



# The roles of CT and EUS in the preoperative evaluation of gastric gastrointestinal stromal tumors larger than 2 cm

Tao Chen<sup>1</sup> · Lili Xu<sup>2</sup> · Xiaoyu Dong<sup>1</sup> · Yue Li<sup>3</sup> · Jiang Yu<sup>1</sup> · Wei Xiong<sup>1,2</sup> · Guoxin Li<sup>1</sup>

Received: 20 August 2018 / Revised: 11 November 2018 / Accepted: 3 December 2018 / Published online: 7 January 2019  
© European Society of Radiology 2019

## Abstract

**Objective** This study aimed to investigate the endoscopic ultrasound (EUS) and computed tomography (CT) features of gastric gastrointestinal stromal tumors (GISTs) for assessing potential malignancy and prognosis.

**Methods** Fifty consecutive patients with primary gastric GISTs larger than 2 cm were retrospectively enrolled in this study. The association of CT and EUS features with malignancy was analyzed using univariate and stepwise logistic regression method. The agreement between EUS/CT lesion size and pathologic tumor size was analyzed by calculating the intraclass correlation coefficient (ICC) value, and the association of imaging features with mitotic counts was further analyzed using univariate analysis. The Kaplan-Meier method and Cox proportional hazards models were used to assess the value of imaging features for predicting the prognosis of GIST patients.

**Results** Tumor size > 5 cm and an exophytic/mixed growth pattern on CT as well as tumor size > 5 cm and the presence of cystic spaces on EUS were independent predictors of highly malignant GISTs (all  $p < 0.05$ ). The ICC values of CT/EUS lesion size relative to pathologic tumor size showed very good reliability (0.853 for EUS and 0.831 for CT). Only tumor shape and growth pattern on CT were significant for predicting mitotic index (both  $p < 0.05$ ). Direct organ invasion on CT ( $p = 0.036$ ; hazard ratio [HR] = 11.891) and serosal invasion on EUS ( $p = 0.015$ ; HR = 8.223) were independent adverse prognostic factors.

**Conclusions** CT features may be more useful than EUS features for predicting tumor mitotic index. In addition, preoperative imaging features can help predict the prognosis of gastric GISTs.

## Key Points

- Both CT and EUS features can be used for risk stratification of gastric GISTs larger than 2 cm.
- CT features performed better than EUS features for predicting tumor mitotic index.
- Preoperative imaging features can help predict the prognosis of gastric GISTs.

**Keywords** Gastrointestinal stromal tumors · Prognosis · Stomach neoplasms · Endosonography · Tomography, x-ray computed

---

Tao Chen and Lili Xu contributed equally to this work.

**Electronic supplementary material** The online version of this article (<https://doi.org/10.1007/s00330-018-5945-6>) contains supplementary material, which is available to authorized users.

✉ Tao Chen  
drchentao@163.com

✉ Wei Xiong  
nick717@126.com

<sup>2</sup> Medical Image Center, Nanfang Hospital, Southern Medical University, Guangzhou 510515, Guangdong Province, China

<sup>1</sup> Department of General Surgery, Nanfang Hospital, Guangdong Provincial Engineering Technology Research Center of Minimally Invasive Surgery, Southern Medical University, No.1838, North Guangzhou Avenue, Guangzhou 510515, Guangdong Province, China

<sup>3</sup> Department of Digestive Endoscopy, Nanfang Hospital, Southern Medical University, Guangzhou 510515, Guangdong Province, China

## Abbreviations

CI	Confidence interval
EUS	Endoscopic ultrasonography
GIST	Gastrointestinal stromal tumor
HR	Hazard ratio
ICC	Intraclass correlation coefficient
NIH	National Institutes of Health
OR	Odds ratio
RFS	Recurrence-free survival
SMT	Submucosal tumor
TKI	Tyrosine kinase inhibitor

## Introduction

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors in the gastrointestinal (GI) tract, accounting for the majority of submucosal tumors (SMTs) [1, 2]. Positive immunohistochemical staining for c-kit is necessary to diagnose and distinguish GISTs from other tumors [3, 4]. GISTs are most frequently located in the stomach (50–60%) and small intestine (30–35%) and are rare in the colorectum (5%) and esophagus (< 1%) [5, 6].

Predicting the behavior of a given GIST is usually challenging unless the tumor is excised or has metastasized. There are several risk classification systems for GISTs [7, 8], mainly based on tumor size and mitotic counts. However, these factors are mainly determined from surgical-excised specimens and less accurately from a biopsy. Additionally, treatment with neoadjuvant tyrosine kinase inhibitors (TKIs) may cause decreases in tumor size in some patients and limit the accuracy in assessing mitotic counts.

Endoscopic ultrasound (EUS) allows assessment of the tumor size, border, internal echoes, layer of the GI wall from which the lesion arises, and other tumor morphological characteristics; therefore, EUS is frequently used to diagnose and characterize GISTs [9, 10]. Computed tomography (CT) is another necessary preoperative evaluation method that depicts the characteristics of GISTs and identifies metastases [11]. CT and EUS findings for malignancy stratification of GISTs are still controversial [12–14], and comparison between them for this purpose has rarely been performed [15].

