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**Synchronous occurrence of gastric cancer and gastrointestinal stromal tumor: A case report and review of the literature**

Liu J *et al.* Gastric cancer concomitant with GIST

Jie Liu, Bin-Jie Huang, Fei-Fei Ding, Fu-Tian Tang, Yu-Min Li

**Jie Liu, Bin-Jie Huang, Fei-Fei Ding, Fu-Tian Tang, Yu-Min Li,** Department of General Surgery, Lanzhou University Second Hospital, Lanzhou 730030, Gansu Province, China

**Jie Liu, Bin-Jie Huang, Fei-Fei Ding, Fu-Tian Tang,** **Yu-Min Li,** Key Laboratory of the Digestive System Tumors of Gansu Province, Lanzhou University Second Hospital, Lanzhou 730030, Gansu Province, China

**Author contributions:** Liu J performed data collection, statistical analysis, literature collection, and manuscript writing; Huang BJ, Tang FT, and Ding FF participated in the investigation and revision; Li YM designed, supervised, and guided this study; and all authors contributed to the article and approved the submitted version.

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**Corresponding author: Yu-Min Li, MD, PhD, Chief Physician, Professor, Surgeon, Surgical Oncologist,** Department of General Surgery, Lanzhou University Second Hospital, No. 80 Cuiyingmen, Lanzhou 730030, Gansu Province, China. liym@lzu.edu.cn

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**Abstract**

BACKGROUND

To evaluate the clinicopathological features and prognosis of gastric cancer (GC) occurring synchronously with gastrointestinal stromal tumor (GIST).

CASE SUMMARY

We report 19 patients with concurrent GC and GIST (17 male and 2 female, median age 62 years). GC was most often located in the lower third of the stomach. GIST was diagnosed preoperatively in four patients. GIST was most often located in the gastric body (*n* = 8, 42%). The most common growth pattern in GIST was extraluminal (*n* = 12, 63%). The positive expression rates of CD117 and CD34 in GIST were 100% and 95%, respectively. Most patients with GIST (*n* = 17, 89%) were very low or low risk. There was no recurrence of GIST during follow-up. The 3-year cumulative survival rate was 73.9%, and the 5-year cumulative survival rate was 59.2%. The combined analysis of this study and literature reports (47 reports, 157 patients) found that GC and GIST were usually located in the lower third (42%) and middle third (51%) of the stomach. GC was usually early (stage I: 42%), poorly differentiated (42%) intestinal-type adenocarcinoma (51%). GISTs were primarily small in diameter (median: 1.2 cm) and very low or low risk (89%).

CONCLUSION

Synchronous GC and GIST may not be rare. They have specific clinicopathological characteristics, and may have mutual inhibition in pathogenesis and progression.

**Key Words:** Gastric cancer; Gastrointestinal stromal tumor; Synchronous occurrence; Diagnosis; Prognosis; Case report

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**Core Tip:** We conclude that there are specific clinicopathological features in gastric cancer (GC) and gastrointestinal stromal tumor (GIST), as is often seen in older men; GC is usually a poorly differentiated enterotype early adenocarcinoma located in the lower third of the stomach. GIST is usually small in diameter, low or very low risk, and located in the body of the stomach. We hypothesized that GC and GIST might be affected by the same unknown carcinogen, leading to the simultaneous proliferation of epithelial and mesenchymal cells. GC and GIST may inhibit each other in the occurrence and development of the disease.

**INTRODUCTION**

Gastric cancer (GC) is a common malignant tumor originating from epithelial tissue. Gastrointestinal stromal tumor (GIST) accounts for 1%-2% of gastrointestinal tumors[1,2]. The prevalence of GC varies widely between western and eastern countries. However, there is no significant difference in GIST[3,4]. GIST is most common in the stomach (60%-70%) and small intestine (20%-30%)[5]. Nevertheless, it is rare for GIST and gastric epithelial tumors to co-occur in the stomach. Maiorana *et al*[6] first reported the synchronous occurrence of gastric epithelial and stromal tumors in 2000. Globally, most studies on concurrent GC and GIST are case reports[7-41]. Collision tumor formed by combined GC and GIST is also rare, a particular case of GC and GIST occurring synchronously[2,32,37-44]. At present, the etiology of GC occurring simultaneously with GIST is unclear. Several studies have reported the synchronous occurrence of GC and GIST with specific pathological features[45]. Some researchers believe that it is an accidental phenomenon[6,11]. Other researchers believe that several unknown carcinogens induce simultaneous proliferation and tumorigenesis of epithelial and stromal cells, such as gene mutation, nitrite, and *Helicobacter pylori*[6,7,9-11,18,30,34,37,38,46-49]. In addition, the impact of co-occurrence of GC and GIST on treatment options and prognosis is controversial.

From December 1, 2011 to December 31, 2021, 5408 GC patients were treated at the Lanzhou University Second Hospital, China. We analyzed 19 patients with synchronously occurring GC and GIST in our institution and reviewed previous studies. The Ethics Committee of Lanzhou University Second Hospital approved this retrospective study (2021A-585). This study aimed to provide some auxiliary data for deepening the understanding of concurrent GC and GIST.

**CASE PRESENTATION**

***Chief complaints***

The chief complaints at initial admission were upper abdominal pain (*n* = 8, 42%), epigastric discomfort (*n* = 6, 32%), abdominal distension (*n* = 4), black stools (*n* = 3), acid reflux (*n* = 2) and progressive dysphagia (*n* = 2). Among them, two patients with the chief complaint of “acid reflux” had symptoms of heartburn and eructation. Some patients had more than one of these symptoms.

***History of present illness***

The disease duration ranged from 15 d to 4 years (median, 4 mo). The outpatients were admitted to the hospital for gastric malignant tumors.

***History of past illness***

Eight patients (42%) had weight loss (range: 1-20 kg) within the last year. Six patients (32%) had prior surgical history, including three cases of cholecystectomy, one of appendectomy, two of fracture surgery and one of cataract surgery. Six patients (32%) had comorbidities, including three with hypertension, two with type 2 diabetes, and one with both.

***Personal and family history***

None of the patients had a family history of GC or GIST.

***Physical examination***

Specialist physical examination showed eight cases (42%) with positive signs; all of which were mild tenderness under the xiphoid process. The median body mass index was 22.8 kg/m2 (range: 13.1-27.9 kg/m2).

