What about Gastric Schwannoma? A systematic review

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Abstract

Background Gastric schwannomas (Gs) are rare mesenchymal neoplasms of the gastrointestinal tract. Diagnosis is commonly achieved by pathological examination of resected specimen. In most cases surgical resection of submucosal gastric lesions is performed with wide margins. New minimally invasive techniques are described in an increasing number of cases.

Methods A Pubmed, Cochrane and Embase systematic review of the literature has been performed. Original papers, review articles, case reports published between 1988 and 2019 were considered eligible. Only papers written in English with full text available have been included. Articles reporting a follow up period, the type of treatment of the primary tumor and the appearance of local or distant recurrence were compared and analysed. Statistical analysis of data has been performed using GraphPad Prism 7 software.

Results 328 articles were found and a total of 102 were included in the analysis. Fifty-three papers reported the follow-up information, ranging from 1-417 months across different studies. Among them, 31 patients underwent endoscopic removal of the gastric lesions, 140 patients local surgery, including wedge resection or partial gastrectomy and 148 patients underwent subtotal or total gastrectomy. The median follow-up was of 27-38-33 months respectively. No recurrence or distant metastasis were detected in endoscopic group. Among local surgery group, liver metastasis was reported in one case; in extended surgery group one patient died for multiple liver metastases.

Conclusions In comparison with endoscopic group, local or more extended surgery involved a larger cohort of patients and reported satisfactory long-term results. Surgical approach in absence of a definite pre-operative diagnosis is considered the gold standard treatment for resectable Gs due to the excellent long-term outcome. Further studies are warranted to define the role of endoscopic treatment.
Keywords: Schwannoma, neurinoma, gastric neurinoma, gastric schwannoma.

Background

Schwannomas, also known as neurilemmomas, are rare tumors arising from Schwann cells in the peripheral aspect of the nerve and are encapsulated by a fibrous band. Epidemiological data from literature indicate that Gastrointestinal schwannomas (GIs) are uncommon neoplasms representing 2–7% of mesenchymal gastrointestinal tumors and account for 0.2% of all gastric tumors. Usually detected during the fifth decade with a female predominance, Gs are considered benign tumors. In most cases patients show unspecific symptoms such as upper abdominal pain, dyspepsia, bleeding, abdominal mass, these symptoms are mostly related to the tumor size and location. Gs usually appear as submucosal or muscular masses, posing a difficult differential diagnosis with GastroIntestinal Stromal Tumors (GISTs), leiomyomas and leiomyosarcomas. Most cases undergo surgical treatment on the basis of a clinical and radiological diagnosis of gastric stromal mass, and the definitive diagnoses of Gs, based on the pathological examination on the surgical specimen, is made only postoperatively. Malignant transformation is uncommon and surgical resection of the primary tumor is recommended.

A systematic review of the literature regarding the incidence, clinical features and treatment options of Gs has also been performed. The association between treatment options, follow-up period and the appearance of local or distant recurrence has also been investigated.

Methods

In order to assess the long-term oncological outcomes of endoscopic resection in comparison with local or more extended surgery for resectable Gs, a systematic review of the literature using PUBMED, COCHRANE and EMBASE databases has been performed.
Keywords used for the research were: schwannoma, neurinoma, gastric neurinoma, gastric schwannoma. Original papers, case reports and review articles published between 1988 and 2019 were considered eligible for the review. Articles reporting a median follow-up were included and analyzed in our research. Only papers written in English with full text available have been included. Papers with repeated case series and incorrect citations were excluded. Factors including year of publication, number of patients for each suitable papers and tumor sizes were also recorded. The choice of treatment (endoscopic, partial or more extended surgery), the median follow-up and the appearance of local or distance recurrence were compared. Statistical analysis of data has been performed using GraphPad Prism 7 software.

Results

Three hundred twenty-eight (n = 328) original articles were found. Two hundred-twenty-six (n = 226) papers were removed because written in other language than English (n = 36), no complete articles or abstract (n = 29), off topic (n = 128) or because no gastric schwannoma (n = 33). Studies selection has been performed using PRISMA flow diagram (Fig.1). One hundred four (n = 102) original articles including ten (n = 10) systematic review of literature, were considered eligible for our search (Table 1). A large cohort of patients (n = 647 patients) with Gs was examined.

