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Higher incidence of gastroesophageal reflux disease after gastric wedge resections of gastric submucosal tumors located close to the gastroesophageal junction

Seung Yeon Ko, Jeong Sun Lee, Jin-Jo Kim, Seung-Man Park

Division of Gastrointestinal Surgery, Department of Surgery, Incheon St. Mary's Hospital, The Catholic University of Korea College of Medicine, Incheon, Korea

Purpose: We hypothesized that gastroesophageal reflux disease (GERD) would be more prevalent after a gastric wedge resection of a submucosal tumor (SMT) located close to the gastroesophageal junction (GEJ) than after a gastric wedge resection of an SMT at other locations because of the damage to the lower esophageal sphincter during surgery.
Methods: Fifty-eight patients with gastric SMT who underwent open or laparoscopic gastric wedge resection between January 2000 and August 2012 at the Department of Surgery, Incheon St. Mary's Hospital were enrolled into this study. The patients were divided into 2 groups according to the location of the tumor, upper or lateral border of the tumor within 5 cm of the GEJ (GEJ ≤ 5 cm group) and upper or lateral border of the tumor greater than 5 cm distal to the GEJ (GEJ > 5 cm group). The surgical records, clinicopathologic findings, postoperative GERD symptoms, postoperative use of acid suppressive medications and preoperative and postoperative endoscopic findings were retrospectively reviewed and compared between the 2 groups.
Results: There was no difference in the frequency of the preoperative GERD symptoms between the 2 groups, whereas postoperative GERD symptoms and postoperative use of acid suppressive medications were more frequent in the GEJ ≤ 5 cm group (P = 0.045 and P = 0.031). However, there were no differences in the follow-up endoscopic findings in terms of reflux esophagitis and Hill's grade between the 2 groups.
Conclusion: The incidence of GERD was higher after gastric wedge resection of SMTs located close to the GEJ. Hence, adequate care should be taken during the follow-up of these patients.
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Key Words: Gastric wedge resection, Esophagogastric Junction, Gastroesophageal reflux

INTRODUCTION

It is difficult to make a preoperative pathologically confirmed diagnosis of a gastrointestinal stromal tumor (GIST) despite the advancement in endoscopic ultrasonography (EUS) and EUS-guided biopsy techniques [1-5]. Therefore, many patients with a gastric submucosal tumor (SMT) undergo gastric wedge resection without a confirmed diagnosis. Gastric wedge resection of an SMT located close to the gastroesophageal junction (GEJ) is technically challenging because there is a substantial risk of stenosis of the GEJ or injury to the lower esophageal sphincter (LES). Much concern has been expressed about these issues in the literature [6-17]. However, to the best of our knowledge, there are no reports on the incidence of stenosis of the GEJ or the incidence of gastroeophageal reflux disease (GERD) caused by injury to the LES after surgery. We

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Corresponding Author: Jin-Jo Kim
Division of Gastrointestinal Surgery, Department of Surgery, Incheon St. Mary's Hospital, The Catholic University of Korea College of Medicine, 56 Dongsu-ro, Bupyeong-gu, Incheon 403-720, Korea
Tel: +82-32-280-5609, **Fax:** +82-32-280-5988
E-mail: kjj@catholic.ac.kr

hypothesized that a wedge resection of an SMT whose upper or lateral border is located within 5 cm of the GEJ, but does not involve the GEJ, may cause injury to the LES, especially to the sling fibers (Fig. 1), and may result in GERD at a later stage. The objective of this study is to determine the incidence of GERD after gastric wedge resections of SMTs located close to the GEJ and compare it with the incidence of GERD after gastric wedge resection of SMTs at other locations in the stomach.

METHODS

From January 2000 to August 2012, 69 patients received surgical treatment for a gastric SMT at the Department of Surgery, Incheon St. Mary's Hospital. Among them, 9 patients underwent formal gastrectomies (2 patients underwent total gastrectomy, and 7 patients underwent distal gastrectomy) because of the location and/or the size of the tumor. Among the 2 patients who underwent total gastrectomy, 1 patient initially underwent laparoscopic enucleation for a 2-cm SMT at the GEJ. However, the final pathologic report revealed a GIST and hence, she underwent a laparoscopic proximal gastrectomy. After the proximal gastrectomy, the patient suffered from severe reflux esophagitis and she finally underwent a laparoscopic completion total gastrectomy at 2 years and 6 months after the proximal gastrectomy. In another 2 patients, gastric SMTs were located at the GEJ. These patients underwent a laparoscopic wedge resection and a prophylactic antireflux surgery, and one of the 2 cases has been reported elsewhere [18]. The remaining 58 patients who underwent open or laparoscopic gastric wedge resection were enrolled in this study. This study was approved by the Institutional Review Board of the Department of Surgery, Incheon St. Mary's Hospital (OC13RISI0002). Fifty-eight patients were divided into 2 groups according to the location of the tumor. The GEJ ≤ 5 cm group included the patients in whom the upper or lateral border of the tumor was located within 5 cm of the GEJ but it did not involve the GEJ, and the GEJ > 5 cm group included the patients in whom the upper or lateral border of the tumor was located more than 5-cm distal to the GEJ. The distance between the GEJ and the tumor was directly measured with endoscope during the preoperative endoscopy.