The aim of this study was to investigate whether EUS and CT features were correlated with the grade of gastric GISTs and to analyze how they could help predict outcome.

## Patients and methods

### Patients

This study was approved by the Institutional Review Board of Southern Medical University Nanfang Hospital. Patients with

primary gastric GISTs who were treated between January 2010 and December 2015 were retrospectively enrolled in this study, and informed consent was waived. Patient characteristics and clinicopathological data were recorded. According to the National Institutes of Health (NIH)–modified criteria [8], patients were divided into very low/low-risk groups (low-grade malignant potential group) and moderate/high-risk groups (high-grade malignant potential group). The inclusion and exclusion criteria were presented in the [Supplementary](#).

### CT imaging analysis

The information and parameters of CT devices and the technique of acquisition of CT examinations were described in the [Supplementary](#). Two radiologists with extensive experience in abdominal CT interpretation (W.X. and X.X.Z.) who were blinded to the pathologic malignant potential of the GISTs independently reviewed the CT images of the GIST patients and recorded the following CT findings: lesion size (cm), shape (regular or irregular), margins (well-defined or ill-defined), growth pattern (endoluminal or exophytic/mixed), enhancement pattern (homogeneous or heterogeneous), presence of enlarged vessels, lymphadenopathy, and invasion of adjacent organs or tissues. The largest dimension of the tumor was measured in a transverse plane. The regular shape was defined as roundish/ovoid, and irregular was lobulated or other shapes. The well-circumscribed border was considered well-defined, and when the tumor border was not clear, or presented with fat infiltration, we defined the border as ill-defined. Enlarged vessels were defined as peritumoral or intratumoral vessels. Lymph nodes with a short-axis diameter longer than 1 cm were considered lymphadenopathy. Artery phase images were used to evaluate the enhancement pattern and enlarged vessels of the lesion. For controversial cases, the two radiologists negotiated to finalize the diagnosis.

### Analysis of EUS features

A radial array echoendoscope (GF-UE260, Olympus Corporation, or EG-530UR, Fujifilm Corporation) was used for EUS. EUS images and written reports for each patient were obtained from the endoscopy database and reviewed by two expert endoscopists (Z.L.H. and Y.L.) who were blinded to the pathologic malignant potential of the GISTs. For each lesion, the following EUS features were recorded: tumor size (cm), borders (regular or not), heterogeneity, and presence of ulceration, hyperechoic foci, cystic spaces, regional lymphadenopathy, and serosal invasion. The EUS readers also resolved disagreements by consensus. Each read was performed by radiologists and endoscopists independently.

## Statistical analysis

All statistical analyses were performed using SPSS software (version 22.0, IBM), with a two-sided  $p$  value  $< 0.05$  considered statistically significant. The statistical analysis was described in the [Supplementary](#).

## Results

### Clinicopathological data

The characteristics of the 50 patients included in this study are shown in Supplemental Table 1. Univariate analysis showed that there was no significant difference in age, gender, or associated symptoms between the low-grade and high-grade malignant potential groups (all  $p > 0.05$ ). However, statistical significance was noted in terms of tumor size ( $3.75 \pm 0.86$  cm vs.  $6.90 \pm 2.74$  cm,  $p < 0.001$ ) and mitotic counts ( $p = 0.001$ ) between the low-grade and high-grade groups.

### Association of imaging features and malignant potential of GISTs

In terms of CT features, tumor size, tumor shape, tumor margins, growth pattern, enhancement pattern, and enlarged vessels were significantly different between the low-grade and high-grade malignant potential groups (Table 1). Tumors larger than 5 cm on CT ( $p < 0.001$ ), those with an irregular shape ( $p = 0.001$ ), those with ill-defined margins ( $p = 0.024$ ), those with an exophytic/mixed growth pattern ( $p = 0.001$ ), those with heterogeneous enhancement ( $p = 0.001$ ), and those associated with enlarged vessels ( $p = 0.029$ ) were more common in the high-grade group than in the low-grade group (Figs. 1 and 2). A stepwise logistic regression using six significant CT features as inputs showed that only tumor size  $> 5$  cm ( $p = 0.002$ ; odds ratio [OR] = 39.895; 95% confidence interval [CI], 3.973–400.587) and exophytic/mixed growth pattern ( $p = 0.011$ ; OR = 7.868; 95% CI, 1.597–38.779) were independent indicators of higher grade tumors (Table 3).

In terms of EUS features, in the univariate analysis, tumor size  $> 5$  cm ( $p < 0.001$ ), the presence of cystic spaces ( $p = 0.001$ ), and serosal invasion ( $p = 0.013$ ) were significantly associated with high-grade malignant potential of GISTs (Table 2, Figs. 3 and 4). In addition, logistic regression analysis showed that tumor size  $> 5$  cm ( $p = 0.004$ ; OR = 39.895; 95% CI, 3.973–400.587) and the presence of cystic spaces ( $p = 0.017$ ; OR = 8.246; 95% CI, 1.455–46.729) were independent risk factors for malignancy (Table 3).

### Imaging methods for determining tumor size and predicting mitotic counts

The ICC values of CT and EUS examinations for predicting the corresponding pathological tumor size showed very good reliability of 0.831 (0.721–0.901) and 0.853 (0.755–0.914), respectively.