Fifty-three (n = 53) articles reported the follow-up information (Table 2). Only three (n = 3) papers reported disease recurrence in 4 patients: one (n = 1) patient with local recurrence and three (n = 3) with liver metastases. No distant or local recurrence during a mean 28-month follow-up period were observed in our two cases. The median follow-up time was 22.75 months (95% CI: 12–36), the median tumor size was 2.9 cm (95% CI: 2.17–4), the median number of cases was 1. Subtotal or total gastrectomy was performed in 46% of the patients, local surgery in 44% and 10% underwent endoscopic surgery. (Fig. 2)
Thirty-one (n = 31) patients underwent endoscopic removal of the gastric lesions and the median follow-up among this group was of 27 months; no recurrence or distant metastasis were detected. Local surgery, including wedge resection or partial gastrectomy were performed among one-hundred forty (n = 140) patients and the median follow-up among this group was of 38 months. Liver metastasis diagnosis 1 year after surgery was reported in 1 case. Despite aggressive chemotherapy the patient died few months later. Extended surgical approach, including subtotal or total gastrectomy, was performed among one hundred forty-eight (n = 148) patients. One patient died for multiple liver metastases despite a surgery with curative intent. The median follow-up among this group was of 33 months. One more local and one distant recurrence are reported but the type of treatment is not recorded for these patients (Table 2).

Discussion

Gastric Submucosal tumors (SMTs) are classified into three groups: myogenic tumors (leiomyomas or leiomyosarcomas), neurogenic tumors (schwannomas, granular cell tumors, and neurofibromas), and GastroIntestinal Stromal Tumors (GISTs). Leiomyomas and schwannomas are usually classified as benign tumors, while GISTs are considered potentially malignant and leiomyosarcomas are considered malignant. Schwannoma is a subtype of neurogenic tumors arising from Schwann cells which form the sheath around the axons of the peripheral nerve, and can develop anywhere along the peripheral course of the nerve\textsuperscript{2}. Gastrointestinal Schwannomas (Gs) are uncommon neoplasms representing 2–7% of mesenchymal gastrointestinal tumors and account for 0.2% of all gastric tumors and 4% of all benign tumors of the stomach\textsuperscript{1}. First described by Daimaru et al. in 1988, Gs are generally slow-growing and asymptomatic, and the prognosis is excellent. Voltaggio et al. estimated that the ratio of gastric GIST to Gs is approximately 45 to 1.
Gs are usually observed in the fifth and sixth decade of life with a female predominance\(^6\), the most common site is the gastric body, followed by gastric antrum and fundus. Clinical detection of these tumors is difficult and patients usually present unspecific symptoms like epigastric discomfort, epigastric pain, gastrointestinal bleeding or palpable mass. Patients may be asymptomatic and the tumor can be discovered incidentally\(^4\).

The preoperative differential diagnosis is still challenging, and the main problem is the differentiation of Gs from GIST and smooth muscle tumors. Compared to GIST on CT examination, schwannomas appear as a mass developing inside the gastric lumen with an exophytic or mixed growth pattern, and do not usually show signs of haemorrhage, necrosis, cystic changes or calcification\(^7\). However smaller GISTs can present as small hypervascular masses with marked enhancement on CT examination, making differentiation from GSs difficult\(^8\). Gastric leiomyomas usually appear as homogeneous hypoattenuating masses with an endoluminal growth pattern on plain CT, and show mild to moderate enhancement on contrast CT. Another typical feature of leiomyomas is involvement of gastric cardia and the esophagogastric junction. Choi et al calculated the growth rate based on computed tomography (CT) images of patients with a series of follow-up: tumor volume doubling times for Gs were significantly longer than those of GISTs (\(p = 0.004\)).