***Laboratory examinations***

Preoperative laboratory tests showed six (32%) patients with elevated tumor markers. The most frequently observed tumor markers with elevated reference values were CEA and CA72-4, followed by CA125 and CA199 (Table 1). Six patients (32%) with anemia (hemoglobin: No. 1 = 108 g/L; No. 7 = 102 g/L; No. 8 = 124 g/L; No. 10 = 129 g/L; No. 11 = 119 g/L; and No. 17 = 88 g/L). Four patients (21%) had positive occult blood tests.

***Imaging examinations***

The results of preoperative abdominal contrast-enhanced computed tomography (CT) and esophagogastroduodenoscopy (EGD) suggested that GC was most commonly located in the lower third of the stomach (*n* = 7, 37%), followed by the middle third (*n* = 6, 31%), upper third (*n* = 5, 26%) and multiple distributions in the stomach (*n* = 1, 5%). The median maximum diameter was 3.5 cm (range, 1.5-10.0 cm). The most common gross appearances were ulcerative type (Figure 1A) (*n* = 10, 53%) and ulcerative infiltrative type (*n* = 4). The detailed clinicopathological data of all GC patients are shown in Table 1. Preoperative CT found suspected GIST in three cases (15%) (Figure 1B and C). All 19 patients underwent EGD, and four (21%) were found to be suspicious of GIST (Figure 1D); of whom, three were diagnosed by endoscopic ultrasonography (Figure 1E). The clinicopathological data of GIST are shown in Table 2.

For the histological subtype, 18 cases were adenocarcinoma (Figure 2A) and one was high-grade intraepithelial neoplasia. Seven cases (39%) were classified as moderately to poorly differentiated, five were moderately differentiated, five were poorly differentiated, and one was well differentiated. For the Lauren classification, six patients (32%) were classified as diffuse type, five as intestinal type and three as mixed type. In pTNM staging, there was one stage 0, three stage IA, three stage IB, three stage IIA, three stage IIB, four stage IIIA, and two stage IIIC.

Intraoperative exploration revealed suspicious GIST in 12 cases (63%). The location of GIST was most commonly in the gastric body (*n* = 8, 42%), followed by gastric fundus (*n* = 3, 15%), gastric antrum (*n* = 2), gastric cardia (*n* = 2), duodenum (*n* = 2), and jejunum (*n* = 2). The median maximum diameter of GIST was 1.4 cm (range: 0.2-12.0 cm), and the diameters of two were 9 cm (Figure 1B) and 12 cm (Figure 1C), respectively. Seven cases (50%) of GIST were subserosal, five were muscular, and two were submucosal. For the growth pattern of GIST, 12 (63%) were extraluminal, two were intraluminal, of which one caused pyloric obstruction (Figure 1B), four were intramural, and one was both intraluminal and extraluminal, with compression of the spleen and left kidney (Figure 1C). Eighteen GISTs had a mitotic index < 5/50 HPF. According to the risk category for malignant behavior of GIST, 17 (89%) patients were classified as low or very low risk, and two as high risk. Sixteen GISTs were composed of spindle cells (Figure 2B), and one of spindle and epithelial cells. All GISTs were positive for CD117 (Figure 2C), 18 were positive for CD34 (Figure 2D), 18 for Dog-1 (Figure 2E), and nine for vimentin. S-100 protein was negative in 17 cases, and SMA protein was negative in 15 cases.

**MULTIDISCIPLINARY EXPERT CONSULTATION**

Xiao Chen, Professor, Chief of Gastroenterology; Ai-lin Song, Professor, Chief of Gastroenterology; Ying-xin Kang, Professor, Chief of Gastroenterology.

**FINAL DIAGNOSIS**

Synchronous occurrence of GC and GIST.

**TREATMENT**

According to the Japanese Classification of Gastric Cancer, all GC patients underwent D2 Lymphadenectomy and postoperative chemotherapy. Complete resection or local resection with adequate margins was performed for all GIST, and oral imatinib mesylate (IM) was administered postoperatively for medium- or high-risk GIST. All 19 patients received radical gastrectomy combined with complete stromal tumor resection, including four (21%) with laparotomy and 15 cases (79%) with laparoscopy. For GC, total gastrectomy was performed in six cases (31%), distal gastrectomy in 11 (58%) and proximal gastrectomy in two (11%). For postoperative treatment of GIST, two patients were given oral IM because GIST was classified as high risk, but the rest were not treated.

**OUTCOME AND FOLLOW-UP**

Patients were followed up by outpatient review or telephone; the primary event was death, and the last follow-up date was March 2022. During follow-up, two patients were lost, 12 survived, and five died of GC recurrence or distant metastasis (Table 1). No recurrence of GIST was found in 17 patients who were successfully followed up. The 3-year cumulative survival rate of 19 patients with synchronously occurring GC and GIST was 73.9%, and the 5-year cumulative survival rate was 59.2% (Figure 3A).

**DISCUSSION**

It has been reported that the incidence of GC accompanied by GIST is 0.29%-0.53%[6,30,52]. As the diagnostic criteria for GIST have changed and awareness has increased, data surveys in the United States and the Netherlands showed that the incidence of GIST has increased year by year[4,53]. Kawanowa *et al*[54] found that microscopic GIST was found in 35% of GC patients undergoing resection. In our series, the incidence of synchronous GC and GIST was 0.35% (19/5408). It is possible that the incidence of GC simultaneously occurring with GIST is higher because most GISTs are small (68% ≤ 2 cm, Table 3) and it is easy to miss diagnosis[7-41]. In addition to the small size of GIST, there are other factors contributing to the low preoperative diagnosis rate: (1) EUS demonstrates superior diagnostic capability for mesenchymal tissue GIST compared to conventional gastroscopy; however, most patients still opt for conventional gastroscopy; (2) Patients with concurrent GC and GIST primarily seek medical attention due to symptoms related to GC, resulting in a rarity of clinical recognition. Consequently, some clinicians may prioritize the diagnosis of GC while overlooking the presence of GIST; and (3) Some GISTs are extraluminal. Studies have shown that epigastric discomfort, dull pain, upper gastrointestinal bleeding, or melena may occur when the diameter of GIST is > 5 cm, and bleeding is the first symptom in most patients[55]. The clinical signs of synchronous GC and GIST lack specificity, and the symptoms of GIST are often masked by GC[45], probably because most GISTs are small in diameter (68% ≤ 2 cm).

