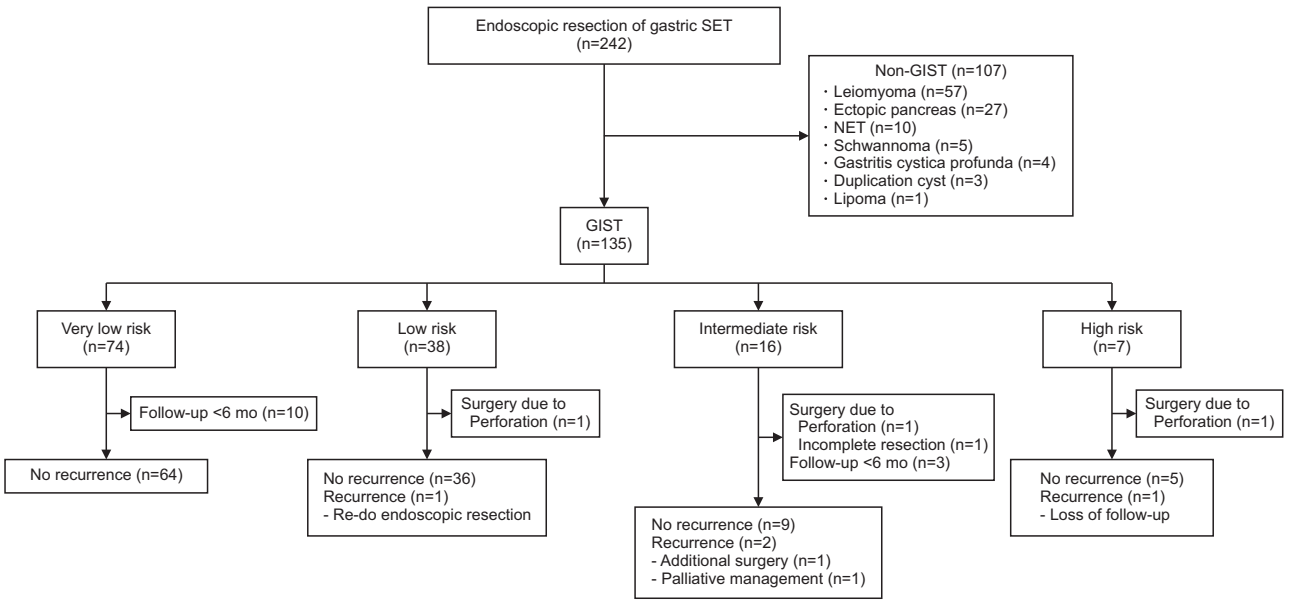

Fig. 3. Flowchart of enrolled patients according to risk stratification by National Institutes of Health Consensus.
SET, subepithelial tumor; GIST, gastrointestinal stromal tumor.

were resected by endoscopic procedures such as ESD, EFTR, and STER, recurrence was rarely reported (0% to 2.7%).[11,17-23] In this study, we enrolled a larger number of endoscopic cases (135 cases) including our previous cases, and the follow-up period was relatively longer than in the other studies (3.3 to 23.3 months). To our knowledge, this is the first study that followed up more than 100 patients who underwent endoscopic resection of gastric GIST with mean duration of follow-up longer than 3 years. The follow-up duration of current study is 36.5±30.1 months that is shorter than our previous report which compared endoscopic resection with surgery (45.5±29.1 months). We consider that newly enrolled patients after August 2014 may affect this shortening. However, we believe that our current study still has strengths in that it demonstrated clinical outcomes of GIST resected by endoscopic procedures during relatively long-term period.

Currently, the standard treatment for GISTs larger than 20 to 30 mm is surgical resection according to several guidelines,[6,9,24-27] and endoscopic resection might be technically unavailable or cause serious complications if the tumor is large (>30 to 40 mm).[28,29] In general, periodic surveillance is recommended in cases of SETs less than 20 mm in the stomach.[6,9,24-27] However, there is no gold standard management strategy in such cases and we should consider that all GISTs have the potential for malignant transformation and distant metastasis.[15,30] Furthermore, when we choose periodic surveillance, several issues such as the risk associated with repeated endoscopic procedures, delayed diagnosis of malignancy, low compliance and stress of the patient, and cost-effectiveness are involved.[31,32] Considering possible recurrence, patients who underwent endoscopic resection of gastric GIST need to be closely followed up with annual endoscopic surveillance and CT scan, which is not different from clinical process of patients who do not undergo endoscopic resection of SET and are followed up with annual EGD. However, these patients may have anxiety that they still have SET and do not know its definite diagnosis, which may cause poor compliance to annual EGD. Endoscopic resection can be helpful to patients in that it solves these problems.