Endoscopy usually reveals a submucosal elevated lesion with a smooth overlying normal mucosa, a central ulcer can be seen in 25–50% of cases, due to ischemic changes in the covering mucosa \(^8\). However, it may be difficult to achieve the correct histological diagnosis with only a standard endoscopic biopsy, because the surface of a gastric SMT is covered with normal epithelium and superficial endoscopic biopsy usually shows normal mucosa. EUS features may be helpful for differentiating gastric schwannomas from other
mesenchymal tumors, especially GISTs. Although endoscopic ultrasonography (EUS) is a useful tool for diagnosing gastric SMTs, it is not always possible to differentiate a schwannoma from a GIST or a leiomyoma by EUS, as the tumor originates from the muscularis propria layer. Endoscopic ultrasonography scans (EUS) can be used to delineate the full depth of the tumor and to direct needle biopsy. Histological diagnosis by an EUS-fine-needle aspiration biopsy (FNAB) represents a reliable, useful and suitable method for the histological evaluation of gastric submucosal tumors (SMTs) including Gs. The overall diagnostic rate for SMT by an EUS-FNAB has been reported to be relatively high (83.9) combining both diagnostic and suspicious results. However, the accuracy diagnostic rate may be influenced by the tumor lesion’s size and only a limited number of patients perform this procedure.

Schwannomas grow as a nodular, well-circumscribed, encapsulated mass on the periphery of a nerve. Histologically are spindle cell neoplasms that typically have two components: compact spindle cell Schwann cell components (Antoni A areas), showing occasional palisading (Verocay Bodies) alternating with and looser hypocellular areas (Antoni B areas). Focal nuclear atypia and mitotic activity may be present. Thick-walled, hyalinized blood vessels are commonly present. By immunohistochemistry, tumor cells are strongly and uniformly positive for S100 protein and usually positive for glial fibrillary acid protein (GFAP); EMA-positivity may be encountered in subcapsular areas. As Schwannomas are negative for CD117, DOG1, CD34, SMA and desmin, they can be easily distinguished from GISTs which are positive for CD117 and DOG-1 or from leiomyoma as they are typically positive for SMA and desmin.

According to literature surgical approach in absence of a definite pre-operative diagnosis is considered the gold standard treatment for respectable Gs due to the excellent long-term outcome².
The disease recurrence was not related to the type of surgery performed. Out of the 4 cases of disease recurrence, one patient underwent to local resection, one patient to more extended surgery and in two cases the type of surgery was not reported. The literature analysis showed that one-hundred forty (n = 140) patients performed a local resection with a median follow-up of thirty-eight (n = 38) months. Extended surgery, including subtotal or total gastrectomy was performed among one hundred forty-eight (n = 148) patients, mean follow up was 33 months. Both groups reported satisfactory long-term results but a significant statistically difference was not observed. Although only few articles regarding the endoscopic resection of Gs reporting a follow-up period have been described in literature, it seems to be a new valid non-invasive alternative treatment due to the benign clinical behaviour of these tumors. The literature analysis showed that only 31 patients underwent to endoscopic removal of the gastric lesions and the median follow-up among this group was of 27 months with no recurrence. A cohort of 14 patients with Gs who received endoscopic resection of the gastric lesions previously detected by EUS, were retrospectively reviewed by Hu J et al. The preoperative diagnosis was based only on imaging and EUS-FNA was not performed in order to minimize the risk of tumor rupture and spread. Ten patients (n = 10) received endoscopic full-thickness resection (EFTR); (n = 3) patients were treated by endoscopic submucosal dissection (ESD) and ligation-assisted endoscopic enucleation (EE-L) was performed for 1 patient. No recurrence or metastases were found during the follow up period (28 months) and mortality rates were not observed. These experiences confirm that currently available advanced endoscopic resection techniques can treat most Gs with a minimally invasive approach. The limited number of patients and a short follow-up (27 vs 35.5) cannot allow to make definitive comparison of prognosis between endoscopic and surgical groups. Nevertheless, endoscopic treatment represents a very appealing option when deemed suitable. US and
CT diagnostic features are not fully reliable, and gastric GIST could present a very high risk of local and distant recurrence when resected with an incomplete surgical margin. Thus, preoperative pathological diagnosis seems to be mandatory in order to perform minimally invasive treatment. EUS-FNAB is safe, reliable and recommended when gastric stromal lesions are detected in order to define the risk features of GIST and select cases with indication to neoadjuvant treatment\textsuperscript{24}. A further benefit of such approach is to identify the cases of Gs that can be treated with a minimally invasive approach. Nowadays surgical resection is currently considered the gold standard treatment: the groups involving a partial or more extended surgery included a larger cohort of patients and reported satisfactory long-term results. However, a statistically significant difference was not observed comparing the groups.

