Article

Necessity of Individualized Approach for Gastric Subepithelial Tumor Considering Pathologic Discrepancy and Surgical Difficulty Depending on the Gastric Location

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Abstract: Background: Depending on the location of gastric subepithelial tumors (SETs), surgical access is difficult with a risk of postoperative complications. This study aimed to evaluate the clinicopathological characteristics of small-sized gastric SETs and their surgical outcomes depending on location and provide considering factors for their treatment plans. Methods: This single-center, retrospective study reviewed patients who underwent surgical resection for gastric SETs (size < 5 cm). SETs were divided into benign SETs and gastrointestinal stromal tumors (GISTs) for comparison. The clinicopathological characteristics of SETs in the cardia were compared to those in the other regions. Results: Overall, 191 patients with gastric SETs (135 GISTs, 70.7%; and 56 benign SETs, 29.3%) were included. In multivariate analysis, age > 65 years (odds ratio (OR), 3.183; 95% confidence interval (CI), 1.310–7.735; p = 0.011), and non-cardiac SETs (OR, 2.472; 95% CI, 1.110–5.507; p = 0.030) were associated with a significant risk of malignancy. Compared to SETs in other locations, cardiac SETs showed more complications (3 versus 0; p = 0.000), and open conversion rates (2 versus 0; p = 0.003). However, the proportion of GISTs of SETs in the cardia is not negligible (52.9%). Conclusions: Considering the malignancy risk of SETs, active surgical resection should be considered in old age and/or location in the non-cardiac area. However, in young patients, SETs located in the gastric cardia have a considerably benign nature and are associated with poor short-term surgical outcomes. An individualized surgical approach for asymptomatic small SETs according to the gastric location is warranted.

Keywords: gastric subepithelial tumor; gastrointestinal stromal tumor; laparoscopic wedge resection

1. Introduction

Gastric subepithelial tumors (SETs) are rare lesions that account for less than 2% of all gastric tumors [1]. The majority of such lesions are small, asymptomatic, and accidentally found during routine upper endoscopy. With the increase in screening through upper endoscopy, gastric SETs are easily encountered [2,3]. The pathologic diagnosis of SETs is diverse, including gastrointestinal stromal tumors (GISTs), leiomyomas, schwannomas, heterotopic pancreas, and other benign or potentially malignant lesions. Among these, GISTs are the most common and potentially malignant lesions [4–6]. Because it is difficult to determine the pathologic diagnosis of SETs before surgery and the potential risk of malignancy, the standard treatment for gastric SETs is surgical resection with negative surgical margins [5,7,8]. In several retrospective studies, based on the location, pathologic discrepancies in gastric SETs have been reported, and benign tumors such as leiomyomas are the most common neoplasms in the cardia [9–11]. After surgical resection, numerous small SETs in the cardia are diagnosed as benign tumors. The surgical resection of such small benign SETs is not mandatory, considering the postoperative risk.
With advancements in technology, laparoscopic wedge resection has been recognized as the optimal choice for the treatment of gastric SETs [1,12]. However, the resection of SETs located in the cardia is extremely difficult and may lead to the risk of several complications, such as leakage, stenosis, and reflux [13–16]. Sometimes, major gastric resections, such as proximal gastrectomy or total gastrectomy, are inevitable. Hence, there is still controversy regarding the diagnosis and treatment plan for SETs in the cardia [17,18]. Therefore, further consensus on the diagnosis and treatment of SETs in the cardia is required to reduce unnecessary invasive surgery.

In this study, we retrospectively reviewed the clinicopathological features of surgically resected small gastric SETs. Depending on the location, we analyzed the pathological discrepancy and surgical outcomes of SETs to identify the factors that determine the individualized surgical approach for gastric SETs.

2. Materials and Methods

2.1. Patients and Methods

A retrospective single-center study involved 191 consecutive patients who underwent surgical resection for gastric SETs (size < 5 cm) at the National Cancer Center, Korea, between January 2000 and April 2020. The data collected were patients’ demographics, operation records, and tumor characteristics, including tumor size, location, change in mucosa, growth pattern, and histopathological findings. Before surgical resection, all the patients were diagnosed with gastric SETs using esophagogastroduodenoscopy (EGD) and computed tomography (CT). When necessary, endoscopic ultrasound (EUS) was performed to estimate the depth of the lesion, whereas endoscopic biopsy was performed to assess the mucosal changes of the lesion. This study was approved by the Institutional Review Board of the National Cancer Center (approval number: NCC2021-0026).