In this study, the median age of concurrent GC and GIST was 62 years and combined with the literature review[7-41], the median age was 70 years (range: 45-93 years, 47 reports, 157 patients) (Table 3), which is similar to the median age at diagnosis for GIST (range: 66-69 years)[55]. Older people may have specific changes in gene expression profiles, lower immunity, and greater susceptibility to synchronous tumors[45]. The male to female ratio in this study was 8.5:1.0, and combined with other studies[7-41], the ratio was 3.4:1.0 (Table 3). The latest statistics report that GC incidence is two times higher in males than in females[56], while GIST has almost equal gender distribution[55].

The preoperative diagnosis rate of synchronous GIST and GC is low, and diagnosis is usually made during intraoperative exploration or postoperative pathological examination[6,30,45]. GIST is often misdiagnosed as metastatic lymph nodes from epithelial-mesenchymal transition or GC recurrence and metastasis. In our study, the preoperative diagnostic rate of suspicious GIST was 15% with CT, 21% with gastroscopy, and 63% with intraoperative exploration. Lin *et al*[45] found that among 42 patients with synchronous GC and GIST, only one (2.4%) was diagnosed preoperatively. Therefore, it is necessary for clinicians to carefully improve imaging examinations such as endoscopy and CT before surgery, and conduct comprehensive and meticulous exploration during surgery. If suspicious lesions are found, a routine biopsy or intraoperative frozen examination is performed to confirm the diagnosis, and a detailed analysis of specimens after surgery is required.

In the present study, the median maximum diameter of the GC was 3.5 cm (range: 1.5-10.0 cm), and the most common appearance of GC was ulcerative (53%), which was similar to that reported by Maiorana *et al*[6] (50%) and Cai *et al*[25] (50%). Summarizing this study and literature review[7-41], we found that the median maximum diameter of the GC was 4 cm (range: 1.0-10.2 cm). GC is usually located in the lower third of the stomach (42%), stage I (42%), poorly differentiated (42%), and intestinal adenocarcinoma (51%) (Table 3). Therefore, we hypothesized that the occurrence of GIST might have an inhibitory effect on the progression of GC. This was a finding not encountered before in the literature. However, this conjecture is solely based on the findings of pertinent global research due to limited case numbers and a dearth of molecular biological mechanism investigations, thereby insufficiently substantiating this conclusion.

In the case of GC occurring concomitantly with GIST, we found that GISTs were most frequently located in the gastric body (42%), with a maximum diameter of 1.4 cm (68% ≤ 2 cm), most often occurred in the subserosal layer, and the most common growth pattern was extraluminal (Table 2). These results were similar to our summary[7-41], with 51% of GISTs located in the middle third of the stomach, and the median largest diameter of GISTs was 1.2 cm (78% ≤ 2 cm) (Table 3). Yan *et al*[30] reported that 93% of GISTs simultaneously occurring with GC were < 2 cm in diameter, and Agaimy *et al*[57] found that 73% of GISTs were < 5 cm in diameter. Liu *et al*[52] found that GISTs that occurred simultaneously with GC were small, with a median diameter of 0.8 cm (range: 0.2-2.5 cm), while the median value of pure GIST was 7.5 cm (range: 1.5-30.0 cm). At present, the most practical value for the diagnosis of GIST is the proto-oncogene c-kit gene expression product CD-117 (80%-100%) and CD-34 (56%-83%)[55-57]. In our study, the positive rates of CD117 and CD34 in GIST co-occurring with GC were 100% and 95%, respectively; similar to the results reported by Liu *et al*[52] (CD117 92.6%, CD34 96.3%). Lin *et al*[45] found that compared with pure GIST, the positive rate of CD117 (66.7%) and CD34 (59.5%) in synchronous GC combined with GIST was lower. On the contrary, Liszka *et al*[26] found that the positive expression rate of CD117 in GIST combined with other tumors and GIST alone was 100%, and the positive rate of CD34 was 54.5% and 56.7%, respectively, with no significant difference. Combined with the literature review[7-41], we found that only two cases were negative for CD117 expression and one was negative for CD34 expression (Table 3). Liu *et al*[52] found that most incidental GISTs (90.7%) had low mitotic activity and low risk, while only 1.9% of clinical GIST cases had low risk. Cai *et al*[25] and Liszka *et al*[26] found that patients with synchronously occurring GIST and other tumors had a lower risk of invasion and a smaller tumor diameter than patients with GIST alone. Yan *et al*[30] reported that almost all GISTs occurring concomitantly with GC were stratified as very low or low risk. We found that 89% of GISTs were low or very low risk. When combined with other studies[7-41], we found that 89% of GISTs co-occurring with GC were classified as low or very low risk (Table 3). Liu *et al*[58] conducted a retrospective analysis on 24 patients diagnosed with GC combined with GISTs. The findings revealed that the occurrence of GIST combined with GC was more prevalent among elderly male patients, while GIST predominantly exhibited low-risk characteristics. Similarly, Liu *et al*[59] conducted an analysis on 26 patients diagnosed with GC and GISTs, revealing that the Fletcher classification typically indicates a very low or low risk of invasion in patients with GIST and GC. These findings may be related to the following factors: Widespread KIT/PDGFRA mutations in early tumorigenesis. Since additional mutations are required for GIST progression, synchronized tumors may influence the environment, release factors that inhibit the acquisition of further genetic changes, or inhibit GIST growth[30]. It may also be incidental that GIST develops later than GC.

At present, the etiology of GC co-occurrence with GIST is unclear. Some researchers believe that it is an accidental phenomenon[6,11], and others believe that several unknown carcinogens induce simultaneous proliferation and tumorigenesis of epithelial and stromal cells, such as gene mutation, nitrite, and Helicobacter pylori[6,7,9,11,18,30,34,37,38,46-49]. Gene mutations may lead to the interaction of two adjacent tissues, interfering with mesothelial and epithelial cell growth regulation, thereby inducing different tumors in two tissues of the same organ. Through next-generation sequencing, Liu *et al*[10] detected that GC and GIST had significantly different gene mutations at the molecular level (TP53 and KIT gene mutations, respectively). Some researchers have hypothesized that there might be a field effect, with etiological cofactors leading to these two lesions[60]. Based on the high correlation between clinical and microscopic GIST and GC, we believe that GC and GIST may be affected by the same unknown carcinogen, resulting in the simultaneous proliferation of epithelial and stromal cells.

