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Role of Multidetector CT Imaging in the Risk Stratification of Gastrointestinal Stromal Tumors (GISTs)–A Retrospective Analysis

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Abstract

Background Gastrointestinal stromal tumors (GISTs) are the most common gastrointestinal mesenchymal neoplasms which can arise from any part of the gastrointestinal tract (GIT) or an extraintestinal location. Size and the organ of origin are the major imaging inputs expected from the radiologist. However, it is worthwhile to find out which imaging characteristics on MDCT correlate with risk stratification. This knowledge would help the clinician in treatment planning and prognostication. The aim of this retrospective study is to evaluate the various MDCT imaging characteristics of GISTs and find out which parameters have significant association with risk and subsequent development of metastasis on follow-up whenever it was possible.

Materials and Methods This is a retrospective study conducted on 45 histopathologically proven cases of GIST from two institutions by searching from the digital archives. The following imaging parameters were analyzed: maximum size in any plane, organ of origin, shape (round, ovoid or irregular), margin (well-defined or ill-defined), surface (smooth or lobulated), percentage of necrosis, growth pattern, enhancement characteristics–both intensity (mild, moderate or significant) and pattern (homogenous vs. heterogenous), calcification, infiltration into adjacent organs, and presence of metastasis at presentation or on follow-up.

Results CT morphological parameters of significance in risk stratification as per our study include tumor necrosis, predominant cystic change, irregular and lobulated shape/surface characteristics, and adjacent organ infiltration.

The parameters which were associated with development of metastasis were size > 5 cm, necrosis > 30%, and the presence of adjacent organ infiltration.

Conclusion The radiologist has an important role in ascertaining the size of tumor as well as the organ of origin accurately to guide the clinician in risk calculation and subsequent prognostication. In addition, certain CT characteristics mentioned above, namely, tumor size, significant necrosis/cystic changes, irregular/lobulated contour, and invasion of adjacent organs, help in risk stratification and in predicting metastasis/poor prognosis.

Keywords
- GIST
- MDCT
- risk stratification

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Introduction

Gastrointestinal stromal tumors (GISTs) were considered as smooth muscle tumors along with leiomyoma, leiomyoblastoma, and leiomyosarcoma before the 1980s. Later with advancements in immunohistochemistry, they were reclassified as a specific group of mesenchymal tumors by Mazur and Clark in 1983, based on their origin from interstitial cells of Cajal.[1] GISTs are the most common mesenchymal neoplasms of the gastrointestinal tract (GIT). The interstitial cells of Cajal which are located in the myenteric plexus express a tyrosine kinase growth factor receptor named c-kit protein (CD-117), a specific immunohistochemical (IHC) marker which is not seen in smooth muscle and other mesenchymal tumors of GIT. This marker enabled targeted therapy using Imatinib and other tyrosine kinase inhibitors.[2]

GISTs can occur anywhere along the GIT, from esophagus to rectum and less commonly in extragastrointestinal locations in the abdominal cavity. Stomach is the most common site of occurrence (►**Fig. 1**) of GIST in GIT (60–70%), followed by small intestine (25–35%) (►**Fig. 2**) and then colon-rectum and appendix (together 5%), with esophagus being the least common site (< 1%). In the abdominal cavity, GIST can also arise from omentum, mesentery, and retroperitoneal compartment (less than 5% of all GISTs).[3]

Depending on the location and size of the GIST, clinical presentation can vary from asymptomatic and incidentally detected lesions to masses, which can cause abdominal pain, bleeding into bowel or abdominal cavity, anemia, dyspepsia, nausea or vomiting, symptoms due to mass effect or, rarely, bowel obstruction.[4] Only one of the cases presented with small bowel obstruction in our study (►**Fig. 3 A, B**). Majority of GISTs are benign lesions with 20 to 30% having malignant potential, which can be identified based on certain imaging and pathological findings.[3,5]

Imaging workup for GIST includes endoscopic ultrasonography, CT, MRI and functional imaging with positron emission tomography (PET)-CT. Contrast-enhanced CT (CECT) is the first-line imaging modality in suspected GISTs.

For patients with comorbidities who are high-risk candidates for surgery and for those who refuse surgery, it will be beneficial if imaging morphology could help to a certain extent in risk stratification of GIST. Imaging-guided biopsy could rarely cause tumor dissemination.[5] It is also a known fact that biopsy specimens are likely to give inaccurate mitotic count due to the small sample size and sampling error, especially in case of a markedly heterogeneous tumor.