2.2. Statistical Analysis

All statistical analyses were performed using R (version 2.12.1, R Foundation for Statistical Computing, Vienna, Austria). Categorical variables were analyzed using the chi-squared test, and continuous data were analyzed using Student’s t-test and were described as mean plus minus standard deviation (mean ± SD). Multivariate analysis was performed using logistic regression analysis to assess the predictive risk factors for GISTs. Statistical significance was considered as a p-value less than 0.05.

3. Results

3.1. Baseline Characteristics of Patients

A total of 191 patients with gastric SETs (less than 5 cm in diameter) who underwent surgical resection were included in this study (Table 1). The mean age was 57.3 ± 11.4 years (range 24–85 years); 83 (43.5%) patients were men, and 108 (56.5%) patients were women. The mean size of SETs was 2.8 ± 0.9 cm (range 0.5–4.9 cm), and 34 SETs (17.85%) were located in the cardia. Wedge resection (laparoscopic resection) was performed in 183 patients (95.8%) and gastrectomy (open resection) in 8 patients (4.2%). One in eight patients who underwent gastrectomy were converted during wedge resection, whereas two of the eight patients underwent open surgery during laparoscopic wedge resection. According to the National Institutes of Health classification, among all SETs, 135 patients (70.7%) were histologically diagnosed with GISTs, and 56 patients (29.3%) were diagnosed with benign SETs, including leiomyomas (18, 9.4%), schwannomas (15, 17.8%), heterotopic pancreas (14, 7.3%), and other benign SETs (9, 4.7%), such as inflammatory pseudo-tumor, fibrotic nodule, and lymphoid hyperplasia. Seventy-three patients underwent endoscopic biopsy or endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) preoperatively, and 13 patients (17.8%) were diagnosed with GISTs or suspicious findings of GIST (data not shown).
3.2. Comparison of Benign SET and GIST/Risk Factors for GISTS

While comparing benign SETs and GISTS, the mean age was significantly higher in the GIST group (51.2 ± 10.9 versus 59.8 ± 10.7; p = 0.000), and the proportion of location in the cardia was significantly higher in benign SETs (28.6% versus 13.3%; p = 0.004). There were no differences in tumor size, growth pattern, and mucosal changes (Table 2). In multivariate analysis, for risk factors of GIST, age > 65 years was a significant risk factor (odds ratio (OR) 3.183; 95% confidence interval (CI): 1.310–7.735; p = 0.011), and tumor location in non-cardia showed a significantly higher odds ratio than other locations (OR 2.472; 95% CI: 1.110–5.507; p = 0.030) (Table 3).

Table 1. Baseline characteristics of patients.

| Variable                  | Total       |
|---------------------------|-------------|
|                           | N = 191     |
| Age (years)               | Mean ± SD   |
| Male                      | 83 (43.5%)  |
| Female                    | 108 (56.5%) |
| BMI (kg/m²)               | Mean ± SD   |
| Cardia                    | 34 (17.8%)  |
| Fundus                    | 26 (13.6%)  |
| Body                      | 109 (57.1%) |
| Antrum                    | 22 (11.5%)  |
| Extent of resection       | Wedge       |
| Gastrectomy               | 8 (4.2%)    |
| Surgical approach         | Laparoscopy |
| Open                      | 183 (95.8%) |
| Hospital stay (days)      | Mean ± SD   |
| GIST                      | 135 (70.7%) |
| NIH classification         | Very low risk|
| Low risk                  | 41 (30.4%)  |
| Intermediate risk         | 26 (19.3%)  |
| Pathology                 | 59 (43.7%)  |
| High risk                 | 9 (3.8%)    |
| Leiomyoma                 | 18 (9.4%)   |
| Schwannoma                | 15 (7.8%)   |
| Heterotopic pancreas      | 14 (7.3%)   |
| Others                    | 9 (4.7%)    |

SD, standard deviation; SET, subepithelial tumor; GIST, gastrointestinal stromal tumor. * One patient underwent gastrectomy conversion during wedge resection. b Two patients underwent open conversion during laparoscopic approach.