Synchronous GC and GIST treatment is comprehensive and based on surgery. The surgical method is mainly based on GC, and adjuvant IM therapy should be given to patients with intermediate- and high-risk GIST after surgery[55]. In our study, all patients were given chemotherapy based on GC after surgery, and imatinib (IM) therapy was also given to patients with high-risk GIST. Xu *et al*[61] demonstrated that apatinib exhibits promising therapeutic potential and tolerability in patients with GC complicated by GISTs who have shown resistance to IM in combination with chemotherapy. However, there is still no conclusion on whether there is any interaction between chemotherapy for GC and IM treatment for GIST and the time sequence of medication.

For patients with synchronously occurring GC and GIST, studies have shown that regardless of the Fletcher grade of GIST, GC is the main factor affecting the prognosis[35,45,51]. Liu *et al*[52] conducted a follow-up study on 22 patients with synchronously occurring GC and GIST who underwent surgery and found that the 5-year survival rate after surgery was 31.8%, and the average survival time was 3 years. Lin *et al*[45] found that GIST risk stratification, postoperative oral IM, and synchronous GC were independent predictors of survival; the 3-year survival rate was 62.6%, the 5-year survival rate was 57.8%, and the 5-year overall survival rate of patients with synchronous GC was lower than that of patients with nonsynchronous GC (very low/low: 60.2% *vs* 98.6%; moderate/high risk: 33.3% *vs* 98.1%). In our study, the 3-year cumulative survival rate of 19 patients with concurrent GC and GIST was 73.9%, and the 5-year cumulative survival rate was 59.2%. We analyzed the survival of 46 patients with synchronous GC and GIST by combining the patients in this study (*n* = 17) and those reviewed in the literature (*n* = 29) (Figure 3B)[6-67]. The 3-year cumulative survival rate was 54.5%, the 5-year cumulative survival rate was 46.7%, the median survival time was 4 years, and none of the GISTs recurred during follow-up. In addition to the report by Liu *et al*[52], the 5-year survival rate of patients with GC combined with GIST in our study and in most studies was higher than that of patients with simple curable GC treated with surgery (5-year survival rate: 45%)[62], and similar to that of patients with simple GIST treated with complete resection (5-year survival rate: 50%-65%)[55]. To our knowledge, this is a finding that has not been encountered before in the literature. The reasons may be as follows: In patients with GC combined with GIST, most GC is early stage (42%), and most GIST is very low or low risk (89%). We hypothesize that there may be mutual inhibition between GC and GIST in the pathogenesis and progression. It is crucial to emphasize that our conjecture is solely based on a comprehensive analysis of current research findings both domestically and internationally. However, in order to validate this hypothesis, extensive medical records and molecular biological investigations are imperative due to the absence of studies elucidating the underlying molecular mechanisms. In contrast, distinct findings emerge when comparing and analyzing GC patients with GIST and those diagnosed solely with GIST. Liu *et al*[58] conducted a comparative analysis between GC patients with GIST (*n* = 24) and gastric GIST patients (*n* = 217), revealing significantly lower 5-year disease-free survival rate and disease-specific survival rate in the former group compared to the non-synchronous group (54.9% *vs* 93.5%, *P* < 0.001; 37.9% *vs* 89.9%, *P* < 0.001). Similarly, Liu *et al*[59] conducted an analysis on a cohort of 26 patients with synchronous GC (group A) and 96 patients with gastric GIST (group B). The findings revealed that the Fletcher classification (*P* < 0.05) and synchronous GC (*P* < 0.01) were identified as independent prognostic factors.

**LIMITATION**

Our study had some limitations. Firstly, the research data quality could be better, with a limited number of cases (19 cases) and insufficient pathological research data. Additionally, more comprehensive test results and genetic and molecular data must be needed to support statistically significant conclusions based on limited information. Methodologically, this study is a retrospective single-centre investigation lacking prospective and case-control studies (including patients with superficial GC and Simple GIST patients) and molecular biological mechanism exploration. Regarding the study’s content, an in-depth investigation of H. pylori was not conducted. Consequently, this study remains at a preliminary stage of exploration. This study concludes that further investigations are required to validate and supplement the conjecture. The future research will require enhancements in data quality, research methods, and a deeper exploration of the content.

**CONCLUSION**

Synchronous of GIST and GC are more common than previously considered. There are specific clinicopathological features between GC and GIST, such as those commonly seen in older men, GC is usually poorly differentiated intestinal-type early adenocarcinoma located in the lower third of the stomach, and GIST is usually small-diameter, low risk or very low risk located in the gastric body. We hypothesize that GC and GIST may be affected by the same unknown carcinogen, resulting in the simultaneous proliferation of epithelial and stromal cells. GC and GIST may have mutual inhibitory effects on the pathogenesis and disease progression. Importantly, a substantial amount of case data and studies on molecular biological mechanisms are imperative to validate this hypothesis.

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**Figure Legends**



**Figure 1 Gastroscopic and imaging features of gastric cancer concomitant with gastrointestinal stromal tumor.** A: Ulcerative gastric adenocarcinoma (patient 6); B: Pyloric adenocarcinoma (thin arrows) and intraluminal gastrointestinal stromal tumor (GIST; thick arrows) leading to pyloric obstruction (patient 1); C: Giant GIST (9.5 cm × 10.9 cm × 11.7 cm, arrow) showing intraluminal and extraluminal growth, compressing the spleen and left kidney (patient 11); D: Suspicious GIST under gastroscopy (patient 6); E: Suspicious GIST on ultrasound Endoscopy (patient 6).



**Figure 2 Pathological and immunohistochemical features of gastric cancer concomitant with gastrointestinal stromal tumor.** A: Microscopically showing gastric adenocarcinoma (patient 6; HE, 100 ×); B: Microscopically showing gastric stromal tumor (patient 6; HE, 100 ×); C: CD117 positive under microscope (patient 6; immunohistochemical staining, 200 ×); D: CD34 positive under microscope (patient 6; immunohistochemical staining, 200 ×); E: Dog-1 positive under microscope (patient 6; immunohistochemical staining, 200 ×).