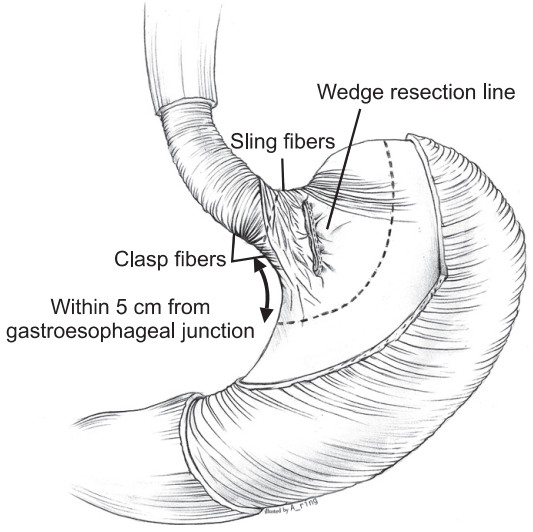

Fig. 1. Illustration for the hypothesis of the development of gastroesophageal reflux disease after a gastric wedge resection for a submucosal tumor located close to the gastroesophageal junction. If the upper or lateral border of the tumor is located within 5 cm from the gastroesophageal junction, there is a substantial risk of damage to the lower esophageal sphincter, especially to the sling fibers after wedge resection for this tumor.

Surgical records, clinicopathologic findings, postoperative GERD symptoms, postoperative use of acid suppressive medications and preoperative and postoperative endoscopic findings were retrospectively reviewed and compared between the 2 groups.

Presence of postoperative GERD symptoms during the follow-up period was assessed with a careful review of the medical records when the patient complained of typical GERD symptoms, such as heartburn and/or acid regurgitation, and when the patient complained of epigastric pain and the endoscopic findings showed any evidence of reflux esophagitis; this symptom was also regarded as a GERD symptom. Postoperative use of acid suppressive medications, such as proton pump inhibitors (PPI), H2 receptor antagonists and antacids, in each patient was investigated and the use of such medications for more than 30-day was recorded. Preoperative endoscopic findings and the last postoperative follow-up endoscopic findings in each patient were reviewed simultaneously by 2 expert endoscopists (J.S.L. and S.M.P.). The degree of reflux esophagitis was graded by the Los Angeles (LA) classification [19] and the endoscopic morphology of the GEJ was classified by Hill's grade [20]. When there was disagreement in the findings between the 2 endoscopists, they discussed the findings and arrived at consensus. Endoscopically, when there was absence of reflux esophagitis or the LA classification grade was M (minimal change), it was considered that the patient did not have reflux esophagitis, and when the LA classification grade was more than A, it was considered that the patient had reflux esophagitis.

If the final pathology result in a patient indicated a GIST, then the patient was regularly followed up. If the final pathology result indicated a benign SMT, then the patient was followed up based on the symptoms.

All continuous variables are expressed as a mean ± standard deviation. A chi-square test was used to compare the categorical variables, and a Student t-test was used to compare the continuous variables. P-value less than 0.05 was considered statistically significant.

RESULTS

There were 25 men and 33 women and the mean age of the patients was 59 years (range, 31–86 years). The clinical characteristics of each group are shown in Table 1. The incidence of preoperative GERD symptoms and preoperative endoscopic findings were not different between the 2 groups. The pathologic analysis of 58 SMTs revealed GIST in 48 cases and other benign SMTs in 10 cases (3 leiomyoma, 3 heterotopic pancreas, 1 Schwanoma, 1 glomus tumor, 1 gastric cyst, and 1 inflammatory myofibroblastic tumor). All of the resection margins were not involved by the tumor. A postoperative complication was noted in one case of the GEJ > 5 cm group. An intraabdominal hematoma developed in this patient and he recovered well after percutaneous drainage and transfusions. There were no cases of stenosis of the GEJ in the GEJ ≤ 5 cm group. There was no postoperative mortality in either group. Among the 48 GIST patients, there was no postoperative recurrence during the mean 30 (±23) months of postoperative follow-up (Table 2).