3.3. Comparison of Cardiac SETs and SETs in Other Locations

A total of 34 SETs were located at the cardia compared to SETs in other locations (Table 4). The mean age was significantly higher in non-cardiac SETs (52.6 ± 13.6 versus 58.3 ± 10.6; p = 0.026). Cardiac SETs appeared larger in size (3.1 ± 1.0 cm versus 2.8 ± 0.9 cm; p = 0.041) and showed a more endophytic growth pattern (73.5% versus 53.5%; p = 0.032) than non-cardiac SETs. The proportion of benign SETs was significantly higher in cardiac SETs (47.0% versus 25.5%; p = 0.012) than in the non-cardiac group. Eight patients (4.2%) underwent open surgery, and two of them underwent open conversion during laparoscopic resection due to difficulty in resection and failure in primary closure after wedge resection. There were more intraoperative complications in cardiac SETs (4 [11.8%] versus 6 [3.8%]; p = 0.069) compared to three complications postoperatively. In addition, the mean operation time (148.1 ± 70.2 min versus 84.9 ± 44.0 min; p = 0.000) and the mean hospital stay (6.4 ± 2.6 days versus 5.2 ± 1.9 days; p = 0.001) were significantly longer in cardiac SETs.
Table 2. Comparison of benign SETs and GISTs.

| Variable                  | Benign SET | GIST       | p-Value |
|---------------------------|------------|------------|---------|
|                           | N = 56     | N = 135    |         |
| Age (years)               |            |            |         |
| Male                      | 24 (42.8)  | 59 (43.7)  | 0.914   |
| Female                    | 32 (57.2)  | 76 (56.3)  |         |
| BMI (kg/m²)               | Mean ± SD  |            |         |
| Male                      | 24.7 ± 3.1 | 24.8 ± 3.3 | 0.783   |
| Female                    | 2.9 ± 1.0  | 2.8 ± 0.9  | 0.306   |
| Size (cm)                 | Mean ± SD  |            |         |
| Endophytic                | 36 (64.3)  | 73 (54.1)  | 0.194   |
| Exophytic                 | 20 (35.7)  | 62 (45.9)  |         |
| Mucosal change            | No         | 40 (71.4)  | 0.350   |
| Yes                       | 16 (28.6)  | 30 (22.2)  |         |
| Location of SET           |            |            |         |
| Cardia                    | 16 (28.6)  | 18 (13.3)  | 0.004   |
| Fundus                    | 1 (1.8)    | 25 (18.5)  |         |
| Body                      | 32 (57.1)  | 77 (57.0)  |         |
| Antrum                    | 7 (12.5)   | 15 (11.1)  |         |
| Extent of gastric resection|           |            |         |
| Wedge resection           | 51 (91.1)  | 132 (97.8) | 0.087   |
| Gastrectomy               | 5 (8.9)    | 3 (2.2)    |         |
| Surgical approach         |            |            |         |
| Laparoscopy               | 52 (92.9)  | 131 (97.0) | 0.189   |
| Open                      | 4 (7.1)    | 4 (3.0)    |         |
| Hospital stay (days)      | Mean ± SD  |            |         |
|                          | 6.0 ± 2.1  | 5.2 ± 2.0  | 0.018   |

SET, subepithelial tumor; GIST, gastrointestinal stromal tumor; SD, standard deviation. * One patient was converted to open proximal gastrectomy during laparoscopic wedge resection for SET at gastric cardia and was finally diagnosed with leiomyoma. ** Two patients were converted to open surgery due to failure of laparoscopic wedge resection.

Table 3. Risk factors of GISTs in multivariate analysis.

| Variable                  | Odds Ratio | 95% CI     | p-Value |
|---------------------------|------------|------------|---------|
| Age ≥65                   | 3.183      | 1.310–7.735| 0.011   |
| Sex Male                  | 1.045      | 0.537–2.034| 0.896   |
| Tumor location Non-cardia| 2.472      | 1.110–5.507| 0.030   |
| Growth pattern Endophytic | 0.441      | 0.390–1.507| 0.441   |
| Tumor size >2 cm          | 1.270      | 0.541–2.981| 0.583   |
| Mucosal change Yes        | 0.687      | 0.325–1.450| 0.324   |

Table 4. Comparison of cardiac and non-cardiac SETs.