Many patients who undergo neoadjuvant therapy with tyrosine kinase inhibitors, especially those with large primary tumors, may face limitation in the mitotic index assessment in the final resected specimen due to therapy-induced tumor changes. It is this knowledge that sparks an interest in assessing the role of tumor imaging morphology in risk stratification and the likelihood of development of metastasis or disease progression.[6]

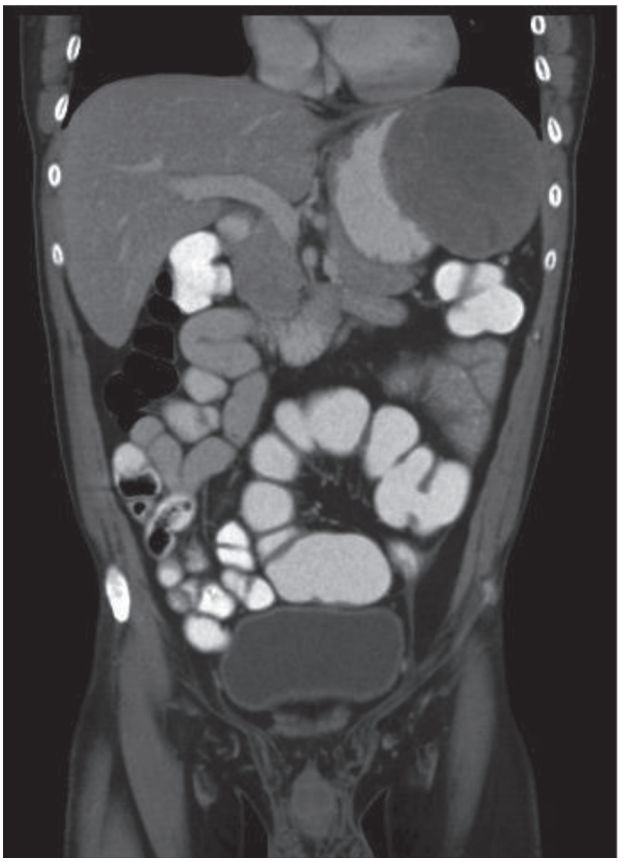

Fig. 1 Coronal contrast-enhanced CT image showing moderate-sized exophytic gastrointestinal stromal tumor (GIST) arising from gastric fundus. High risk. Mitotic index (MI): > 5/50 HPF. Size: 10.3 cm.

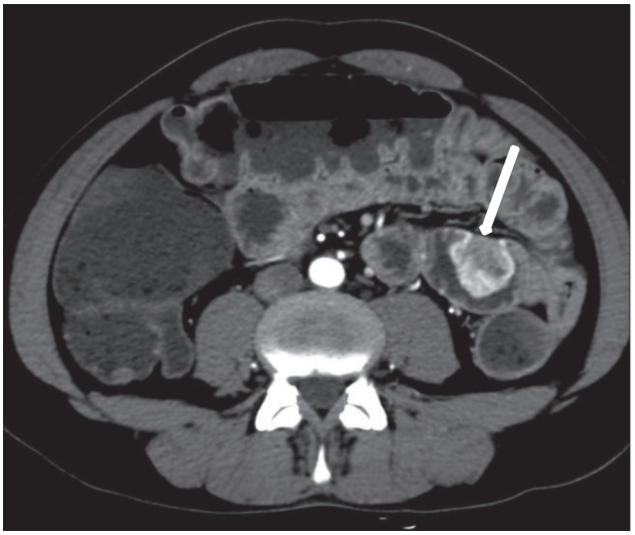

Fig. 2 Axial contrast-enhanced CT image showing intensely enhancing completely endophytic jejunal gastrointestinal stromal tumor (GIST). Low risk. Mitotic index (MI) < 5/50 HPF. Size: 3 cm.