Considering the malignant potential of GISTs and the problems with surveillance, a definitive diagnosis is necessary for a small GIST, obtaining appropriate tissue is essential. However, the diagnostic yields of other methods such as "bite on bite" (<38%), jumbo forceps (60%), and EUS-guided fine needle aspiration (38% to 84%) are unsatisfactory.[26] In this situation, endoscopic resection, another technique to obtain tissue, may provide an accurate diagnosis and appropriate therapy as well. It also avoids frequent re-examinations and reassures patients and has several advantages over surgical approaches as it is minimally invasive and reduces hospital stays and cost.[14,33-35] Given the aforementioned concerns, we suggest that endoscopic resection would be an alternative treatment strategy for gastric GISTs according to a definite diagnosis, although careful patient selection considering tumor size and the presence of high-risk features at the pre-procedure EUS findings is necessary. Endoscopic resection of gastric GIST may have strengths over laparoscopic approach if tumors are located in the cardia or esophagogastric junction where laparoscopic approach is difficult. However, two of our recurrent cases were located in the cardia and high body, and all tumors were larger than 2.0 cm. Therefore, it would be more appropriate to consider surgical resection rather than endoscopic procedure regardless of tumor location, if tumor size is larger than 2.0 cm and pre-procedural EUS findings suggest high risk of malignancy.

When we resect GISTs endoscopically rather than surgically, the safety of the endoscopic treatment becomes a major concern. The safety of endoscopic treatment for GISTs should be evaluated in terms of the clinical outcomes such as complications and oncological safety regarding the risk of recurrence during the long-term follow-up period. The most common complication was microperforation in 6.7% of the patients, but all were successfully treated by endoscopic closure using hemostatic clips and recovered with conservative care. Macroperforation occurred in 4.4% of the patients, for which laparoscopic closure was needed. Although the microperforation rate was relatively high as a complication after endoscopic resection, it can be managed conservatively without surgical intervention in most patients. However, more than half of patients with SET who underwent endoscopic resection were diagnosed as non-GIST. Considering similar complication rate during endoscopic resection of non-GIST gastric SETs, this procedure needs to be carefully performed after sufficient pre-procedural evaluation and selection of cases with a high possibility of gastric GIST.

In our study, the histopathologic evaluation showed low R0 resection rates and high R1 resection rates. The endoscopic resection method mostly used was ESD (85.2%), and a portion of gastric GISTs are widely connected with muscularis propria layer or even outpouching, which would be difficult to secure negative resection margin and contribute to low R0 resection rate. However, a relatively low rate of recurrence (3.4%) was found during the mean 36.5-month follow-up period. A previous study analyzed the predictive factors of recurrence after resection in 136 patients with small (5 cm or less) primary gastric GISTs who underwent mainly surgical resections. Microscopically positive resection margins were noted in 10.3% of the patients. However, there was no recur-

rence during a mean follow-up of 32 months. Interestingly, five patients (4%) who had tumors with a high mitotic index but free resection margins, showed recurrence during a median follow-up of 23 months. Thus, the authors concluded that the main predictor of recurrence was tumor biology such as abnormal p53 expression and a high mitotic index but not the microscopic marginal status.[36] Another prospective study reported the clinical outcomes of 200 patients who underwent surgical resection of gastric GISTs. In this study, a trend of early recurrence of tumors larger than 10 cm was shown. However, other factors including microscopically positive resection margins did not predict recurrence. Furthermore, only tumor size was a predictive factor for disease-specific survival, and microscopic margins did not influence survival outcome.[5] Based on these previous studies and our current data, we suggest that careful surveillance after the endoscopic resection of GISTs may be considered even when R1 resection is noted. Considering our recurrent cases, particularly careful follow-up is necessary for patients in relatively high National Institutes of Health risk groups. Among the four recurrent cases, two were corresponding to intermediate risk, and each one from the other two was low and high risk, respectively. Therefore, it would be necessary to recommend additional surgery if pathologic finding of endoscopic resection is not corresponding to very low-risk group. Additionally, if tumor has typical EUS findings suggesting malignancy such as irregular border, cystic spaces, echogenic foci and heterogeneity, surgery would be a better option than endoscopic resection. In addition, the current guidelines recommend imatinib therapy for at least 3 years in patients diagnosed with a high-risk GIST after surgery.[27,37] However, little is known about adjuvant imatinib therapy after endoscopic resection. Further large-scale studies are needed.