**Figure 3 Kaplan-Meier survival curves.** A: 19 patients with gastric cancer (GC) accompanying gastrointestinal stromal tumor (GIST) in this study; B: 46 patients with GC accompanying GIST in this study and the literature reviewed.

**Table 1 Clinicopathological features, treatment and outcome of gastric cancer in 19 patients**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **No.** | **Age in yr** | **Sex** | **BMI** | **Chief complaint** | **Disease duration (mo)** | **Comorbidities in yr** | **Tumor marker** | **Primary site** | **Size (cm)** | **pTNM** | **Gross appearance** | **Differentiation** | **Lauren type** | **Outcome** |
| 1 | 66 | M | 17.9 | Epigastric discomfort | 12.0 | HBP/20 | (-) | Pylorus | 1.5 | T3N0M0/IIA | Ulcerativeinfiltrative  | M-P | Mixed | 38 m, PFS |
| 2 | 56 | M | 24.2 | CT found by accident | 2.0 | No | (-) | Cardia, body, antrum | 10.0 | T3N1M0/IIB | Diffuse infiltrative | P, SRCC | Diffuse | NA |
| 3 | 53 | M | 19.5 | Upper abdominal pain | 0.5 | No | CA72-4↑ | Body | 4.5 | T3N0M0/IIA | Ulcerative infiltrative | P, SRCC | NA | 48 m, PFS |
| 4 | 71 | M | 21.5 | Epigastric discomfort | 6.0 | No | (-) | Body | 2.0 | T2N0M0/IB | NA | M-P | Mixed | 53 m, PFS |
| 5 | 45 | M | 21.8 | Bloating, acid reflux | 6.0 | No | (-) | Pylorus | 3.5 | T3N2M0/IIIA | Ulcerative | M-P, SRCC | Diffuse | 48 m, DOD |
| 6 | 55 | M | 25.5 | Epigastric discomfort | 2.0 | No | (-) | Antrum | 4.0 | T1bN0M0/IA | Ulcerative | M-P, SRCC | Intestinal | 6 m, PFS |
| 7 | 79 | F | 22.2 | Heartburn, abdominal pain, black stools | 2.0 | HBP/10, DM/10 | (-) | Antrum | 3.0 | TisN0M0/0 | NA | HGIEN | NA | 27 m, PFS |
| 8 | 58 | M | 27.9 | Upper abdominal pain | 4.0 | No | (-) | Antrum | 5.0 | T4aN0M0/IIB | Ulcerative | P | Diffuse | 26 m, PFS |
| 9 | 71 | M | 23.8 | Epigastric pain, acid reflux | 1.0 | HBP/10 | (-) | Antrum | 3.5 | T1bN0M0/IA | NA | M | Intestinal | 23 m, PFS |
| 10 | 56 | M | 23.2 | Upper abdominal pain, choking eating, black stools | 1.0 | No | (-) | Cardia | 1.5 | T2N0M0/IB | Ulcerative infiltrative | M | Intestinal | NA |
| 11 | 55 | M | 23.7 | Abdominal distension | 9.0 | No | CEA↑ | Fundus | 3.0 | T4aN3bM0/IIIC | Ulcerative | M | Intestinal | 10 m, DOD |
| 12 | 59 | M | 23.1 | Abdominal distension, black stools | 1.0 | DM/6 | (-) | Body | 5.0 | T2N0M0/IB | Ulcerative | P | Diffuse | 20 m, PFS |
| 13 | 62 | M | 22.9 | Upper abdominal pain | 12.0 | No | CEA↑, CA724↑ | Body | 2.0 | T3N0M0/IIA | Ulcerative | P, SRCC | Diffuse | 9 m, PFS |
| 14 | 49 | M | 13.1 | Epigastric discomfort | 12.0 | No | (-) | Cardia, fundus | 5.0 | T4bN0M0/IIIA | Ulcerative | M-P | Mixed | 45 m, PFS |
| 15 | 65 | F | 23.6 | Epigastric discomfort, abdominal distension | 12.0 | No | (-) | Cardia, body | 2.5 | T4aN1M0/IIIA | Ulcerative | M | NA | 5 m, DOD |
| 16 | 73 | M | 21.3 | Epigastric discomfort | 48.0 | No | CA724↑ | Body | 5.0 | T4aN3bM0/IIIC | Ulcerative | M-P | Diffuse | 12 m, DOD |
| 17 | 62 | M | 22.8 | Upper abdominal pain | 6.0 | DM/6 | CEA↑, CA125↑ | Antrum | 3.5 | T4aN0M0/IIB | Ulcerative infiltrative | M | Intestinal | 70 m, PFS |
| 18 | 62 | M | 21.2 | Progressive dysphagia | 3.0 | HBP/30 | CA199↑  | Cardia | 4.5 | T4aN2M0/IIIA | Ulcerative | M-P | Mixed | 12 m, DOD |
| 19 | 72 | M | 22.4 | Upper abdominal pain | 0.5 | No | (-) | Body | 1.5 | T1bN0M0/IA | NA | W | NA | 63 m, PFS |

M: Male; F: Female; HBP: High blood pressure; DM: Diabetes Mellitus (Type 2); TG: Total gastrectomy; DG: Distal gastrectomy; PG: Proximal gastrectomy; pTNM: Pathological tumor-node-metastasis; SRCC: Signet-ring cell carcinoma; HGIEN: High-grade intraepithelial neoplasia; NA: Not assessed; PFS: Progression-free survival; DOD: Dead of disease; M-P: Moderately to poorly differentiated; M: Moderately differentiated; P: Poorly differentiated; W: Well differentiated.