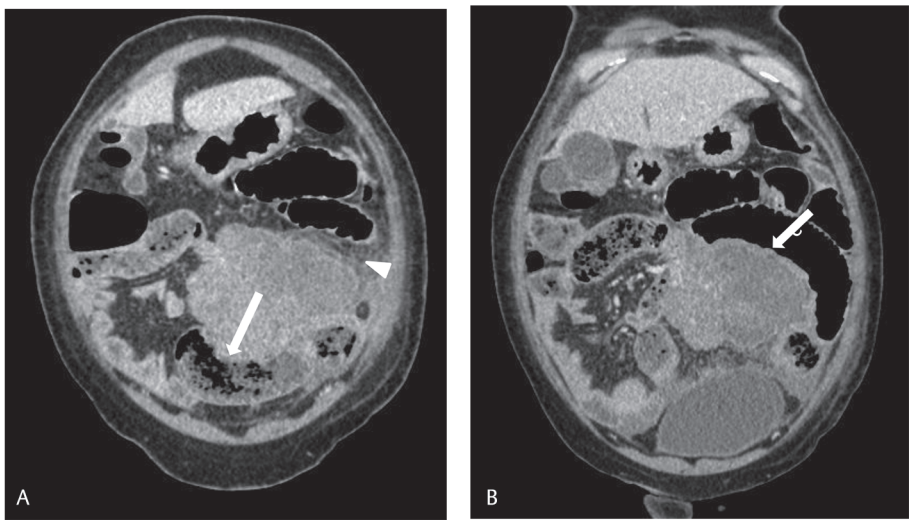

Fig. 3 (**A**, **B**) Coronal contrast-enhanced CT images of a 44-year-old female with jejunal gastrointestinal stromal tumor (GIST) showing lobulated and irregular contour, invasion into adjacent small bowel loops (white arrows) and omentum (white arrowhead) with coexistent adhesion causing bowel obstruction. High risk. Size: 11.4 cm. Mitotic index (MI) >5/50 HPF.

The aim of this study is to evaluate the imaging features of GISTs on CECT and assess its role in risk stratification in a selected South Indian population.

Materials and Methods

Study Population

This is a retrospective study conducted by consecutive sampling of all patients registered in the oncology departments of the participating institutions in the 6-year period from January 2014 to December 2019, who have undergone CECT and who were subsequently (post-surgical resection) proven to have GISTs based on histopathology and IHC (CD 117/DOG1 positivity). Whenever feasible, the cases were followed-up for a period ranging from 6 to 60 months to look for development of metastasis and correlate the same with mitotic index (MI) and risk stratification. Out of the 45 cases included in this study, only 33 cases could be followed-up.

Data was retrieved from electronic radiology database. A total of 45 patients (26 males and 19 females) met the inclusion criteria and were included in the study after excluding patients who did not have pretreatment (prior to surgery or systemic therapy) CT images available for evaluations. We have included gastric, small and large bowel GISTs in our study, all of whom underwent multidetector (MD) CECT prior to surgery or neoadjuvant therapy. We did not have any case of esophageal or extragastrointestinal GIST.

Imaging Technique

Patients were kept fasting for a minimum period of 6 hours before the abdominal and pelvic CT examination and were made to drink 1000 to 1200 mL of gastrografin or mannitol prior to the CT examination. Whenever indicated per rectal contrast was also administered. Patients were in supine position and scanned from domes of diaphragm to pubic symphysis, using 64-slice MDCT GE Lightspeed or 128 slice MDCT, OPTIMA 660 from GE healthcare, Milwaukee, WI, USA. Following the unenhanced CT, 80 to 120 mL (1.5 mL/kg body weight) of Iohexol (350 mg iodine/mL; Omnipaque, GE Healthcare, Shanghai, China) or Iopromide (Ultravist, Bayer Zydus Pharma Ltd, NJ, USA) was administered intravenously at a flow rate of 4 mL/s using a dual head pressure injector (Medrad Stellant CT Injector System, Indianola, PA, US). CECT images were obtained in late arterial phase (35 seconds) and hepatic venous phase (70 seconds). CT parameters were as follows: 120 kVp, automatic tube current modulation, 5 mm slice thickness with 0.625 mm reconstruction, 35 to 50 cm field of view and 512 × 512 matrix. Raw data was reconstructed in coronal and sagittal planes.

MRI with contrast was done as a correlative study in few patients ($n = 4$), especially when CT showed very large or predominantly cystic tumor.

Image Analysis

Three abdominal radiologists (with more than 10 years of experience) reviewed the images in consensus. The images were reviewed on picture archiving and communication system (PACS).

The following imaging parameters were analyzed: maximum size in any plane, organ of origin, shape (round, ovoid or irregular), margin (well-defined or ill-defined), surface (smooth or lobulated), percentage of necrosis, growth pattern, enhancement characteristics–both intensity (mild, moderate or significant) and pattern (homogenous vs. heterogenous), calcification, infiltration into adjacent organs, and presence of metastasis at presentation or on follow-up.