Mortality and recurrence were not observed in endoscopic group, which includes a smaller number of cases. Further studies encouraging the use of endoscopic resection for Gs and reporting a follow-up period are needed.

**Conclusion**

Surgical approach in absence of a definite pre-operative diagnosis is considered the gold standard treatment for resectable Gs due to the excellent long-term outcome. Further studies are warranted in order to define the role of endoscopic treatment.

**Abbreviations**

Gs: Gastric schwannomas

GIs: GastroIntestinal schwannomas

GISTs: GastroIntestinal Stromal Tumors

SMTs: Submucosal tumors

EGD: Esophagogastroduodenoscopy
EUS: Endoscopic ultrasonography
CECT: Contrast-enhanced computed tomography
CT: Computed tomography
SMA: Smooth muscle actin
FNAB: EUS-fine-needle aspiration biopsy
GFAP: Glial fibrillary acid protein
EFTR: Full-thickness resection
ESD: Endoscopic submucosal dissection
EE-L: Ligation-assisted endoscopic enucleation

Declarations

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Not applicable.

Consent for publication
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Availability of data and materials
None.

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Tables
| Author                  | Year of Publication | Number of cases | Treatment                                                |
|------------------------|---------------------|-----------------|---------------------------------------------------------|
| Wang W et al (9)        | 2019                | 19              | Surgical treatment                                      |
| Wang J et al (26)       | 2019                | 38              | Not reported                                            |
| Paramythiotis D et al (2) | 2018              | 2               | Open surgical treatment                                 |
| Pesenti C et al (28)    | 2019                | 1               | Not reported                                            |
| Drago J et al (1)       | 2019                | 1               | Laparoscopic resection                                  |
| Mekras A et al (29)     | 2018                | 4               | (n=2) laparoscopic resection; (n=2) open gastric wedge  |
| Sanei B et al (30)      | 2018                | 1               | Open surgery, subtotal gastrect gastrectejunost         |
| Sunkara T et al (31)    | 2018                | 1               | Open surgery, subtotal gastrect gastrectejunost         |
| Bae H et al (32)        | 2018                | 85              | Partial gastrect                                        |
| Shawgi M et al (33)     | 2018                | 1               |                                                                 |
| Lyros O et al (34)      | 2017                | 1               | "rendez-vous" endoscopic-laparoscopic resection         |
| Takasumi M et al (35)   | 2017                | 3               | Follow-up                                               |
| Choi KW et al (36)      | 2017                | 1               | Open subtotal gastrectomy with Roux-en-Y gastrojejunost |
| Hu J et al (22)         | 2017                | 14              | Endoscopic resection                                    |
| Hu BG et al (37)        | 2017                | 1               | Laparoscopy converted to laparotomy for resection of the |
| Liu J et al (38)        | 2017                | 12              | Surgery                                                 |
| Shimizu S et al (39)    | 2017                | 1               | Laparoscopic distal gastrectomy dissection              |
| Choi CW et al (40)      | 2017                | 2               | Not reported                                            |
| Kamata K et al (41)     | 2017                | 5               | Surgical resection                                      |
| Romdhane H et al (42)   | 2016                | 1               | Laparoscopic partial gastrect                           |
| Koizumi S et al (43)    | 2016                | 3               | 2 patients: surgical 1 patient: follow-up               |
| Álvarez Higuera FJ et al (44) | 2016            | 1               | Conservative management                                 |
| Vargas Flores E et al (45) | 2016             | 1               | Surgical laparoscopic subtotal gastrect                 |
| Kudose S et al (46)     | 2016                | 1               | Distal gastrect                                         |
| Mohanty SK et al (47)   | 2016                | 1               | Open surgery                                           |
| Lee Sj et al (48)       | 2016                | 27              | Not reported                                            |
| Oh Sj et al (49)        | 2016                | 1               | Subtotal gastrectomy with D-2 lymph node dissection     |
| Lavy Ds et al (50)      | 2016                | 1               | Laparoscopic partial wedge                             |
| Tatangelo F. et al (51) | 2016                | 1               | Subtotal omento-gastrrect                               |