**Table 2 The clinical, histological and immunohistochemical characteristics of gastrointestinal stromal tumor in 19 patients**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **No.** | **CT** | **EGD** | **Location** | **Origin** | **Size (cm)** | **Type** | **Growth pattern** | **Mitotic index (HPF)** | **Risk category** | **CD117** | **CD34** | **Dog-1** | **S-100** | **SMA** | **VIM** | **IM** |
| 1 | GIST | GIST | Antrum | Submucosal | 9.0 | Spindle, epithelioid | Intraluminal | < 5/50 | High | + | + | + | - | - | NA | Yes |
| 2 | (-) | (-) | Body | Muscularis | 0.4 | NA | Intramural  | < 5/50 | Very low | ++ | +++ | +++ | - | - | NA | No |
| 3 | (-) | (-) | Body | Subserous | 1.0 | Spindle | Extraluminal | < 5/50 | Low | + | + | + | - | - | + | No |
| 4 | Mass | (-) | Duodenum | NA | 2.0 | Spindle | Extraluminal | < 5/50 | Low | + | + | + | - | - | + | No |
| 5 | (-) | (-) | Jejunum | NA | 1.5 | Spindle | Extraluminal | < 5/50 | Low | ++ | + | +++ | - |  | NA | No |
| 6 | (-) | GIST | Fundus | Muscularis | 1.5 | Spindle | Extraluminal | < 5/50 | Low | + | + | + | - | - | + | No |
| 7 | GIST | GIST | Body | NA | 5.0 | Spindle | Extraluminal | < 5/50 | Low | + | + | + | - | - | + | No |
| 8 | Mass | Mass | Fundus  | Subserous | 1.0 | Spindle | Intraluminal  | < 5/50 | Low | + | + | + | - | NA | NA | No |
| 9 | (-) | Mass | Duodenum | NA | 4.0 | Spindle | Extraluminal | < 5/50 | Low | + | + | + | - | - | + | No |
| 10 | (-) | (-) | Cardia | Subserous | 0.2 | Spindle | Extraluminal | < 5/50 | Very low | + | + | + | - | - | NA | No |
| 11 | GIST | GIST | Body | Muscularis | 12.0 | Spindle | Extraluminal, intraluminal  | 6-10/50 | High | + | + | + | - | - | + | Yes |
| 12 | (-) | (-) | Jejunum | NA | 4.0 | Spindle | Extraluminal | < 5/50 | Low | + | - | + | - | - | + | No |
| 13 | (-) | (-) | Body | Muscularis | 0.4 | Spindle | Intramural  | < 5/50 | Very low | + | + | + | - | - | NA | No |
| 14 | (-) | (-) | Fundus | Subserous | 0.4 | Spindle | Extraluminal | < 5/50 | Very low | ++ | +++ | +++ | - | NA | NA | No |
| 15 | (-) | (-) | Body | Submucosal | 0.6 | Spindle | Intramural  | < 5/50 | Very low | + | + | + | - | - | NA | No |
| 16 | (-) | (-) | Body | Subserous | 3.0. | Spindle | Extraluminal | < 5/50 | Low | + | + | + | - | - | + | No |
| 17 | (-) | (-) | Antrum | Muscularis | < 1.0 | NA | Intramural  | < 5/50 | Very low | + | + | NA | NA | NA | NA | No |
| 18 | (-) | (-) | Cardia, fundus | Subserous | 0.4 | Spindle | Extraluminal | < 5/50 | Low | + | + | + | NA | - | NA | No |
| 19 | (-) | (-) | Body | Subserous | 1.3 | Spindle | Extraluminal | < 5/50 | Very low | + | + | - | - | NA | + | No |

NA: Not assessed; CT: Computed tomography; EGD: Esophagogastroduodenoscopy; V-L: Very low; L: Low; IN: Intermediate; H: High; IM: Imatinib mesylate; GC: Gastric cancer; GIST: Gastrointestinal stromal tumor.