In terms of CT features, there were significant differences in tumor shape and growth pattern between the low and high mitotic count groups in the univariate analysis. An irregular tumor shape and exophytic/mixed growth pattern were more common in the high mitotic count group than in the low mitotic count group ( $p = 0.038$  and  $0.009$ , respectively). However, in terms of EUS features, none were found to be significantly associated with the mitotic counts of GISTs (all  $p > 0.05$ ) (Tables 1 and 2).

### Imaging morphology for predicting prognosis

Among the total 50 patients, nine were lost to follow-up; thus, they were excluded from the recurrence-free survival (RFS) analysis. After a median follow-up interval of 42 (range, 4–89) months, regional recurrence or distal metastasis developed in six (6/41, 14.6%) patients. Of these patients, one was in the low-grade malignant potential group, and five were in the high-grade malignant potential group.

In the univariate analysis, a heterogeneous enhancement pattern, the presence of enlarged vessels, adjacent tissue invasion, and lymphadenopathy on CE-CT were significant indicators for a shorter RFS ( $p = 0.018$ ,  $0.020$ ,  $0.013$ , and  $0.001$ , respectively) (Fig. 5 and Table 4). When these significant features were entered into the Cox regression model, only adjacent tissue invasion (hazard ratio [HR] = 1.891; 95% CI, 1.171–120.782;  $p = 0.036$ ) was an independent risk factor for tumor recurrence. In terms of EUS features, only serosal invasion was significantly associated with RFS ( $p = 0.015$ ; HR = 8.223; 95% CI, 1.500–45.069) (Fig. 5 and Table 4).

## Discussion

This study indicated that CT (size  $> 5$  cm and exophytic/mixed growth pattern) and EUS features (size  $> 5$  cm and the presence of cystic spaces) were independent predictors of high malignant potential of gastric GISTs larger than 2 cm. Agreement between size assessed by CT/EUS and pathology was very good. Certain CT features like irregular tumor shape and exophytic/mixed growth pattern were predictors of higher mitotic counts, while EUS features were not. Adjacent tissue invasion on CT and serosal invasion on EUS were independent risk factors for tumor recurrence.

The most frequent symptoms of GISTs are GI bleeding and abdominal pain, dyspepsia, constipation, or diarrhea [16–19]. However, in our cohort, no statistically significant difference

**Table 1** Comparison of CT features in patients with gastric GISTs (*n* [%])

CT features	Low-grade group <sup>a</sup> ( <i>n</i> = 27)	High-grade group <sup>b</sup> ( <i>n</i> = 23)	<i>p</i> <sup>c</sup>	Low mitotic counts ( <i>n</i> = 41)	High mitotic counts ( <i>n</i> = 9)	<i>p</i> <sup>c</sup>
Tumor size (cm)			< 0.001			0.520
≤ 5	26 (93.6)	9 (39.1)		30 (73.2)	5 (55.6)	
> 5	1 (3.7)	14 (60.9)		11 (26.8)	4 (44.4)	
Tumor shape			0.001			0.038
Regular	19 (70.4)	5 (21.7)		23 (56.1)	1 (11.1)	
Irregular	8 (29.6)	18 (78.3)		18 (43.9)	8 (88.9)	
Tumor margin			0.024			0.105
Well-defined	23 (85.2)	13 (56.5)		32 (78.0)	4 (44.4)	
Ill-defined	4 (14.8)	10 (43.5)		9 (22.0)	5 (55.6)	
Growth pattern			0.001			0.009
Endoluminal	21 (77.8)	7 (30.4)		27 (65.9)	1 (11.1)	
Exophytic/mixed	6 (22.2)	16 (69.6)		14 (34.1)	8 (88.9)	
Enhancement pattern			0.001			0.689
Homogeneous	21 (77.8)	7 (30.4)		24 (58.5)	4 (44.4)	
Heterogeneous	6 (22.2)	16 (69.6)		17 (41.5)	5 (55.6)	
Enlarged vessels			0.029			0.287
Absent	26 (96.3)	16 (69.6)		36 (87.8)	6 (66.7)	
Present	1 (3.7)	7 (30.4)		5 (12.2)	3 (33.3)	
Adjacent tissues invasion			0.490			0.560
Absent	26 (96.3)	20 (87.0)		38 (92.7)	8 (88.9)	
Present	1 (3.7)	3 (13.0)		3 (7.3)	1 (11.1)	
Lymphadenopathy			0.181			0.456
Absent	27 (100.0)	20 (87.0)		39 (95.1)	8 (88.9)	
Present	0 (0.0)	3 (13.0)		2 (4.9)	1 (11.1)	

GISTs gastrointestinal stromal tumors

<sup>a</sup> Low-grade group: low-grade malignant potential group

<sup>b</sup> High-grade group: high-grade malignant potential group

<sup>c</sup> Chi-square test or Fisher's exact test was used for comparison



**Fig. 1** A 54-year-old woman with gastric gastrointestinal stromal tumor (GIST). Arterial phase contrast-enhanced CT image shows a round-shaped, well-defined, homogeneously enhanced tumor with an endoluminal growth pattern (arrow). The tumor had a low risk of aggressive behavior with a tumor size of 3.2 cm and mitotic count of 1/50 high-power fields

was found in the clinical symptoms of patients in the low-grade and high-grade groups.