The lesions were classified as those with size less than 5 cm (small) or more than 5 cm (large). Lesions arising from stomach, small bowel, large bowel, and rectum were separately classified. The percentage of necrosis in the tumor was categorized as less than 30%, 30 to 50%, more than 50% and predominantly cystic (when more than 50% of the tumor showed well defined cystic change).

Growth patterns were classified as endophytic, exophytic, or mixed. Endoluminal growth was noted when a tumor was attached to the gastric or bowel wall and was completely within the lumen without bulging into the extraluminal space (►**Fig. 4A, B**). Exophytic growth was stated when a mass was confined to the extraluminal space without bulging into the gastric or bowel lumen. When tumors had both endo and exophytic components they were said to have mixed growth pattern (►**Fig. 5A–C**).

To determine the tumor enhancement intensity, CT attenuation values of the lesion were measured in Hounsfield units (HU). Mild enhancement was when the HU was less than 60, moderate in the range of 60 to 100 HU, and significant being more than 100 HU.

The histopathological correlation has been done with cell type (spindle cell, epithelioid cell or mixed), MI (less than or more than 5 mitosis per 50 high power field [HPF]), and IHC characteristics especially CD-117 and DOG1.

Risk stratification was done in our study using Miettinen and Lasota's risk stratification criteria (2006). This risk stratification system is based on three parameters, that is, MI, organ of origin and largest diameter of the tumor. Based on this, when the mitotic count is > 5/50HPF, all GISTs > 5 cm in size, irrespective of site of GIT origin, fall into high-risk category.

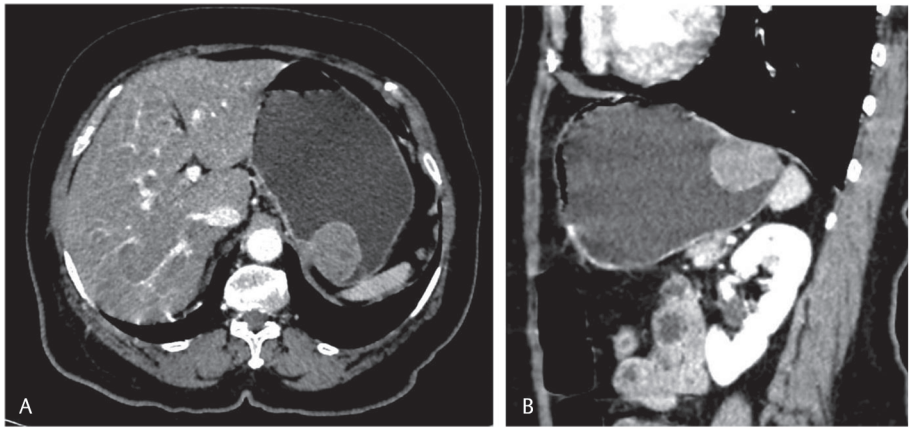

Fig. 4 (**A**) Axial and (**B**) sagittal reformatted contrast-enhanced CT images of 64-year-old female with totally endophytic gastric gastrointestinal stromal tumor (GIST). Size 3.7 cm. Mitotic index (MI) < 5/50 HPF. Low risk.