The mean follow-up periods in the GEJ ≤ 5 cm group and the GEJ > 5 cm group were 26.3 (±22.1) months and 21.3 (±20.7) months, respectively. During the follow-up, many patients complained of various upper gastrointestinal symptoms (Table 3), and the patients in the GEJ ≤ 5 cm group had a tendency for developing more upper gastrointestinal symptoms than the patients in the GEJ > 5 cm group, but there was no statistically significant difference (P = 0.072). Eight patients (23.5%) complained of GERD symptoms in the GEJ ≤ 5 cm group and a greater number of patients complained of GERD symptoms in the GEJ ≤ 5 cm group than in the GEJ > 5 cm group (P = 0.045). The postoperative use of acid suppressive medications for more than 30 days was more frequently observed in the GEJ ≤ 5 cm group (P = 0.031). The mean duration of GERD symptoms of 8 patients in the GEJ ≤ 5 cm group was 21.8 (±18.1) months, and the duration of GERD symptoms of 1 patient in the GEJ > 5 cm group was 18 months. Among 8 patients with GERD symptoms in the GEJ ≤ 5 cm group, symptoms improved by PPI medication for not more than 6 months in 3 patients and symptoms improved by PPI medication for not more than

Table 1. Clinical characteristics of the patients with gastric submucosal tumor

Characteristic	GEJ ≤ 5 cm (n = 34)	GEJ > 5 cm (n = 24)	P-value
Gender			0.373
Male	13 (38.2)	12 (50.0)	
Female	21 (61.8)	12 (50.0)	
Age (yr)	57 ± 13	61 ± 12	0.231
Preoperative GERD symptoms			0.564
Yes	1 (2.9)	2 (8.3)	
No	33 (97.1)	22 (91.7)	
Preoperative EGD finding			
Reflux esophagitis			0.640
Yes	2 (5.9)	3 (12.5)	
No	32 (94.1)	21 (87.5)	
Hill's grade			0.564
≤2	33 (97.1)	22 (91.7)	
>2	1 (2.9)	2 (8.3)	

Values are presented as number (%) or mean ± standard deviation.
GEJ, gastroesophageal junction; GERD, gastroesophageal reflux disease; EGD, esophagogastroduodenoscopy.

Table 2. Postoperative outcomes after gastric wedge resections

Variable	GEJ ≤ 5 cm (n = 34)	GEJ > 5 cm (n = 24)	P-value
Pathology			0.922
GIST	28 (82.4)	20 (83.3)	
Benign SMT	6 (17.6)	4 (16.7)	
Tumor size (cm)	3.5 ± 1.7	5.2 ± 4.6	0.098
Surgical margin			-
Involved	0 (0)	0 (0)	
Not involved	34 (100)	24 (100)	
Type of surgery			0.839
Open	5 (14.7)	4 (16.7)	
Laparoscopic	29 (85.3)	20 (83.3)	
Operation time (min)	146 ± 85	125 ± 74	0.321
Oral feeding (day)	3.3 ± 1.5	3.0 ± 1.5	0.512
Postoperative hospital stay (day)	7.1 ± 3.1	7.4 ± 6.6	0.783
Postoperative complication			0.414
Yes	0 (0)	1 (4.2)	
No	34 (100)	23 (95.8)	
Recurrence			-
Yes	0 (0)	0 (0)	
No	34 (100)	24 (100)	

Values are presented as number (%) or mean ± standard deviation.
GEJ, gastroesophageal junction; GIST, gastrointestinal stromal tumor; SMT, submucosal tumor.

Table 3. Postoperative upper gastrointestinal complaints after gastric wedge resections

Variable	GEJ ≤ 5 cm (n = 34)[a]	GEJ > 5 cm (n = 24)
Indigestion	4	2
Epigastric pain	5	3
Heartburn	4	0
Regurgitation	4	1
Gas bloat	2	0
Dysphagia	1	0
Nausea	0	1

GEJ, gastroesophageal junction.
[a]There were more than one symptoms in some patients.