**Fig. 2** A 68-year-old man with gastric gastrointestinal stromal tumor (GIST). Arterial phase contrast-enhanced CT image shows an irregular, heterogeneously enhanced tumor with exophytic growth pattern and enlarged vessels (arrow). The tumor had a high risk of malignancy, because its maximum diameter was 7.2 cm, and mitotic count was 40/50 high-power fields

**Table 2** Comparison of EUS features in patients with gastric GISTs (*n* [%])

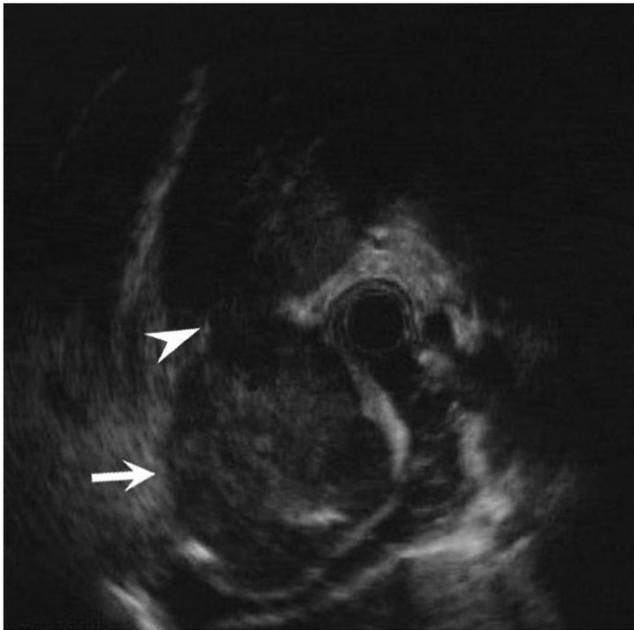
EUS features	Low-grade group <sup>a</sup> ( <i>n</i> = 27)	High-grade group <sup>b</sup> ( <i>n</i> = 23)	<i>p</i> <sup>c</sup>	Low mitotic counts ( <i>n</i> = 41)	High mitotic counts ( <i>n</i> = 9)	<i>p</i> <sup>c</sup>
Tumor size (cm)			< 0.001			0.422
≤ 5	26 (93.6)	10 (43.5)		31 (75.6)	5 (55.6)	
> 5	1 (3.7)	13 (56.5)		10 (24.4)	4 (44.4)	
Irregular border			0.408			0.764
Absent	10 (37.0)	6 (26.1)		14 (34.1)	2 (22.2)	
Present	17 (63.0)	17 (73.9)		27 (65.9)	7 (77.8)	
Heterogeneity			0.092			0.345
Absent	7 (25.9)	1 (4.3)		8 (19.5)	0 (0.0)	
Present	20 (74.1)	22 (95.7)		33 (80.5)	9 (100.0)	
Ulceration			0.100			0.689
Absent	18 (66.7)	10 (43.5)		24 (58.5)	4 (44.4)	
Present	9 (33.3)	13 (56.5)		17 (41.5)	5 (55.6)	
Cystic spaces			0.001			0.145
Absent	16 (59.3)	3 (13.0)		18 (43.9)	1 (11.1)	
Present	11 (40.7)	20 (87.0)		23 (56.1)	8 (88.9)	
Hyperechoic foci			1.000			1.000
Absent	22 (81.5)	19 (82.6)		34 (82.9)	7 (77.8)	
Present	5 (18.5)	4 (17.4)		7 (17.1)	2 (22.2)	
Regional lymphadenopathy			0.850			1.000
Absent	25 (92.6)	20 (87.0)		37 (90.2)	8 (88.9)	
Present	2 (7.4)	3 (13.0)		4 (9.8)	1 (11.1)	
Serosal invasion			0.013			1.000
Absent	26 (96.3)	15 (65.2)		34 (82.9)	7 (77.8)	
Present	1 (3.7)	8 (34.8)		7 (17.1)	2 (22.2)	

GISTs gastrointestinal stromal tumors, EUS endoscopic ultrasound

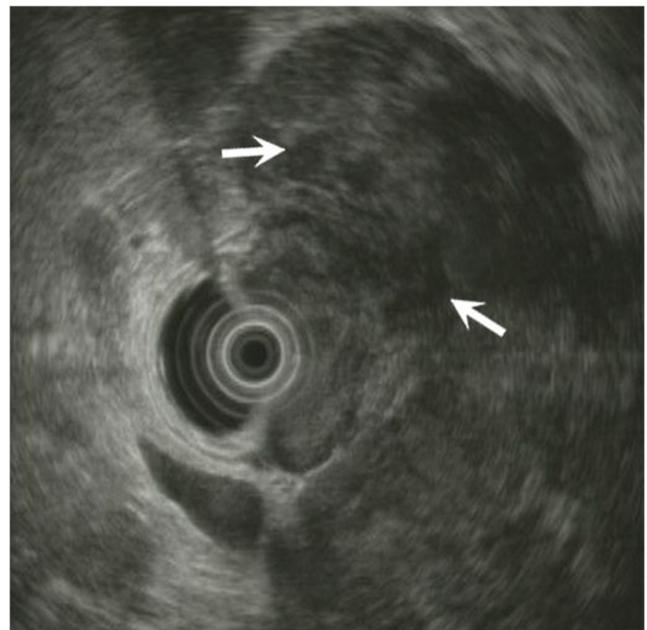
<sup>a</sup>Low-grade group: low-grade malignant potential group