| Variable                  | Cardia | Non-Cardia | p-Value |
|---------------------------|--------|------------|---------|
|                           | N = 34 | N = 157    |         |
| Age (years)               | Mean ± SD | 52.6 ± 13.6| 58.3 ± 10.6| 0.026   |
| Sex                       | Male   | 15 (44.1)  | 68 (43.3)| 0.932   |
| Female                    | 19 (55.9)| 89 (56.7)|         |
| BMI (kg/m²)               | Mean ± SD | 24.9 ± 2.8| 24.8 ± 3.4| 0.919   |
| Size (cm)                 | Mean ± SD | 3.1 ± 1.0 | 2.8 ± 0.9 | 0.041   |
| Mucosal change No         | 25 (73.5)| 120 (76.4)| 0.615   |
| Yes                       | 9 (26.5)| 37 (23.6)|         |
| Growth pattern Endophytic | 25 (73.5)| 84 (53.5)| 0.032   |
| Exophytic                 | 9 (26.5)| 73 (46.5)|         |
| Diagnosis                 | Benign | 16 (47.0)| 40 (25.5)| 0.012   |
| GIST                      | 18 (52.9)| 117 (74.5)|         |
| Extent of gastric resection| Wedge resection | 31 (91.2)| 152 (96.8)| 0.137   |
| Gastrectomy               | 3 (8.8)| 5 (2.5)|         |
| Surgical approach         | Laparoscopy | 30 (88.2)| 153 (97.5)| 0.015   |
| Open                      | 4 (11.8)| 4 (2.5)|         |
| Operation time (minutes)  | Mean ± SD | 148.1 ± 70.2| 84.9 ± 44.0| 0.000   |

Complications
Table 4. Cont.

| Variable   | Cardia      | Non-Cardia | \( p \)-Value |
|------------|-------------|------------|---------------|
| N = 34     | N = 157     |            |               |
| Intraoperative 4 (11.8) | 6 (3.8)     | 0.069      |
| Postoperative 3 (8.8)   | 0 (0)       | 0.000      |
| Hospital stay (days) Mean ± SD 6.4 ± 2.6 | 5.2 ± 1.9   | 0.001      |

SD, standard deviation; BMI, body mass index; GIST, gastrointestinal stromal tumor.

3.4. Complications

There were ten intraoperative complications and three postoperative complications. Intraoperative complications consisted of five bleeding events at the resection site (one in cardiac SETs, four in non-cardiac SETs), three gastric serosal injuries (one in cardiac SETs, two in non-cardiac SETs), and two perforations at the suture line after resection of cardiac SETs. Postoperative complications included cases of suspected micro-perforations at the stapled line, which were treated conservatively.

4. Discussion

In this retrospective study, we reviewed 191 gastric SETs and evaluated the clinico-pathological differences of SETs in the cardia compared to those of SETs in the other locations. Our results reveal that, in the cardiac SETs, the proportion of benign tumors was significantly higher, with more perioperative complications, a longer operation time, and prolonged hospital stay postoperatively. In a multivariate analysis, an age over 65 years and the location of the non-cardiac area were significant risk factors for GISTs.

Gastric SETs exhibit various clinical courses, ranging from benign to malignant. Most SETs are small, asymptomatic, and clinically insignificant at the time of detection [4,19]. Because these lesions arise from the muscles of neural origin and are covered with normal gastric mucosa, it is difficult to histologically diagnose them before surgical resection. Preoperative CT scan, EGD, or EUS have limitations in determining whether these lesions are benign or potentially malignant [19]. Therefore, surgical resection is usually recommended for gastric SETs larger than 2 cm [5,20]. Numerous patients undergo surgery without a definite histological diagnosis; however, controversy persists over the diagnostic and treatment plans for gastric SETs.

SETs located in the cardia are extremely difficult to surgically access, and there are concerns regarding postoperative complications such as luminal leakage, stenosis, and gastroesophageal reflux [16,21,22]. However, in patients who have undergone surgery, a significant number of benign SETs (not requiring immediate surgery) are sometimes diagnosed postoperatively. Several studies have reported that cardiac SETs are difficult to surgically resect with adequate margins, and postoperative complications, such as gastroesophageal reflux, stenosis, or leakage, may occur [1,13,15]. Our results also show a higher complication rate in cardiac SETs. Furthermore, two patients underwent open conversion during laparoscopic surgery. One of them failed to suture the gastric lumen after laparoscopic wedge resection and was converted to open surgery. The gastric lumen was sutured ineffectively after conversion, and proximal gastrectomy with double-tract reconstruction was performed. Although only two patients underwent open conversion, the results indicate that the resection of SETs in the cardia may increase the risk of open conversion during minimally invasive surgery.