In conclusion, the endoscopic resection of gastric GISTs appeared to be feasible and safe when performed in selected patients by skilled endoscopists, and oncologically safe with a low risk of recurrence once complete resection was achieved, even though the R0 resection rates were low. However, additional surgery should be considered if pathologic outcomes are corresponding to intermediate- or high-risk groups considering higher recurrence rate in those subgroups.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTIONS

Study concept and design: J.J.P., M.K.J. Data acquisition: all authors. Data analysis and interpretation: M.K.J., Y.H.L. Drafting of the manuscript; M.K.J., J.J.P., Y.H.L. critical revision of the manuscript for important intellectual content: B.J.L., J.J.P., S.W.L., H.J.C. Statistical analysis: all authors. Administrative, technical, or material support; study supervision: S.M.K., W.S.K., A.Y.Y. Approval of final manuscript: all authors.

ORCID

Moon Kyung Joo https://orcid.org/0000-0001-6050-3695
Jong-Jae Park https://orcid.org/0000-0002-4642-5405
Yeon Ho Lee https://orcid.org/0000-0001-8257-1306
Beom Jae Lee https://orcid.org/0000-0003-2449-4968
Seong Min Kim https://orcid.org/0000-0003-4438-2955
Won Shik Kim https://orcid.org/0000-0003-4431-6472
Ah Young Yoo https://orcid.org/0000-0002-3474-2016
Hoon Jai Chun https://orcid.org/0000-0002-5539-361X
Sang Woo Lee https://orcid.org/0000-0003-3491-0371

REFERENCES

1. Chak A, Canto MI, Rösch T, et al. Endosonographic differentiation of benign and malignant stromal cell tumors. Gastrointest Endosc 1997;45:468-473.
2. Palazzo L, Landi B, Cellier C, Cuillerier E, Roseau G, Barbier JP. Endosonographic features predictive of benign and malignant gastrointestinal stromal cell tumours. Gut 2000;46:88-92.
3. Brand B, Oesterhelweg L, Binmoeller KF, et al. Impact of endoscopic ultrasound for evaluation of submucosal lesions in gastrointestinal tract. Dig Liver Dis 2002;34:290-297.
4. Biondi A, Persiani R, Cananzi F, et al. R0 resection in the treatment of gastric cancer: room for improvement. World J Gastroenterol 2010;16:3358-3370.
5. DeMatteo RP, Lewis JJ, Leung D, Mudan SS, Woodruff JM, Brennan MF. Two hundred gastrointestinal stromal tumors: recurrence patterns and prognostic factors for survival. Ann Surg 2000;231:51-58.
6. Koo DH, Ryu MH, Kim KM, et al. Asian Consensus Guidelines for the diagnosis and management of gastrointestinal stromal tumor. Cancer Res Treat 2016;48:1155-1166.
7. Standards of Practice Committee, Faulx AL, Kothari S, et al. The role of endoscopy in subepithelial lesions of the GI tract. Gastrointest Endosc 2017;85:1117-1132.
8. National Comprehensive Cancer Network (NCCN). NCCN