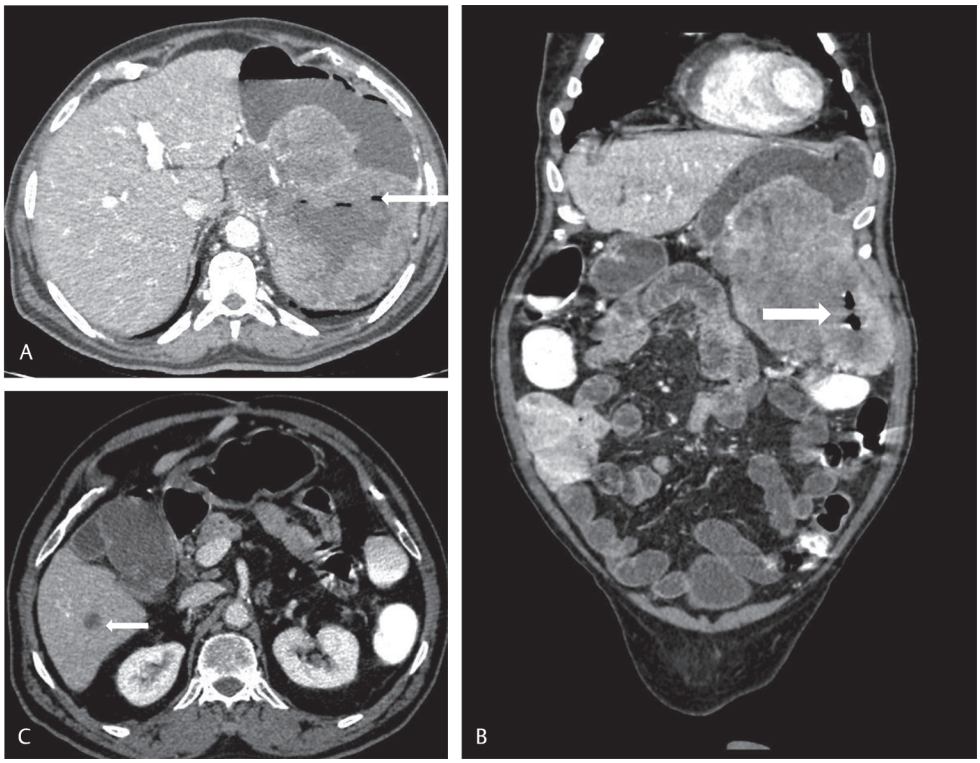

Fig. 5 (**A**) Axial and (**B**) coronal reformatted contrast-enhanced CT images of a large gastric gastrointestinal stromal tumor (GIST) showing endo-exophytic growth pattern and associated fistulous communication with gastric lumen. White arrows point to air pockets within the central necrotic portion of tumor. Tumor had > 30% necrosis. High risk. Mitotic index (MI) > 5 /50 HPF. Size 16.2cm. (**C**) Axial CECT taken 6 months after surgery shows cystic metastasis within central necrotic portion of tumor which confirms fistulous communication in right lobe of liver (white arrow).

When the size is between 2 and 5 cm, gastric GISTs fall into intermediate risk, whereas small and large bowel tumors stay in high-risk category. When the size is < 2cm, even with mitotic count > 5/50HPF, gastric GISTs have only negligible risk, whereas small bowel and colorectal GISTs fall in the high-risk category. When the mitotic count is < 5/50HPF, gastric GISTs of size > 10 cm fall into intermediate risk, whereas small bowel and colorectal tumors > 5 cm fall into intermediate or high-risk category.

Statistical Analysis

Categorical and quantitative variables were expressed as frequency (percentage) and mean ± SD, respectively. Diagnostic statistics such as sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy have been calculated to assess predictive accuracy of CT imaging morphological parameters of the tumor in detecting risk and mitotic index. Kappa statistics was performed to find the agreement of results of CT imaging parameters with risk and MI. Chi-square test, odds ratio with 95% CI was used to find association of risk and MI with selected CT imaging parameters. $p < 0.05$ was considered as the threshold for statistical significance. Statistical analyses were performed by using a statistical software package SPSS, version 20.0.

Results

Each of the 12 imaging parameters were analyzed. Note was also made of the age and sex distribution of the study population. In our study, the patients were in the age ranging from 35 to 82 years. Of this, 51.1% of cases belonged to the 6th and 7th decades. The average age was 61 years with SD of 12.31. As much as 57.8% of our cases were males and 42.2% of the cases were females.

►**Table 1** shows the percentage distribution of the sample according to the various CT imaging characteristics. As many as 29 of the 45 cases (64.4%) showed size more than 5 cm. All the patients who showed homogenous tumor enhancement had size < 5 cm. Reports were analyzed separately with percentage of tumor necrosis cutoff at 50% and also at 30%. Those with > 50% necrosis (n = 9) or predominantly cystic change (n = 7) together constituted 35.6% (n = 16). Those with necrosis more than 30% combined with tumors with cystic change constituted 51% (n = 23). Adjacent organ infiltration was seen in 28.8% of the cases (►**Fig. 6 A–D**). As much as 66.6% cases had either irregular or lobulated shape/surface (n = 30). As much as 87% cases were of spindle cell type on histopathologic evaluation. Out of 45 patients, 43 showed CD 117 positivity. DOG-1 positivity was documented in the two patients who were CD 117 negative. As much as 42.2% of cases (n = 19) had mitotic rate of > 5/50 HFP and 57.8% (n = 26) had mitotic rate of < 5/50 HPF.

Most of our patients (57.8%) were in the high-risk category, 15.6% were in the moderate/intermediate risk group, followed by 13.3% in the very low, 11.1% in the low-risk group and 2.2% had zero risk. In our study, cases with no risk, very low risk and low risk were together included as low-risk group, constituting 26.6% (n = 12). Moderate and high-risk cases were together included under high-risk group, constituting 73.4% (n = 33). One gastric GIST showed fistulous communication with lumen (►**Fig. 5 A**, **B**) .