<sup>b</sup>High-grade group: high-grade malignant potential group

<sup>c</sup>Chi-square test or Fisher's exact test was used for comparison



**Fig. 3** A 66-year-old man with gastric gastrointestinal stromal tumor (GIST). EUS image shows a heterogeneous tumor with lobulated border (arrow). The tumor partially invades the serosal layer and extended into the liver (arrowhead). The mitotic count of the tumor was greater than 10/50 high-power fields, and its tumor size was 10.5 cm; therefore, it was considered to have a high risk of aggressive behavior. Local liver invasion was demonstrated during surgery



**Fig. 4** An 83-year-old man with gastric gastrointestinal stromal tumor (GIST). EUS image shows a heterogeneous tumor located in the stomach with an irregular border and internal cystic spaces (arrows). According to the modified NIH criteria, the patient was classified into the intermediate risk group with a pathological tumor size of 9.0 cm and a mitotic count of 5/50 high-power fields

**Table 3** Results of logistic regression for significant CT/EUS Features

CT features	$\beta$	SE	Wald	<i>p</i>	Odds ratio (95% CI)
Tumor size <sup>a</sup>	3.686	1.177	9.810	0.002	39.895 (3.973–400.587)
Growth pattern <sup>b</sup>	2.063	0.814	6.426	0.011	7.868 (1.597–38.779)
EUS features	$\beta$	SE	Wald	<i>p</i>	Odds ratio (95% CI)
Tumor size <sup>a</sup>	3.382	1.176	8.269	0.004	29.443 (2.936–295.286)
Cystic spaces <sup>c</sup>	2.110	0.885	5.682	0.017	8.246 (1.455–46.729)

EUS endoscopic ultrasound, CI confidence interval

<sup>a</sup> > 5 cm vs.  $\leq$  5 cm

<sup>b</sup> Exophytic/mixed vs. endoluminal

<sup>c</sup> Present vs. absent

Risk stratification of gastric GISTs relies on lesion size and mitotic count, determined on resected specimens. However, neoadjuvant TKI treatment may induce subsequent changes, making the assessment of mitotic counts in resection specimens less reliable than those in naïve patients [20, 21]. As preoperative evaluation methods, CT and EUS estimate the size of treatment-naïve tumors and provide imaging features that may be representative of a tumor's biological behavior [13, 22–24]. Therefore, using pretreatment imaging morphology for risk stratification of GISTs may be helpful for treatment planning and determining appropriate follow-up intervals.

Previously, several studies have investigated the value of CT for preoperative assessment of malignancy in GISTs. The study by Zhou et al [13] showed that primary GISTs with CT features of a lesion size > 10 cm or 5–10 cm, a mixed growth pattern, and enlarged vessels feeding or draining the mass were more likely to have higher grade risk than those with a smaller lesion, endoluminal growth pattern, and no enlarged feeding vessels. Tateishi et al reported that an extrinsic epicenter and an unclear border were the most significant predictors for high-grade tumors, as identified by using a multiple step-wise logistic regression method [25]. In our series, tumor size, shape, margins, growth pattern, enhancement pattern, and the presence of enlarged vessels were found to be statistically significant factors for risk stratification of GISTs in the univariate analysis, but the logistic regression showed that only lesion size > 5 cm and exophytic/mixed growth pattern were independent predictors for high malignant potential.