Lee et al. [9] reported histological characteristics of gastric SETs based on their location. The results reveal that, in the cardia, the characteristics of gastric SETs were significantly different from those at the other locations. Several studies reported that leiomyomas were the most common SET in the cardia. The results of this study show that benign SETs were more frequent in the cardia than in other locations (47.0% versus 25.5%; \( p = 0.012 \)), and all the 16 benign SETs were histologically diagnosed as leiomyomas. However, nearly
50% of the cardiac SETs are still GISTs. Therefore, ignorance of malignancy at the cardia is alarming.

There are controversies regarding the diagnosis and treatment of gastric SETs [17,19]. Hence, most patients undergo surgery based on the size of the tumor or the presence of symptoms. Sometimes, surgeons find it difficult to perform immediate surgical procedures for SETs at difficult locations due to the risk of postoperative complications. Therefore, the literature recommends a tailored approach for SETs in the cardia [23,24], but there are concerns about the difficulty and complications of surgery.

Because benign SETs are the most common tumors in the cardia, there should be an accurate histological diagnosis before surgery. Several studies have reported the safety and feasibility of endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) and/or fine-needle biopsy (FNB) [25–28]. However, it is difficult to distinguish GISTs from benign tumors due to the insufficient amount of tissue obtained by EUS-FNA; therefore, it is not used as a routine diagnostic tool in gastric SETs [11,29,30]. As mentioned above, the cardia is a difficult and risky location to surgically access; such preoperative diagnostic tools might be helpful in establishing a treatment plan. If benign histological diagnosis can be confirmed before surgery, endoscopic surveillance without immediate surgery is a reasonable treatment plan for asymptomatic patients, and invasive surgery can be avoided.

This study has some limitations. First, it was a retrospective, single-institutional study with a limited sample size, and there might be selection bias. Second, since a number of patients have not undergone preoperative EUS-FNA and FNB in this study, further prospective studies are required to verify the efficacy of the preoperative pathological diagnosis via EUS-FNA and FNB.

In conclusion, old age and non-cardiac location were risk factors for GISTs in the multivariate analysis. SETs located in the cardia are difficult to surgically access, and surgery in this complicated location can lead to longer operation times, a prolonged hospital stay, and more complications. Therefore, a treatment plan for asymptomatic small-sized SETs should be individualized depending on the location of SETs. Because benign tumors are more frequent in the cardia than other locations, an accurate pathological diagnosis should be obtained preoperatively through further diagnostic tools such as EUS-FNA and FNB. Further studies for the better preoperative diagnosis of these diagnostic tools should be conducted in the future.

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References
1. Cheng, H.L.; Lee, W.J.; Lai, I.R.; Yuan, R.H.; Yu, S.C. Laparoscopic wedge resection of benign gastric tumor. Hepato Gastroenterol. 1999, 46, 2100–2104.
2. Papanikolaou, I.S.; Triantafyllou, K.; Kourikou, A.; Rösch, T. Endoscopic ultrasonography for gastric submucosal lesions. World J. Gastrointest. Endosc. 2011, 3, 86–94. [CrossRef]
3. Ye, L.S.; Li, Y.; Liu, W.; Yao, M.H.; Khan, N.; Hu, B. Clinical course of suspected small gastrointestinal stromal tumors in the stomach. World J. Gastrointest. Surg. 2020, 12, 171–177. [CrossRef] [PubMed]
4. Wiech, T.; Walch, A.; Werner, M. Histopathological classification of nonneoplastic and neoplastic gastrointestinal submucosal lesions. Endoscopy 2005, 37, 630–634. [CrossRef] [PubMed]
5. Casali, P.G.; Blay, J.Y.; Bertuzzi, A.; Bielack, S.; Bjerkehagen, B.; Bonvalot, S.; Boukowinas, I.; Bruzzi, P.; Tos, A.P.D.; Dileo, P. Gastrointestinal stromal tumours: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann. Oncol.* 2014, 25 (Suppl. S3), iii21–iii26.