Table 1 CT morphological characteristics of patients selected for study.

CT characteristics		Count	Percentage
Size	< 5	16	35.6
	5–10	13	28.9
	> 10	16	35.6
Shape	Round	15	33.3
	Ovoid	20	44.4
	Irregular	10	22.2
Margins	Well-defined	42	93.3
	Ill-defined	3	6.7
Surface	Smooth	15	33.3
	Lobulated	30	66.7
Shape/surface	Irregular and lobulated	10	22.2
	Regular and lobulated	20	44.4
	Regular and smooth	15	33.3
Enhancement intensity	Mild	21	46.7
	Moderate	18	40.0
	Significant	6	13.3
Pattern of Enhancement	Heterogeneous	36	80.0
	Homogeneous	9	20.0
Necrosis	Absent	11	24.4
	Less than 30%	11	24.4
	30–50%	7	15.6
	> 50%	9	20.0
	Predominantly cystic	7	15.6
Type of calcification	Present	11	24.4
	Absent	34	75.6
Organ of metastasis	Nil	35	77.8
	Liver	4	8.9
	Lung	0	0.0
	Lymph node	0	0.0
	Bone	0	0.0
	Peritoneum	3	6.7
	Liver, lymph node	1	2.2
	Liver, peritoneum	2	4.4
Organ of origin	Stomach	26	57.8
	GE junction	0	0.0
	Small bowel	12	26.7
	Large bowel	2	4.4
	Rectum	5	11.1
	Others	0	0.0
Growth pattern	Exophytic	25	55.6
	Endophytic	18	40.0
	Mixed	2	4.4

Abbreviation: GE, gastroesophageal.

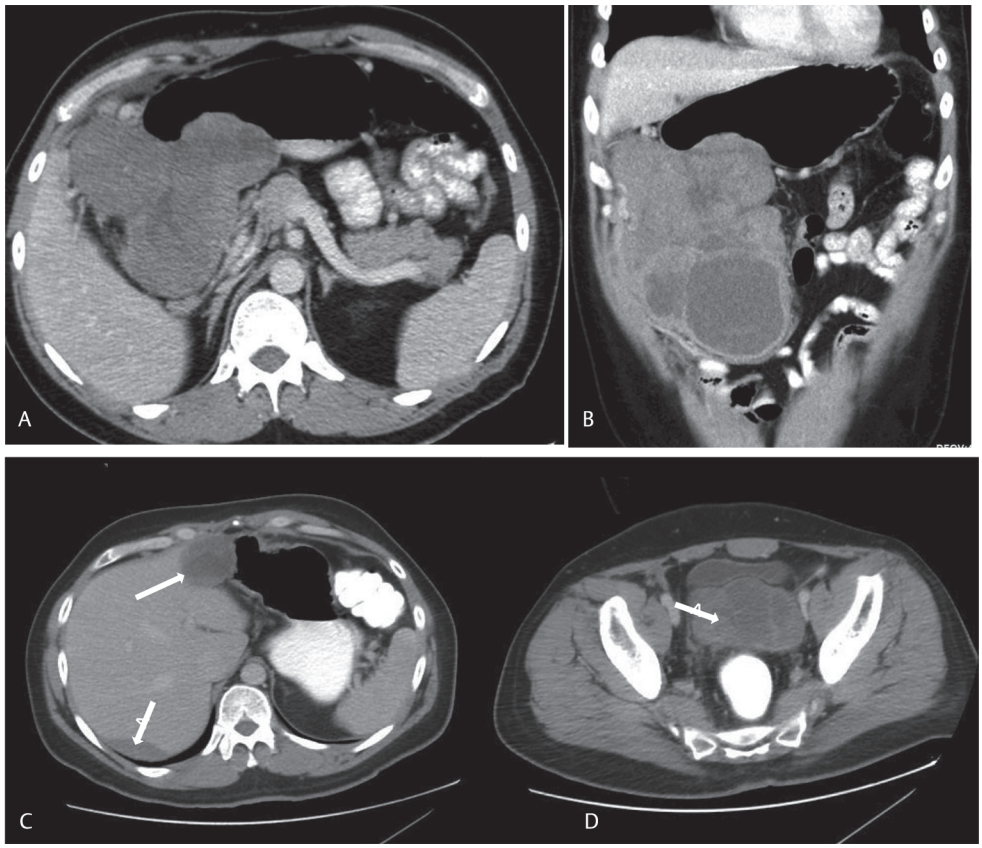

Fig. 6 (A) Axial and (**B**) coronal contrast-enhanced CT images showing markedly necrotic ascending colonic gastrointestinal stromal tumor (GIST) with lobulated and slightly irregular contour in right hypochondrium and lumbar region, displacing the bowel loops medially and with infiltration into stomach. High risk. Mitotic index (MI) > 5/50HPF. Size 15.8 cm. (**C**) axial upper abdomen and (**D**) axial pelvic contrast-enhanced CT images of follow-up scan, 1-year postsurgery showing recurrence at the postoperative site near the stomach as well as perihepatic and pelvic deposits (white arrows).