**Table 3 Details of the clinical, histological, immunohistochemical, and outcomes of concurrent gastric cancer and gastrointestinal stromal tumor summarized in this study and literature review**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ref.** | **Sex** | **Age in yr** | **GC** | **GIST** | **Outcome** |
| **Location** | **Size (cm)** | **TNM status** | **Lauren** | **Differentiation** | **Location** | **Size (cm)** | **Risk** | **CD117** | **CD34** |
| Maiorana *et al*[6], 2000 | F | 81 | Cardias | 4.0 | T2bN0M0, IB | Intestinal | NA | Fundus | 5.0 | L | NA |  | 21 m, DOD |
| F | 79 | Antrum | 2.0 | T1bN0M0, IA | Diffuse |  | Pylorus | 6.0 | H |  | + | 54 m, PFS |
| M | 75 | Antrum | 4.0 | T2bN1M0, IIA | Intestinal |  | Antrum | 5.0 | L |  |  | 12 m, PFS |
| F | 79 | Pylorus | 1.2 | T2aN1M0, IIA | Intestinal |  | Cardias | 5.0 | L |  | + | 28 m, PFS |
| M | 79 | Antrum | 2.0 | T2aN0M0, IB | Intestinal |  | Cardias | 0.6 | V-L |  | + | 75 m, PFS |
| Bircan *et al*[7], 2004 | 71 | Antrum | 5.7 | T3NxM0 | Intestinal | P | Cardias | 0.5 | V-L | + | + | NA | 71 |
| 77 | Cardias | 7.5 | T2N1M0, IIA | NA | M | Cardias | 0.6 | V-L | + | + | NA | 77 |
| Villias *et al*[8], 2008 | M | 78 | Antrum | NA | T1N0M0, IA | Intestinal | M | Antrum | 0.9 | V-L | + | + | NA |
| Lin *et al*[9], 2006 | F | 70 | Cardias | 1.7 | T1N0M0, IA | NA | P, SRCC | Fundus | 1.1 | V-L | + | + | 14 m, PFS |
| Liu *et al*[10], 2018 | M | 72 | Antrum | 4.0 | T2N1M0, IIA | NA | M | Fundus | 2.0 | V-L | + | + | 18 m, PFS |
| Wronski *et al*[11], 2006 | F | 64 | Antrum | 5.0 | T4N0M0, IIB | Diffuse | NA | Cardias | 2.0 | L | + | + | NA |
| M | 66 | Cardias | 1.0 | T1N0M0, IA | Intestinal | NA | Cardias | 1.0 | V-L | + | + | NA |
| Theodosopoulos *et al*[63], 2011 | M | 80 | Antrum | 6.5 | T1N0M0, IA | Intestinal | W | Body | 3.0 | IN | + | NA | 12 m, PFS |
| Rauf *et al*[46]， 2006 | F | 70 | Antrum, body | 10.0. | T4N1M0, IIIA | Diffuse | P, SRCC | Body | 2.0 | L | + | + | 18 m, DOD |
| Namikawa *et al*[14], 2021 | M | 74 | Body | 2.0 | T2N0M0, IB | NA | M | Body | 2.2 | L | NA | NA | 1 m, PFS |
| Shimodate *et al*[15], 2014 | M | 79 | Body | 3.0 | T1bN0M0, IA | NA | NA | Body | 1.3 | V-L | + | + | NA |
| Khoshnevis *et al*[16], 2013 | F | 64 | Pylorus | 6.0 | T4N0M0, IIIA | Diffuse | P, SRCC | Fundus, body | 1.0 | H | + | NA | 4 m, PFS |
| Namikawa *et al*[17], 2016 | M | 58 | Body | 9.0 | T2N1M0, IIA | Diffuse | SRCC | Body | 21.0 | H | NA | NA | 4 m, PFS |
| Kaffes *et al*[18], 2002 | M | 78 | Antrum | NA | T1N0M0, IA | Diffuse | P | Body | 1.5 | ND | NA | + | 20 m, PFS |
| Uchiyama *et al*[19], 2007 | M | 74 | Antrum | 1.5 | T1aN0M0, IA | Intestinal | M-P | Body | 0.8 | L | + | + | NA |
| Salemis *et al*[20], 2008 | F | 78 | Antrum | 6.5 | T4N2M0, IIIA | Diffuse | P | Body | 1.0 | L | + | + | 14 m, DOD |
| Narasimhamurthy *et al*[21], 2010 | M | 65 | Cardias | 4.0 | T4NxM0 | Diffuse | P | Antrum | 2.5 | L | + | NA | NA |
| Ferreira *et al*[22], 2010 | M | 52 | NA | 10.2 | T3N1M0, IIB | NA | NA | NA | 1.1 | V-L | + | + | NA |
| F | 65 | NA | 4.8 | T3N1M0, IIB | NA | NA | NA | 0.7 | V-L | + | + |  |
| Gonçalves *et al*[23], 2010 | M | 74 | NA | NA | NA | NA | NA | NA | 1.2 | V-L | NA | NA | 5 m, DOD |
| M | 67 | NA | NA | NA | NA | NA | NA | 0.3 | V-L | NA | NA | 2 m, DOD |
| Jeong *et al*[24], 2011 | M | 74 | Antrum | 3.3 | T1aN0M0, IA | Intestinal | M | Body | 2.0 | V-L | + | + | NA |
| Cai *et al*[25], 2013 | M | 47 | Cardias | 8.0 | T3N1M0, IIB | NA | P | Cardias | 2.0 | V-L | + | + | NA |
| M | 80 | Antrum | 2.0 | T1N0M0, IA |  | P | Cardias | 1.5 | V-L | + | + |  |
| M | 60 | Antrum | 8.0 | T3N0M0, IIA |  |  | Antrum | 0.6 | V-L | + | + |  |
| F | 67 | Antrum | 4.0 | T3N1M0, IIB |  |  | Body | 0.8 | V-L | + | + |  |
| M | 78 | Pylorus | 6.0 | T4N2M0, IIIA |  |  | Body | 2.5 | L | + | + |  |
| M | 78 | Body | 10.0 | T3N1M0, IIB |  |  | Body | 1.4 | L | + | + |  |
| F | 59 | Body | 4.0 | T2N1M0, IIA |  | P | Body | 0.8 | L | + | + |  |
| M | 80 | Antrum | 6.0 | T2N0M0, IB |  | P | Body | 5.0 | L | + | + |  |
| Liszka *et al*[26], 2007 | M | 53 | NA | NA | NA | NA | NA | NA | NA | V-L | + | NA | NA |
| M | 63 | NA | NA | NA | NA | NA | NA | NA | L | + | NA |  |
| Yamamoto *et al*[27], 2012 | M | 67 | Body | 3.0 | T4N0M0, IIB | Diffuse | P | Body | 3.0 | L | + | + | NA |
| Gülpınar *et al*[28], 2014 | M | 75 | Antrum | NA | T1N1M0, IB | NA | M | Antrum | 1.0 |  | NA | NA | NA |
| Trihia *et al*[29], 2019 | M | 79 | Cardias | 8.5 | NA | Intestinal | M-P | Body | 0.9 | L | + | + | Days, DOD |
| Yan *et al*[30], 2013 | M | 53 | U | NA | T4N0M0, IIIA | NA | P | NA | 0.4 | V-L | NA |  | NA |
| M | 51 | U | NA | T4N3M0, IIIB |  | M-P |  | 0.8 | V-L | + |  |  |
| M | 62 | U | NA | T4N2M0, IIIA |  | P |  | 0.8 | V-L | NA |  |  |