6. Landi, B.; Blay, J.Y.; Bonvalot, S.; Brassier, M.; Coindre, J.M.; Emile, J.F.; Hautefeuille, V.; Honore, C.; Hartigau, E.; Mantion, G.; et al. Gastrointestinal stromal tumours (GISTs): French Intergroup Clinical Practice Guidelines for diagnosis, treatments and follow-up (SNFGE, FFCD, GERCOR, UNICANCER, SFCD, SFED, SFRG). *Dig. Liver Dis. Off. J. Ital. Soc. Gastroenterol. Ital. Assoc. Study Liver* 2019, 51, 1223–1231. [CrossRef] [PubMed]

7. Nishimura, J.; Nakajima, K.; Omori, T.; Takahashi, T.; Nishitani, A.; Ito, T.; Nishida, T. Surgical strategy for gastric gastrointestinal stromal tumors: Laparoscopic vs. open resection. *Surg. Endosc.* 2007, 21, 875–878. [CrossRef]

8. Koo, S.Y.; Lee, J.S.; Kim, J.J.; Park, S.M. Higher incidence of gastroesophageal reflux disease after gastric wedge resections of gastric fundus. *JSLS J.* 2010, 14, 108–119.e3. [CrossRef] [PubMed]

9. Lee, H.H.; Hur, H.; Jung, H.; Jeon, H.M.; Park, C.H.; Song, K.Y. Analysis of 151 consecutive gastric submucosal tumors according to tumor location. *J. Surg. Oncol.* 2011, 104, 72–75. [CrossRef]

10. Min, Y.W.; Park, H.N.; Min, B.H.; Choi, D.; Kim, K.M.; Kim, S. Preoperative predictive factors for gastrointestinal stromal tumors: Analysis of 375 surgically resected gastric subepithelial tumors. *J. Gastrointest. Surg. Off. J. Soc. Surg. Aliment. Tract* 2015, 19, 631–638. [CrossRef]

11. Kim, G.H.; Ahn, J.Y.; Gong, C.S.; Kim, M.; Na, H.K.; Lee, J.H.; Jung, K.W.; Kim, D.H.; Choi, K.D.; Song, H.J.; et al. Efficacy of Endoscopic Ultrasound-Guided Fine-Needle Biopsy in Gastric Subepithelial Tumors Located in the Cardia. *Dig. Dis. Sci.* 2020, 65, 583–590. [CrossRef] [PubMed]

12. Basso, N.; Rosato, P.; De Leo, A.; Picconi, T.; Trentino, P.; Fantini, A.; Silecchia, G. Laparoscopic treatment of gastric stromal tumors. *Surg. Endosc.* 2000, 14, 524–526. [CrossRef]

13. Llorente, J. Laparoscopic gastric resection for gastric leiomyoma. *Surg. Endosc.* 1994, 8, 887–889. [CrossRef]

14. Singaporewalla, R.M.; Baladas, G.H.; Lee, T.D. Laparoendoscopic removal of a benign gastric stromal tumor at the cardia. *Ann. Surg. Treat. Res.* 2000, 583–590. [CrossRef] [PubMed]

15. Tagaya, N.; Mikami, H.; Kogure, H.; Kubota, K.; Hosoya, Y.; Nagai, H. Laparoscopic intragastric stapled resection of gastric submucosal tumors located near the esophagogastric junction. *Surg. Endosc.* 2002, 16, 177–179. [CrossRef]

16. Ko, S.Y.; Lee, J.S.; Kim, J.J.; Park, S.M. Higher incidence of gastroesophageal reflux disease after gastric wedge resections of gastric submucosal tumors located close to the gastroesophageal junction. *Ann. Surg. Treat. Res.* 2014, 86, 289–294. [CrossRef] [PubMed]

17. Blay, J.Y.; Bonvalot, S.; Casali, P.; Choi, H.; Debieic-Richter, M.; Dei Tos, A.P.; Emile, J.F.; Gronchi, A.; Hogendoorn, P.C.; Joensuu, H.; et al. Consensus meeting for the management of gastrointestinal stromal tumors. Report of the GIST Consensus Conference of 20–21 March 2004, under the auspices of ESMO. *Ann. Oncol. Off. J. Eur. Soc. Med. Oncol.* 2005, 16, 566–578. [CrossRef] [PubMed]

18. Hwang, S.H.; Park, D.J.; Kim, Y.H.; Lee, K.H.; Lee, H.S.; Kim, H.H.; Lee, H.J.; Yang, H.K.; Lee, K.U. Laparoendoscopic removal of a benign gastric submucosal tumor at the cardia. *JSLS J. Soc. Laparoendosc. Surg.* 2006, 10, 117–121.