Diagnostic Accuracy of CT Variables in Predicting Risk

With regard to size of tumor and risk, there was sensitivity and specificity of 81.8% and 83.3%, respectively, with PPV of 93.1%, accuracy of 82.2%, Kappa 0.59 (moderate agreement) and *p*-value of < 0.01. The diagnostic accuracy of margins in predicting risk was only 33.3, with 100% specificity and PPV, but very low sensitivity. Similarly, intensity of enhancement, enhancement pattern, tumor calcification, and growth pattern failed to show significant agreement in risk stratification.

High percentage of necrosis, irregular or lobulated shape/surface characteristics and adjacent organ infiltration were the imaging parameters which had agreement and significant association with high risk ($p < 0.05$; ►**Fig. 7 A, B**).

There was significant association between percentage of necrosis > 30% and risk category with *p*-value of < 0.01, sensitivity 69.7%, specificity and PPV of 100% each, Kappa = 0.55 and diagnostic accuracy of 77.8%. None of the low risk cases had > 30% necrosis. Percentage of necrosis showed fair agreement in predicting risk when cutoff was 50% and moderate agreement when the cutoff was fixed at 30%. All the cases with predominant cystic changes were in the high-risk category.

Tumors with lobulated and irregular shape/surface characteristics showed significant association with risk category with *p*-value of 0.01. Adjacent organ infiltration showed moderate agreement in risk prediction with Kappa = 0.26, specificity and PPV of 100% each, and *p*-value of 0.01.

GISTs in extragastric location had a greater chance of being high risk when compared with gastric GIST. Only 61.5% of gastric GISTs were in high-risk category, whereas 83.3% of small bowel GISTs and 100% each of rectal and colonic GISTs were in the high-risk category.

Diagnostic Accuracy of CT Variables in Predicting Mitotic Index

Size of lesion > 5 cm showed significant association with MI with *p*-value of 0.003. Irregular/lobulated shape/surface characteristics had association with MI with *p*-value of 0.04. As far as growth pattern was concerned, 72% of tumors with exophytic growth pattern had low MI, whereas 55.6% with endophytic pattern showed high MI with *p*-value of 0.04. Out of the 13 tumors in our study that showed adjacent organ infiltration, 10 showed high MI (76.9%), while 23 cases which lacked adjacent infiltration (71.8%) had low MI, with *p*-value of 0.003. There was no significant association between percentage of necrosis and MI in our study