Clinical Practice Guideline in Oncology: Gastrointestinal Stromal Tumors (GISTs) version 1 [Internet]. Plymouth Meeting: NCCN; c2021 [cited 2020 Oct 30]. Available from: https://www.nccn.org/guidelines/category_1 .
9. Demetri GD, von Mehren M, Antonescu CR, et al. NCCN Task Force report: update on the management of patients with gastrointestinal stromal tumors. J Natl Compr Canc Netw 2010;8 Suppl 2:S1-S41.
10. De Vogelaere K, Hoorens A, Haentjens P, Delvaux G. Laparoscopic versus open resection of gastrointestinal stromal tumors of the stomach. Surg Endosc 2013;27:1546-1554.
11. An W, Sun PB, Gao J, et al. Endoscopic submucosal dissection for gastric gastrointestinal stromal tumors: a retrospective cohort study. Surg Endosc 2017;31:4522-4531.
12. Pang T, Zhao Y, Fan T, et al. Comparison of safety and outcomes between endoscopic and surgical resections of small (≤ 5 cm) primary gastric gastrointestinal stromal tumors. J Cancer 2019;10:4132-4141.
13. Dai WJ, Liu G, Wang M, et al. Endoscopic versus laparoscopic resection of gastric gastrointestinal stromal tumors: a multicenter study. Oncotarget 2017;8:11259-11267.
14. Joo MK, Park JJ, Kim H, et al. Endoscopic versus surgical resection of GI stromal tumors in the upper GI tract. Gastrointest Endosc 2016;83:318-326.
15. Fletcher CD, Berman JJ, Corless C, et al. Diagnosis of gastrointestinal stromal tumors: a consensus approach. Hum Pathol 2002;33:459-465.
16. Ahn JY, Jung HY, Choi KD, et al. Endoscopic and oncologic outcomes after endoscopic resection for early gastric cancer: 1370 cases of absolute and extended indications. Gastrointest Endosc 2011;74:485-493.
17. Meng Y, Li W, Han L, et al. Long-term outcomes of endoscopic submucosal dissection versus laparoscopic resection for gastric stromal tumors less than 2 cm. J Gastroenterol Hepatol 2017;32:1693-1697.
18. He Z, Sun C, Zheng Z, et al. Endoscopic submucosal dissection of large gastrointestinal stromal tumors in the esophagus and stomach. J Gastroenterol Hepatol 2013;28:262-267.
19. Andalib I, Yeoun D, Reddy R, Xie S, Iqbal S. Endoscopic resection of gastric gastrointestinal stromal tumors originating from the muscularis propria layer in North America: methods and feasibility data. Surg Endosc 2018;32:1787-1792.
20. Tan Y, Tang X, Guo T, et al. Comparison between submucosal tunneling endoscopic resection and endoscopic full-thickness resection for gastric stromal tumors originating from the muscularis propria layer. Surg Endosc 2017;31:3376-3382.
21. Huang LY, Cui J, Liu YX, Wu CR, Yi DL. Endoscopic therapy for gastric stromal tumors originating from the muscularis propria. World J Gastroenterol 2012;18:3465-3471.
22. Wang L, Ren W, Fan CQ, et al. Full-thickness endoscopic resection of nonintracavitary gastric stromal tumors: a novel approach. Surg Endosc 2011;25:641-647.
23. Chen T, Zhang C, Yao LQ, et al. Management of the complications of submucosal tunneling endoscopic resection for upper gastrointestinal submucosal tumors. Endoscopy 2016;48:149-155.
24. Hwang JH, Rulyak SD, Kimmey MB; American Gastroenterological Association Institute. American Gastroenterological Association Institute technical review on the management of gastric subepithelial masses. Gastroenterology 2006;130:2217-2228.
25. Dumonceau JM, Deprez PH, Jenssen C, et al. Indications, results, and clinical impact of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline: updated January 2017. Endoscopy 2017;49:695-714.
26. Khashab MA, Pasricha PJ. Conquering the third space: challenges and opportunities for diagnostic and therapeutic endoscopy. Gastrointest Endosc 2013;77:146-148.
27. Casali PG, Abecassis N, Aro HT, et al. Gastrointestinal stromal tumours: ESMO-EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2018;29(Suppl 4):iv267.
28. Park JJ. Long-term outcomes after endoscopic treatment of gastric gastrointestinal stromal tumor. Clin Endosc 2016;49:232-234.
29. Zhang X, Modayil R, Criscitelli T, Stavropoulos SN. Endoscopic resection for subepithelial lesions-pure endoscopic full-thickness resection and submucosal tunneling endoscopic resection. Transl Gastroenterol Hepatol 2019;4:39.
30. Miettinen M, Lasota J. Gastrointestinal stromal tumors: pathology and prognosis at different sites. Semin Diagn Pathol 2006;23:70-83.
31. Koga T, Hirayama Y, Yoshiya S, et al. Necessity for resection of gastric gastrointestinal stromal tumors ≤ 20 mm. Anticancer Res 2015;35:2341-2344.
32. Casali PG, Jost L, Reichardt P, Schlemmer M, Blay JY; ESMO Guidelines Working Group. Gastrointestinal stromal tumours: ESMO clinical recommendations for diagnosis, treatment and follow-up. Ann Oncol 2009;20 Suppl 4:64-67.
33. Meng Y, Cao C, Song S, Li Y, Liu S. Endoscopic band ligation versus endoscopic submucosal dissection and laparoscopic resection for small gastric stromal tumors. Surg Endosc 2016;30:2873-2878.
34. Feng F, Liu Z, Zhang X, et al. Comparison of endoscopic and open resection for small gastric gastrointestinal stromal tumor. Transl Oncol 2015;8:504-508.
35. Kim HH. Endoscopic treatment for gastrointestinal stromal tumor: advantages and hurdles. World J Gastrointest Endosc 2015;7:192-205.
36. Kim MY, Park YS, Choi KD, et al. Predictors of recurrence

after resection of small gastric gastrointestinal stromal tumors of 5 cm or less. J Clin Gastroenterol 2012;46:130-137.
37. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Soft Tissue Sarcoma [Internet]. Plymouth Meeting: NCCN; c2019 [cited 2022 Sep 15]. Available from: https://www.nccn.org/guidelines/category_1.