| Yoon JM et al (14)      | 2016                | 27              | Surgical excision                                       |
| Stephen Kinsey-Trotma et al (52) | 2016        | 1               | Subtotal omento-gastrrect                               |
| Singh A et al (10)      | 2016                | 1               | No surgical intervention. Regular follow-up             |
| Cai MY et al (20)       | 2016                | 14              | Endoscopic en bloc resection. In one case, endoscopy suspended. In one case the patient underwent laparoscopic surgery. |
| Authors                     | Year | Patients | Procedure                                      |
|-----------------------------|------|----------|------------------------------------------------|
| Meng FS et al (53)          | 2016 | 1        | Endoscopic submucosa                            |
| Shah AS et al (54)          | 2015 | 1        | Exploratory laparotomy with gastric resection   |
| Crouthamel MR et al (55)    | 2015 | 2        | Laparoscopic sleeve gastrectomy                 |
| Tao K et al (8)             | 2015 | 30       | Laparoscopic surgical resection                 |
| Ikehara H. et al (15)       | 2015 | 2        | Surgical resection                             |
| Sreevathsa MR et al (56)    | 2015 | 1        | Minilaparotomy and sleeve resection            |
| Manji M et al (57)          | 2015 | 1        | Gastroscopy with resection                      |
| Enshaei A et al (59)        | 2015 | 1        | Surgical resection                             |
| Hong X et al (60)           | 2015 | 1        | Laparoscopic partial resection                  |
| Zhang Y et al (61)          | 2015 | 1        | Laparoscopic subtotal resection                 |
| Sousa D et al (62)          | 2015 | 1        | Surgical resection                             |
| Yang LH et al (63)          | 2015 | 1        | Total gastrectomy                              |
| Yang JH et al (19)          | 2015 | 1        | Conventional laparotomy with gastrectomy       |
| Park HC et al (65)          | 2015 | 31       | Not reported                                   |
| Li B et al (21)             | 2014 | 6        | Endoscopic intervention                        |
| Ji JS et al (66)            | 2015 | 8        | Not reported                                   |
| Liu-Ye Huang et al (67)     | 2014 | 1        | Not found                                      |
| Zheng L et al (4)           | 2014 | 29       | All patients were treated by surgery including:
|                            |      |          | - gastrectomy (n = 13), gastric wedge resection (n = 8), subtotal gastrectomy (n = 7), and total gastrectomy (n = 1). |
| Rodriguez E. et al (68)     | 2014 | 1        | Not reported                                   |
| Wang G et al (18)           | 2014 | 1        | Surgical treatment. Abdominal                  |
| Lee SS et al (69)           | 2013 | 1        | Surgical treatment                             |
| Di Cataldo A et al (70)     | 2013 | 1        | Wedge resection                                |
| Juan F. Alvarez et al (71)  | 2013 | 1        | Laparoscopic resection                          |
| Atmatzidis S et al (72)     | 2012 | 1        | Surgical treatment: partial gastric resection   |
| Choi J W et al (13)         | 2012 | 16       | Surgical treatment                             |
| Hong SW et al (73)          | 2012 | 1        | Laparoscopic gastric wedge resection            |
| Zhong DD et al (74)         | 2012 | 4        | (n=2) laparotomy and resection of gastrectomy  |
| Jai Hyang Go et al (75)     | 2012 | 1        | Total Gastrectomy                              |
| Yoon W et al (76)           | 2012 | 1        | Laparoscopic partial gastrectomy               |
| Fujiwara S et al (77)       | 2013 | 14       | Laparoscopic partial gastrectomy               |
| Williamson JM et al (11)    | 2012 | 3        | Surgical: tumours were resected or wedge gastric resection |
| Takemura M et al (12)       | 2012 | 1        | Distal gastrectomy with lymph node dissection  |
| Euanorasetr C et al (78)    | 2011 | 1        | Hemigastrectomy with Billroth II               |
| Fukuchi M et al (79)        | 2012 | 1        | Laparoscopy-assisted distal gastrectomy        |
| Voltaggio L et al (7)       | 2012 | 51       | Surgical treatment                             |
| References                                      | Case Number | Tumor size (cm) | Treatment                                      | Follow up time median month (range) |
|------------------------------------------------|-------------|----------------|-----------------------------------------------|-------------------------------------|
| Paramythiotis D et al (2)                      | 2           | (n=1) 2.8×1.5×1.8 (n=1) 5 | Local lpt* resection                          | (n=1) 1 (n=1) NA                     |
| Mekras A et al (29)                            | 4           | 1.5 ± 2.5       | Local lps* resection (n=2) Lpt gastric wedge resection(n=2) | 102.5 (20-185)                     |