Table 4. Findings of postoperative follow-up after gastric wedge resections

Variable	GEJ ≤ 5 cm (n = 34)	GEJ > 5 cm (n = 24)	P-value
Postoperative upper gastrointestinal symptoms			0.072
Yes	18 (52.9)	7 (29.2)	
No	10 (47.1)	17 (70.8)	
Postoperative GERD symptoms			0.045
Yes	8 (23.5)	1 (4.2)	
No	26 (76.5)	23 (95.8)	
Postoperative use of acid suppressive medication			0.031
Yes	11 (32.4)	2 (8.3)	
No	23 (67.6)	22 (91.7)	
Postoperative EGD findings[a)]			
Reflux esophagitis			1.000
Yes	2 (8.3)	1 (7.7)	
No	22 (91.7)	12 (92.3)	
Hill's grade			0.690
≤2	17 (70.8)	10 (76.9)	
>2	7 (29.2)	3 (23.1)	

Values are presented as number (%).
GEJ, gastroesophageal junction; GERD, gastroesophageal reflux disease; EGD, esophagogastroduodenoscopy.
[a)]Postoperative follow-up endoscopies were not performed in 10 patients of the GEJ ≤ 5 cm group and in 9 patients of the GEJ > 5 cm group because of benign pathology, old age, etc.

24 months in another 3 patients. However, the remaining 2 patients became chronic PPI users. One of the 2 chronic PPI users who underwent antireflux surgery at 4 years after developing symptoms recovered.

The postoperative follow-up endoscopies were not performed in 10 patients of the GEJ ≤ 5 cm group and in 9 patients of the GEJ > 5 cm group because of benign pathology, old age, etc. There were no differences in the endoscopic findings in terms of reflux esophagitis and Hill's grade between the 2 groups (Table 4).

DISCUSSION

The treatment for a gastric GIST is complete surgical resection with a microscopically negative margin [17]. Although it appears to be simple, sometimes it is very difficult to perform such a simple task, especially when the tumor is located close to the GEJ or the pylorus. Some investigators have suggested performing an enucleation or an enucleation-like resection when the tumor is located at or very close to the GEJ [8,13,21]. However, this approach can be dangerous because there is high risk of a microscopically positive margin resulting in a negative impact on the patient's survival [22]. Uchikoshi et al. [8] reported a case of recurrence at 2 years after enucleation of a GIST located near the GEJ. There were no cases of recurrent disease and all of the tumors were excised with negative surgical margins in our study. We think that this was possible because of our surgical policy of performing an open or a laparoscopic complete wedge resection of a gastric SMT measuring more than 2 cm in size, whenever possible. We performed a formal gastrectomy rather than an enucleation when a complete wedge resection was not possible. There was one exception to our surgical policy as previously mentioned. The patient is recovering well after 6 years of the initial operation (laparoscopic enucleation) without any evidence of recurrence and after 3 years and 6 months of the laparoscopic completion total gastrectomy without any symptoms of reflux esophagitis.

If the upper or lateral border of an SMT involves the GEJ and the wedge resection line for the tumor crosses the GEJ, there is an apparent resultant damage to the LES. However, it is not certain whether this will result in GERD at a later stage because there is a lack of data about this subject in the literature. Then what will happen in cases in which the lateral border of the tumor is located close to the GEJ but it does not involve the GEJ? As shown in Fig. 1, LES is composed of 2 muscular components; clasp and sling fibers. If the clasp and sling fibers are damaged at the same time, as in the wedge resection of an SMT located at the GEJ, there will be an apparent weakening of the LES and resultant development of GERD. What will happen if the damage is limited to some parts of the sling fibers only, as in the wedge resection of a SMT located near the GEJ but does not reach the GEJ? The objective of the current study was to find an answer to this question.

The incidence of GERD after gastric wedge resection of an SMT located close to the GEJ in our study was 23.5%. It was higher than the incidence of GERD in patients who underwent gastric wedge resections of gastric SMTs at other locations in the stomach and the incidence of GERD among the general population in Korea [23]. Moreover, the postoperative use of acid suppressive medications for more than one month was more frequently observed in the GEJ ≤ 5 cm group. This finding supports the higher incidence of GERD in the GEJ ≤ 5 cm group. Many patients complained of various upper gastrointestinal symptoms after gastric wedge resection as shown in Table 3. However, most of the symptoms except for the symptoms of GERD did not persist for more than one month. Hence, we set the cutoff for the duration of medication at one month.

The LA classification and Hill's grade were used as indicators of GERD in endoscopic finding because Hill's grade correlates well with the existence and severity of GERD [24]. We failed to demonstrate increased frequency of GERD in the GEJ ≤ 5 cm group with endoscopic findings. However, we think that this was because of a lack of endoscopic follow-up in some of the patients in both groups for several reasons. Therefore, a

prospective study in a large number of patients is needed.

In conclusion, the incidence of GERD was 23.5% after wedge resection of a gastric SMT located close to the GEJ. The incidence of GERD after wedge resection of a gastric SMT located close to the GEJ was higher than the incidence of GERD after wedge resection of an SMT at other locations in the stomach. Therefore, adequate care should be taken during the follow-up of these patients.

CONFLICTS OF INTEREST

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

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