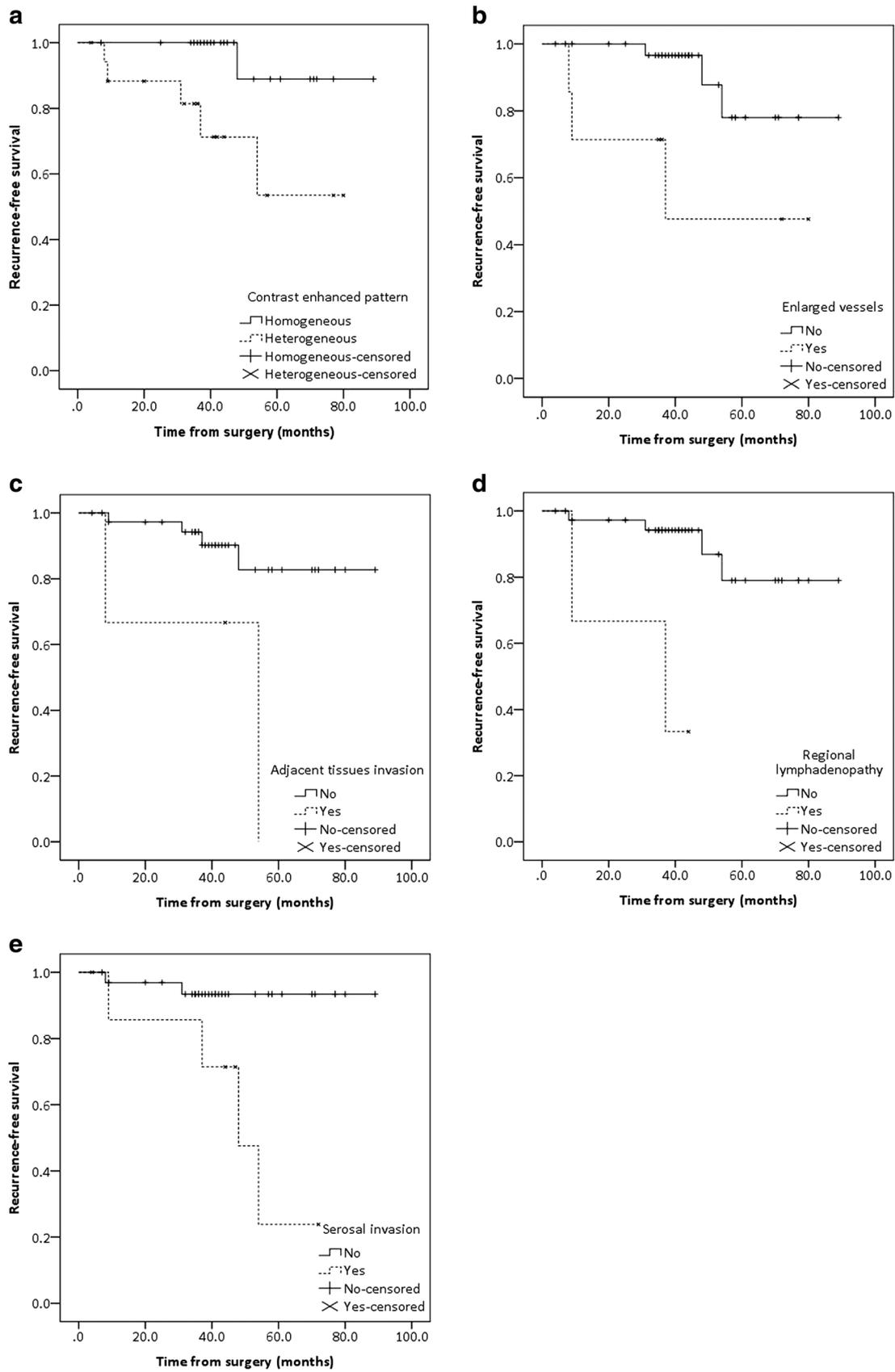
Fewer studies have evaluated EUS features of GISTs for risk classification than CTs. Shah et al [26] reported that EUS features of tumor size > 5 cm, irregular extraluminal borders, local invasion, and the presence of heterogeneity were significantly associated with intermediate- to high-risk malignant potential. Nevertheless, this study had a small sample size of only 26 patients. Other EUS features, such as cystic changes and surface ulceration, have also been demonstrated to be predictive of malignant GISTs [23]. Kim et al [12] retrospectively enrolled 75 patients with 2–5-cm gastric GISTs and analyzed the association of EUS features with the risk of malignancy; however, no features were statistically different between

patients in the very low- and moderate-risk groups, implying that EUS findings might have limitation in preoperatively predicting the malignancy of medium-sized (2–5 cm) GISTs. In our study, lesion size and the presence of cystic spaces and serosal invasion were more common in highly malignant GISTs than in GISTs with low malignant potential in the univariate analysis; however, only lesion size > 5 cm and the presence of cystic spaces remained significant predictors of malignancy in the logistic regression analysis. Compared with the study of Kim et al [12] which focused on medium-sized gastric GISTs, our study evaluated GISTs larger than 2 cm, including tumors > 5 cm. Besides, rather than the Armed Forces Institute of Pathology (AFIP) criteria, our study applied modified NIH criteria for risk stratification that are most commonly used in daily. This might explain discrepancy.

Tumor size is a significant factor for evaluating the biological behavior of GISTs. In our study, the agreement between EUS/CT and pathologically determined size was very good, both with ICC values > 0.80, as previously reported by Williams et al [27]. Nevertheless, tumor size alone is not enough to accurately evaluate the malignant potential of GISTs. Some small GISTs may be aggressive and have a poor prognosis [28], while the risk of malignant potential in some larger tumors might be overestimated [29].

In our series, GISTs with a high mitotic count were more likely to have an exophytic/mixed growth pattern and irregular tumor shape on CT. Mitotic counts can reflect the proliferative activity of tumors, and the association between CT features and mitotic counts indicates that tumors with a mixed growth pattern and an irregular shape may have more aggressive biological behavior than tumors without. Nevertheless, Kim et al [30] previously reported that tumor size was the only CT finding that was a significant predictor of a high mitotic rate; no significance was noted in terms of growth pattern and tumor shape. Comparatively, this study included more large-sized GISTs, with 26 (32.1%) tumors more than 10 cm; while our data only included three cases (6.0%) with tumor diameter > 10 cm. As we enrolled only patients who received surgical resection without neoadjuvant treatment, the consequence is that very large tumors were probably excluded from our analysis. In terms of EUS findings, Chen et al [23] found that mitotic counts were associated with lesion size and not with other parameters. However, mitotic counts were not associated with any EUS features in our series, which may be due to the limitation of EUS to visualize the entire tumor, especially large tumors. In addition, to our knowledge, research on the correlation between tumor mitoses and imaging features is scarce. Therefore, further studies with large sample size are needed to evaluate the relevance.