Table 2 (n=53) articles reported the follow-up information.
| Study Reference | Sample Size | Dimension | Procedure | Follow-up |
|-----------------|-------------|-----------|-----------|-----------|
| Sanei B et al (30) | 1 | 5 × 6 | Local lpt resection | NA |
| Sunkara T et al (31) | 1 | 3.2 × 3.7 × 4.1 | Local lpt resection | 2 |
| Bae H et al (32) | 85 | NA | Surgery | 72 (19–125) |
| Takasumi M et al (35) | 3 | NA | (n=2) Follow-up (n=1) local lpt resection | 93 (83-103) |
| Choi KW et al (36) | 1 | 3.2 × 2.5 | Lpt subtotal gastrectomy | 24 |
| Hu J et al (22) | 14 | 0.5 ± 2.5 | Complete endoscopic resection | 28.5 (4–53) |
| Hu BG et al (37) | 1 | 4 × 3 | Lpt complete resection of the tumor | 12 |
| Shimizu S et al (39) | 1 | 6.5 × 4.5 × 3.5 | Lps distal gastrectomy | 5 |
| Romdhane H et al (42) | 1 | 2.5 | Lps partial gastrectomy | 12 |
| Koizumi S et al (43) | 3 | NA | Surgical resection (n=2) Follow up (n=1) | 48 (24.3-71.7) |
| Vargas Flores E et al (45) | 1 | 1.6 × 1.3 | Lps tumor resection | NA |
| Kudose S et al (46) | 1 | NA | Distal gastrectomy | 12 |
| Mohanty SK et al (47) | 1 | 7 × 6.2 × 8 | Lpt subtotal gastrectomy | 3 |
| Cai MY et al (20) | 14 | 1.73±1.10 | (n=12) endoscopic en bloc resection; (n=1) endoscopic was suspended; (n=1) lps surgery | 47 (17-77) |
| Shah AS et al (54) | 1 | 4-5 | Exploratory lpt with gastric resection | 1 |
| Crouthamel MR et al (55) | 2 | NA | Lps sleeve gastrectomy | Regular fup |
| Tao K et al (8) | 30 | 1.3±8 | (n=11) lps wedge resection; (n=4) lpt wedge resection; (n=2) lps partial gastrectomy; (n=3) lpt partial gastrectomy; (n=7) lpt subtotal gastrectomy; (n=3) lpt total gastrectomy | 50 (12-97) |
| Manji M et al (57) | 1 | 5x6 | Lpt gastrotomy with resection of the mass | 6 |
| Li B et al (21) | 5 | 0.8±2.05 | 2/5 EFR***, 2/5 ESE, 1/5 STER | 5.9 (4.4-7.4) |
| Zheng et al (4) | 29 | 2.1±7.9 | (n=13) Partial gastrectomy; (n=8) gastric wedge resection; (n=7) subtotal gastrectomy; (n=1) total gastrectomy | 47 (6-157) |
| Wang G et al (18) | 1 | 5.6x5.3x4 | Lpt surgical resection | 12 |
| Atmatzidis S et al (72) | 1 | 5x3x2.5 | Partial gastrectomy | 12 |
| Study                          | Cases | Tumor Size | Procedure                        | Tumor Excision | Notes |
|-------------------------------|-------|------------|----------------------------------|----------------|-------|
| Zhong DD et al (74)           | 4     | 3.3±8.1    | (n=2) Lps wedge resection; (n=2) Subtotal gastrectomy | 21,5 (4-39)    |       |
| Fujiwara et al (77)           | 14    | 2±7.5      | Lps partial gastrectomy          |                | 55 (25-243) |
| Takemura M et al (12)         | 1     | 6x5        | Distal gastrectomy               |                | 3     |
| Fukuchi M et al (79)          | 1     | 3.2x3x2.3  | Lps subtotal gastrectomy         |                | 36    |
| Voltaggio et al (7)           | 51    | 1±10.5     | (n=21) Partial gastrectomy; (n=18) Local excision or wedge resection; (n=2) biopsy; (n=2) NA | 214.5 (12-417) |       |
| Watanabe A et al (80)         | 1     | 1.9x1.8    | Lps partial gastrectomy          |                | 24    |