19. Cho, J.W. Current Guidelines in the Management of Upper Gastrointestinal Subepithelial Tumors. *Clin. Endosc.* 2016, 49, 235–240. [CrossRef]

20. Demetri, G.D.; Benjamin, R.S.; Blanke, C.D.; Blay, J.Y.; Casali, P.; Choi, H.; Corless, C.L.; Debieic-Richter, M.; DeMatteo, R.P.; Ettinger, D.S.; et al. NCCN Task Force report: Management of patients with gastrointestinal stromal tumor (GIST)–update of the NCCN clinical practice guidelines. *J. Natl. Compr. Cancer Netw.* 2007, 5 (Suppl. S2), S1–S29, quiz S30. [CrossRef] [PubMed]

21. Tagaya, N.; Mikami, H.; Kubota, K. Laparoscopic resection of gastrointestinal mesenchymal tumors located in the upper stomach. *Surg. Endosc.* 2004, 18, 1469–1474. [CrossRef] [PubMed]

22. Ye, X.; Yu, J.; Kang, W.; Ma, Z.; Xue, Z. Short- and Long-Term Outcomes of Endoscope-Assisted Laparoscopic Wedge Resection for Gastric Submucosal Tumors Adjacent to Esophagogastric Junction. *J. Gastrointest. Surg. Off. J. Soc. Surg. Aliment. Tract* 2018, 22, 402–413. [CrossRef] [PubMed]

23. Song, K.Y.; Kim, S.N.; Park, C.H. Tailored-approach of laparoscopic wedge resection for treatment of submucosal tumor near the esophagogastric junction. *Surg. Endosc.* 2007, 21, 2272–2276. [CrossRef]

24. Sasaki, A.; Koeda, K.; Obuchi, T.; Nakajima, J.; Nishizuka, S.; Terashima, M.; Wakabayashi, G. Tailored laparoscopic resection for suspected gastric gastrointestinal stromal tumors. *Surgery* 2010, 147, 516–520. [CrossRef]

25. De Moura, D.T.H.; McCarty, T.R.; Jirapinyo, P.; Ribeiro, I.B.; Flumignan, V.K.; Najdawai, F.; Ryu, M.; Lee, L.S.; Thompson, C.C. EUS-guided fine-needle biopsy sampling versus FNA in the diagnosis of subepithelial lesions: A large multicenter study. *Gastrointest. Endosc.* 2020, 92, 108–119.e3. [CrossRef] [PubMed]

26. Mekky, M.A.; Yamao, K.; Sawaki, A.; Mizuno, N.; Hara, K.; Nafeh, M.A.; Osman, A.M.; Koshikawa, T.; Yatabe, Y.; Bhatia, V. Diagnostic utility of EUS-guided FNA in patients with gastric submucosal tumors. *Gastrointest. Endosc.* 2010, 71, 913–919. [CrossRef] [PubMed]

27. Sepe, P.S.; Moparty, B.; Pitman, M.B.; Saltzman, J.R.; Brugge, W.R. EUS-guided FNA for the diagnosis of GI stromal cell tumors: Sensitivity and cytologic yield. *Gastrointest. Endosc.* 2009, 70, 254–261. [CrossRef] [PubMed]
28. Kamata, K.; Kurita, A.; Yasukawa, S.; Chiba, Y.; Nebiki, H.; Asada, M.; Yasuda, H.; Shiomi, H.; Ogura, T.; Takaoka, M.; et al. Utility of a 20G needle with a core trap in EUS-guided fine-needle biopsy for gastric submucosal tumors: A multicentric prospective trial. *Endosc. Ultrasound* **2021**, *10*, 134–140. [CrossRef]

29. Lee, M.; Min, B.H.; Lee, H.; Ahn, S.; Lee, J.H.; Rhee, P.L.; Kim, J.J.; Sohn, T.S.; Kim, S.; Kim, K.M. Feasibility and Diagnostic Yield of Endoscopic Ultrasonography-Guided Fine Needle Biopsy with a New Core Biopsy Needle Device in Patients With Gastric Subepithelial Tumors. *Medicine* **2015**, *94*, e1622. [CrossRef]

30. Na, H.K.; Lee, J.H.; Park, Y.S.; Ahn, J.Y.; Choi, K.S.; Kim, D.H.; Choi, K.D.; Song, H.J.; Lee, G.H.; Jung, H.Y.; et al. Yields and Utility of Endoscopic Ultrasonography-Guided 19-Gauge Trucut Biopsy versus 22-Gauge Fine Needle Aspiration for Diagnosing Gastric Subepithelial Tumors. *Clin. Endosc.* **2015**, *48*, 152–157. [CrossRef]