In this study, certain imaging features were useful for predicting the prognosis of GISTs. Patients with adjacent tissue invasion on CT or serosal invasion on EUS were more likely to develop recurrent or metastatic lesions than patients without.



**Fig. 5** Recurrence-free survival as assessed by CT features including contrast-enhancing pattern (a), enlarged vessels (b), adjacent tissue invasion (c), and regional lymphadenopathy (d); and serosal invasion (e) on EUS

**Table 4** Univariate and multivariate analyses of RFS in patients with gastric GISTs

CT features	Univariate <i>p</i>	Multivariate <i>p</i>	Hazard ratio (95% CI)
Tumor size <sup>a</sup>	0.099	–	–
Tumor shape <sup>b</sup>	0.130	–	–
Tumor margin <sup>c</sup>	0.129	–	–
Growth pattern <sup>c</sup>	0.170	–	–
Enhancement pattern <sup>f</sup>	0.018	0.506	2.339 (0.191–28.665)
Enlarged vessels <sup>d</sup>	0.020	0.174	4.293 (0.525–35.082)
Adjacent tissues invasion <sup>d</sup>	0.013	0.036	11.891 (1.171–120.782)
Lymphadenopathy <sup>d</sup>	0.001	0.111	7.432 (0.632–87.398)
EUS features	Univariate <i>p</i>	Multivariate <i>p</i>	Hazard ratio (95% CI)
Tumor size <sup>a</sup>	0.322	–	–
Irregular border <sup>d</sup>	0.227	–	–
Heterogeneity <sup>d</sup>	0.711	–	–
Ulceration <sup>d</sup>	0.591	–	–
Cystic spaces <sup>d</sup>	0.054	–	–
Hyperechoic foci <sup>d</sup>	0.478	–	–
Regional lymphadenopathy <sup>d</sup>	0.211	–	–
Serosal invasion <sup>d</sup>	0.004	0.015	8.223 (1.500–45.069)

*GISTs* gastrointestinal stromal tumors, *EUS* endoscopic ultrasound, *RFS* recurrence-free survival, *CI* confidence interval

<sup>a</sup> > 5 cm vs. ≤ 5 cm

<sup>b</sup> Irregular vs. regular

<sup>c</sup> Ill-defined vs. well-defined

<sup>d</sup> Present vs. absent

<sup>e</sup> Exophytic/mixed vs. endoluminal

<sup>f</sup> Heterogeneous vs. homogeneous

The retrospective nature of the analysis is a limitation of this study. Moreover, our study enrolled only gastric GISTs, because EUS can only be done on gastric or duodenal GISTs but not small bowel lesions. Nevertheless, our cohort of patients who underwent both EUS and CT is larger than those included in previous studies, and this study might supplement the current literature on preoperative risk evaluation for gastric GISTs.

In summary, both CT and EUS features can be used for risk stratification of gastric GISTs larger than 2 cm. Specifically, tumors larger than 5 cm on both imaging modalities, those with an exophytic/mixed growth pattern on CT, and those with cystic spaces on EUS were likely to be highly malignant lesions. In addition, CT features may be more useful for discriminating low and high mitotic count tumors than EUS features. Furthermore, patients with tumors with adjacent tissue invasion on CT and serosal invasion on EUS had a shorter RFS than patients with tumors without.

**Acknowledgements** We thank Xixi Zhao and Zelong Han for their contributions.

**Funding** This study has received funding by the State's Key Project of Research and Development Plan (2017YFC0108300 and 2017YFC0108303).

## Compliance with ethical standards

**Guarantor** The scientific guarantor of this publication is Tao Chen.

**Conflict of interest** The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

**Statistics and biometry** No complex statistical methods were necessary for this paper.

**Informed consent** Written informed consent was waived by the Institutional Review Board.

**Ethical approval** Institutional Review Board approval was obtained.

## Methodology

- retrospective
- diagnostic or prognostic study
- performed at one institution

## References

1. Polkowski M (2005) Endoscopic ultrasound and endoscopic ultrasound-guided fine-needle biopsy for the diagnosis of malignant submucosal tumors. *Endoscopy* 37:635–645