| Ohno T et al (82)             | 2     | -4.7x3.4x4.5 -2.2x1.8x1.7 | Lps wedge resection            |                | 15 (6-24) |
| Komatsu D et al (86)          | 1     | 2.5x2.5x1.5 | LPS partial gastrectomy          |                | 10    |
| Agaimy A et al (85)           | 58    | 0.7±15.5   | NA                              |                | 39.5 (2-77) |
| Ogasawara N et al (87)        | 1     | 5          | Surgical resection               |                | 6     |
| Hong HS et al (89)            | 16    | 1.2 ± 8    | NA                              |                | NA    |
| Yoon HY et al (88)            | 1     | 6 × 5.5 × 4 | Subtotal gastrectomy            |                | 36    |
| Tozbikian G et al (90)        | 1 ( two lesions) | -3.8 x 3 x 3 -1.2 x 1 x 0.6 | Subtotal gastrectomy |                | 13    |
| Chen YY et al (92)            | 1     | 5          | Wedge resection                  |                | 36    |
| Khan AA (93)                  | 1     | 4x2.5      | Lpt Wedge resection              |                | 12    |
| Fujii Y et al (95)            | 1     | 4.3 x 4.2 x 3.6 | Partial resection                |                | 5     |
| Uchikoshi F et al (96)        | 1     | 2.7±7.5    | Lps intragastric enucleation/resection |                | NA    |
| Iwamoto CA et al (97)         | 1     | 3          | Surgical resection               |                | NA    |
| Povoski CA et al (101)        | 1     | 5          | Lpt Subtotal gastrectomy         |                | 30    |
| Janowitz P. et al (98)        | 1     | 4.5x3      | Fundectomy                       |                | 36    |
| Rymarczyk G et al (102)       | 1     | 2±10       | Tumor excision                   |                | 8     |
| Otani Y et al (103)           | 3     | 0.8±6      | Lps wedge resection              |                | 60    |
| Prévot et al (104)            | 3     | 2±11       | Surgical removal                 |                | 90.5 (1-180) |
| Melvin WS et al (108)         | 3     | NA         | Tumor excision                   |                | NA    |
| Silecchia G et al (106)       | 1     | 2.5        | Lps resection of the gastric wall under endoscopic guidance | 13 |       |
| Sarlomo-Rikala M et al (107)  | 6     | 2±9        | NA                              |                | 162 (36-288) |
| Bandoh T et al (109)          | 11    | NA         | Tumor enucleation                |                | 60    |
| Gennatas CS et al (112)       | 1     | NA         | Tumor excision + chemotherapy    |                | 12    |
** Figures **

| Daimaru Y et al (6) | 23 | 2.8 (0.5-7) | Surgical resection | 112.5 (4-221) |

* lps = laparoscopy; lpt = laparotomy
** NA = not available
*** EFR: endoscopic full-thickness resection, ESE: endoscopic submucosal excavation; STER: submucosal tunelling endoscopic resection.

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**Figure 1**

PRISMA Flow Diagram for studies selection.
Figure 2

a) Tumor size in centimeters; b) Number of patients; c) Months of follow-up d) Type of treatment.

Supplementary Files

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