| F | 73 | L | NA | T4N3M0, IIIB |  | P, SRCC |  | 0.2 | V-L | NA |  |  |
| M | 68 | M | NA | T1N0M0, IA |  | M |  | 0.8 | V-L | NA |  |  |
| F | 46 | L | NA | T1bN0M0, IA |  | P, SRCCM |  | 2.5 | L | + |  |  |
| M | 78 | U | NA | T4N1M0, IIIA |  | M |  | 1.5 | V-L | + |  |  |
| M | 66 | U | NA | T4N3M0, IIIB |  | M-P |  | 1.5 | V-L | + |  |  |
| M | 85 | U, M | NA | T4N2M0, IIIA |  | P |  | 1.0 | V-L | + |  |  |
| M | 68 | L | NA | T4N0M0, IIB |  | M |  | 0.8 | V-L | + |  |  |
| M | 69 | U | NA | T4N0M0, IIB |  | P, SRCC |  | 2.0 | V-L | + |  |  |
| M | 77 | U | NA | T2N1M0, IIA |  | M |  | 0.2 | V-L | + |  |  |
| M | 71 | L | NA | T4N3M0, IIIB |  | M-P |  | 0.6 | V-L | + |  |  |
| F | 77 | L | NA | T4N3M0, IIIB |  | M-P |  | 0.5 | V-L | + |  |  |
| F | 70 | L | NA | T1bN0M0, IA |  |  |  | 0.6 | V-L | + |  |  |
| Vogel *et al*[31], 2011 | M | 79 | Body | 6.0 | T1N0M0, IA | Diffuse | P, SRCC | Body | 0.8 | V-L | + | NA | 12 m, PFS |
| 1Ozgun *et al*[32], 2009 | M | 78 | Body | NA | NA | NA | NA | Antrum | 10.0 | H | + | + |  |
| Hsiao *et al*[33], 2009 | M | 75 | Cardias | 1.0 | T1N0M0, IA | NA | W | Cardias | 3.3 | L | + | + | 6 m, DOD |
| Kountourakis *et al*[34], 2008 | F | 72 | NA | NA | NA | Diffuse | NA | NA | 1.8 | V-L | + | + | 6 m, PFS |
| Lee *et al*[35], 2007 | M | 82 | Body | 9.5 | T4NxM1, IV | NA | NA | Body | 1.5 | L | + | + | NA |
| Chen *et al*[36], 2001 | M | 72 | Pylorus | 1.5 | NA | NA | NA | Body | 2.5 | V-L | + | + | NA |
| 1Katsoulis *et al*[37], 2007 | F | 78 | Cardias | NA | T4N3aM0, IIIB | Diffuse | P | Antrum | 0.9 | V-L | + | NA | NA |
| 1Liu *et al*[38], 2002 | M | 70 | Cardia, fundus | 8.5 | T4N0M1, IV | Intestinal | NA | Cardia | NA | V-L | + | + | 3 m, DOD |
| 1Toyoda *et al*[39], 2009 | F | 83 | Body | 9.0 | T4NxM0 | Intestinal | P | Body | 4.5 | H | + | + | 6 m, DOD |
| 1Matsuno *et al*[40], 2021 | M | 68 | Body | 5.0 | T3N0M0, IIA | NA | M | Body | 0.5 | V-L | + | NA | 2.5 yr, PFS |
| 1Kleist *et al*[41], 2010 | F | 86 | Body | 6.0 | NA | Intestinal | SRCC | Body | 6.0 | IN | + | + | 11 m, PFS |
| M | 78 | Body | 6.0 | NA | NA | SRCC | Body | 5.5 | IN | + | + | 4 m, DOD |
| 1Trabelsi *et al*[42], 2008 | M | 54 | NA | NA | NA | Diffuse | NA | NA | 1.0 | V-L | NA | NA | NA |
| 1Zámecník *et al*[64],2005 | F | 93 | Fundus | NA | LGIN, 0 | NA | NA | Fundus | 4.5 | L | + | + | NA |
| 1Idema *et al*[43], 2008 | M | 71 | Body | 5.0 | T4N2M0, III A | Intestinal | srcc | Body | 0.6 | V-L | + | + | 30 m, DOD |
| Alkaaki *et al*[65], 2018 | M | 55 | Cardia  | 1.7 | T1aNxM0 | NA | NA | Antrum | 10 | H | - | + | NA |
| 1Bi *et al*[66], 2009 | F | 73 | Fundus, body | 4.0 | T4N2M0, III A | Intestinal | W | Fundus | 4 | L | + | + | NA |
| 1Firat *et al*[44], 2010 | M | 63 | Cardia | 9.0 | T4N3bM0, IIIB | Intestinal | NA | Cardia | 0.4 | V-L | + | + | 13 m, DOD |
| M | 60 | Body | 4.0 | T1N0M0, IA | Intestinal |  | Body | 0.5 | V-L | + | + | 12 m, PFS |
| Telugu *et al*[67], 2016 | M | 63 | Cardia | 4.0 | T3N1M0, IIB | NA | M | Fundus | 1.0 | V-L | - | + | 7 m, PFS |
| Lin *et al*[45], 2014 | M (32), F (10) | > 60 (30), ≤ 60 (12) | NA | NA | IA (14), IB (8), IIA (5), IIB (1), IIIA (7), IIIB (4), III C (3) | NA | W (6), M (21), P (10), SRCC (5) | U (14), M (20), L (8) | ≤ 2 (35), 2-5 (7) | V-L (35), L (4), IN (2), H (1) | + (28) | + (25) | 3-yr (62.6), 5-yr (57.8%) |
| Liu *et al*[52], 2009 | M (19), F (3) | 64.5, (Med) | NA | NA | NA | NA | NA | Cardias (1), fundus (7), body (13), antrum (1) | 0.8 (Med) | < L |  |  | 5-yr (31.8%) |
| Present study | M (17), F (2) | 62 (Med) | U (5), M (6), L (7), W (1) | 3.5 (Med) | 0 (1), IA (3), IB (3), IIA (3), IIB (3), III A (4), IIIC (2) | Diffuse (6), intestinal (5), mixed (3) | M-P (7), M (5), P (5), W (1) | Body (8), fundus (3), antrum (2), Cardia (2) | 1.4 (Med) | L (10), V-L (7), H (2) | + (19) | + (18), - (1) | 3-yr (73.9%), 5-yr (59.2%) |
| All | M (122), F (35) | 70 (Med) | U (26), M (23), L (35) | 4 (Med) | 0 (2), IA (33), IB (16), IIA (17), IIB (13), IIIA (21), IIIB (11), IIIC (5), IV (2) | Diffuse (19), intestinal (23), mixed (3) | M-P (13), M (38), P (45), W (10) | U (43), M (66), L (20) | 1.2 (Med) | V-L (84), L (35), IN (5), H (9) | - (2) | - (1) | 3-yr (54.5%), 5-yr (46.7%) |

1Collision tumor.

GC: Gastric cancer; GIST: Gastrointestinal stromal tumor; M: Male; F: Female; Med: Median; DOD: Dead of disease; U: Upper one-third of the stomach; M: Middle one-third of the stomach; L: Lower one-third of the stomach; LGIN: Low-grade intraepithelial neoplasia; M-P: Moderately to poorly differentiated; M: Moderately differentiated; P: Poorly differentiated; W: Well differentiated; SRCC: Signet-ring cell carcinoma; V-L: Very low; L: Low; IN: Intermediate; H: High; SRCC: Signet-ring cell carcinoma; NA: Not assessed; PFS: Progression-free survival; pTNM: Pathological tumor-node-metastasis.