2. Polkowski M, Butruk E (2005) Submucosal lesions. *Gastrointest Endosc Clin N Am* 15:33–54 viii
3. Miettinen M, El-Rifai W, H L Sobin L, Lasota J (2002) Evaluation of malignancy and prognosis of gastrointestinal stromal tumors: a review. *Hum Pathol* 33:478–483
4. Okai T, Minamoto T, Ohtsubo K et al (2003) Endosonographic evaluation of c-kit-positive gastrointestinal stromal tumor. *Abdom Imaging* 28:301–307
5. Joensuu H, Hohenberger P, Corless CL (2013) Gastrointestinal stromal tumour. *Lancet* 382:973–983
6. Corless CL, Barnett CM, Heinrich MC (2011) Gastrointestinal stromal tumours: origin and molecular oncology. *Nat Rev Cancer* 11: 865–878
7. Miettinen M, Lasota J (2006) Gastrointestinal stromal tumors: pathology and prognosis at different sites. *Semin Diagn Pathol* 23:70–83
8. Joensuu H (2008) Risk stratification of patients diagnosed with gastrointestinal stromal tumor. *Hum Pathol* 39:1411–1419
9. Chak A (2002) EUS in submucosal tumors. *Gastrointest Endosc* 56:S43–S48
10. Nishida T, Kawai N, Yamaguchi S, Nishida Y (2013) Submucosal tumors: comprehensive guide for the diagnosis and therapy of gastrointestinal submucosal tumors. *Dig Endosc* 25:479–489
11. Kang JH, Lim JS, Kim JH et al (2009) Role of EUS and MDCT in the diagnosis of gastric submucosal tumors according to the revised pathologic concept of gastrointestinal stromal tumors. *Eur Radiol* 19:924–934
12. Kim MN, Kang SJ, Kim SG et al (2013) Prediction of risk of malignancy of gastrointestinal stromal tumors by endoscopic ultrasonography. *Gut Liver* 7:642–647
13. Zhou C, Duan X, Zhang X, Hu H, Wang D, Shen J (2016) Predictive features of CT for risk stratifications in patients with primary gastrointestinal stromal tumour. *Eur Radiol* 26:3086–3093
14. Rimondini A, Belgrano M, Favretto G et al (2007) Contribution of CT to treatment planning in patients with GIST. *Radiol Med* 112: 691–702
15. Belloni M, De Fiori E, Mazzarol G, Curti A, Crosta C (2002) Endoscopic ultrasound and computed tomography in gastric stromal tumours. *Radiol Med* 103:65–73
16. Caterino S, Lorenzon L, Petrucciani N et al (2011) Gastrointestinal stromal tumors: correlation between symptoms at presentation, tumor location and prognostic factors in 47 consecutive patients. *World J Surg Oncol* 9:13
17. Nilsson B, Bümming P, Meis-Kindblom JM et al (2005) Gastrointestinal stromal tumors: the incidence, prevalence, clinical course, and prognostication in the preimatinib mesylate era—a population-based study in western Sweden. *Cancer* 103:821–829
18. Mucciarini C, Rossi G, Bertolini F et al (2007) Incidence and clinicopathologic features of gastrointestinal stromal tumors. A population-based study. *BMC Cancer* 7:230
19. Bümming P, Ahlman H, Andersson J, Meis-Kindblom JM, Kindblom LG, Nilsson B (2006) Population-based study of the diagnosis and treatment of gastrointestinal stromal tumours. *Br J Surg* 93:836–843
20. Gronchi A, Raut CP (2012) The combination of surgery and imatinib in GIST: a reality for localized tumors at high risk, an open issue for metastatic ones. *Ann Surg Oncol* 19:1051–1055
21. Ford SJ, Gronchi A (2016) Indications for surgery in advanced/metastatic GIST. *Eur J Cancer* 63:154–167
22. O'Neill AC, Shinagare AB, Kurra V et al (2016) Assessment of metastatic risk of gastric GIST based on treatment-naive CT features. *Eur J Surg Oncol* 42:1222–1228
23. Chen TH, Hsu CM, Chu YY et al (2016) Association of endoscopic ultrasonographic parameters and gastrointestinal stromal tumors (GISTs): can endoscopic ultrasonography be used to screen gastric GISTs for potential malignancy? *Scand J Gastroenterol* 51:374–377
24. Kim JS, Kim HJ, Park SH, Lee JS, Kim AY, Ha HK (2017) Computed tomography features and predictive findings of ruptured gastrointestinal stromal tumours. *Eur Radiol* 27:2583–2590
25. Tateishi U, Hasegawa T, Satake M, Moriyama N (2003) Gastrointestinal stromal tumor. Correlation of computed tomography findings with tumor grade and mortality. *J Comput Assist Tomogr* 27:792–798
26. Shah P, Gao F, Edmundowicz SA, Azar RR, Early DS (2009) Predicting malignant potential of gastrointestinal stromal tumors using endoscopic ultrasound. *Dig Dis Sci* 54:1265–1269
27. Williams KB, Bradley JF, Wormer BA et al (2013) Pre-operative evaluation of gastric gastrointestinal stromal tumors: endoscopic ultrasound vs CT scan. Annual Meeting of the SAGES: Society of American Gastrointestinal and Endoscopic Surgeons. Available via <https://www.sages.org/meetings/annual-meeting/abstracts-archive/?search=Pre-operative+Evaluation+of+Gastric+Gastrointestinal+Stromal+Tumors&meeting=2013>. Accessed 13 Dec 2018
28. Wada N, Kurokawa Y, Nishida T et al (2014) Subgroups of patients with very large gastrointestinal stromal tumors with distinct prognoses: a multicenter study. *J Surg Oncol* 109:67–70
29. Joensuu H, Rutkowski P, Nishida T et al (2015) KIT and PDGFRA mutations and the risk of GI stromal tumor recurrence. *J Clin Oncol* 33:634–642
30. Kim HC, Lee JM, Kim KW et al (2004) Gastrointestinal stromal tumors of the stomach: CT findings and prediction of malignancy. *AJR Am J Roentgenol* 183:893–898