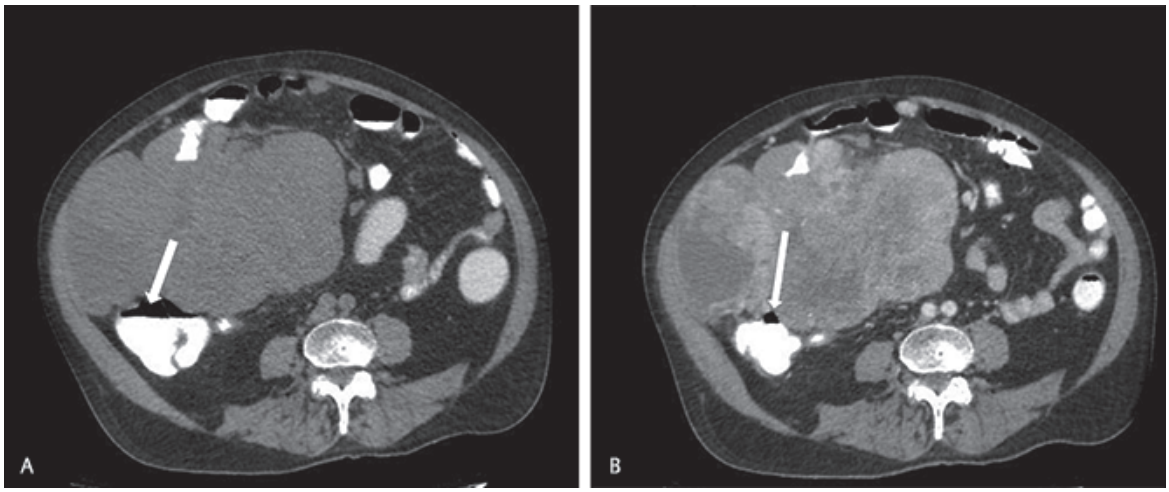

Fig. 7 (**A**) Plain and (**B**) contrast-enhanced CT axial images show large exophytic moderately enhancing jejunal gastrointestinal stromal tumor (GIST) with central necrosis and lobulated and irregular contour. There was invasion of adjacent ascending colon (white arrow) High risk. Mitotic index (MI): > 5 / 50 HPF. Size: 21 cm.

(*p*-value = 0.157). The remaining CT imaging parameters did not show statistically significant association with MI.

Correlation of CT Characteristics of Those Tumors that Metastasized, with MI and Risk Category

Among the 33 patients who could be followed up, only 10 developed metastases during the period of observation. Liver was the most common site of metastasis followed by peritoneum/omentum.

As much as 90% of cases ($n = 9$) that developed metastasis had high MI. Only one small bowel GIST which subsequently metastasized had low MI. Thus, there was significant association between MI and development of metastasis ($p < 0.01$).

It was also found that there was significant association between risk category and occurrence of metastasis at presentation or on follow-up with a *p*-value of 0.01. The specificity and PPV were 100% each, but with low sensitivity (30.3%) and accuracy (48.9%). None of the low-risk cases developed metastasis, but 50% of the high-risk cases developed metastasis on follow-up.

►**Table 2** shows association of metastasis with selected CT imaging characteristics. The individual CT morphological parameters in tumors with metastasis were analyzed, and it was found that among these, size > 5cm ($p < 0.01$), extent of necrosis more than 30% ($p < 0.01$) and presence of adjacent organ infiltration ($p < 0.001$) showed significant association with metastasis. None of the patients with less than 30% necrosis developed metastasis in our study.

Discussion

GISTs are the most common mesenchymal tumors of the GIT and comprise a subset of tumors with marked heterogeneity. GISTs are potentially malignant tumors with nearly 20 to 30% being malignant. They exhibit a wide range of morphological appearance. GISTs are mostly spindle cell tumors with 20 to 25% of tumors having epithelioid morphology and some having a combination of spindle and epithelioid cells.

Most GISTs show strong and diffuse expression of KIT (CD117). C-kit mutations are seen in around 80 to 85% of GIST, with recent studies showing other mutations in GIST like PDGFRA (Platelet derived growth factor receptor α), BRAF V600E and SDH (succinate dehydrogenase gene) mutations.[7]

A small minority (< 5%) may lack KIT expression. An equally sensitive and specific marker is DOG1 (Discovered on GIST-1), which is a recently described protein expressed in GISTs irrespective of mutation status. This is positive in up to 50% of KIT negative GISTs.

Although GIST can occur in any age group, it is most frequently seen in those above 50 years, with equal prevalence among both sexes. Most of the GISTs occur sporadically with few cases seen in association with inherited syndromes like neurofibromatosis type I (NF1), Carney triad, Carney–Stratakis syndrome and familial GIST.[8]

Although CT is the first-line and most preferred imaging modality in suspected GISTs, MRI is also beneficial in predicting the malignant potential of GIST (like presence of intratumoral large cystic changes and low apparent diffusion coefficient [ADC] values). It may also be helpful in very large GISTs where organ of origin may be difficult to ascertain. Diffusion-weighted imaging is said to have a role in prediction of risk.

PET-CT is mostly concerned with post therapy response evaluation and follow-up of GIST, especially in detection of local/distant recurrence, resulting in significant impact on clinical management.[9]

The goal of this study was to evaluate the MDCT imaging morphology of GISTs and more importantly to analyze its role in risk stratification, which has a huge bearing on the treatment and prognostication.

Majority of our cases were in their 6th and 7th decades, with slight male predominance, and stomach being the most common site, followed by small bowel and colorectal GISTs. With regard to the various CT parameters assessed, majority of tumors had size > 5 cm, well-defined margins, lobulated or

Table 2 Association of metastasis with selected CT imaging variables

		Organ of metastasis				χ^2	*p*-Value	Odds (95% CI)
		Absent		Present				
		Count	Percentage	Count	Percentage			
Size	> 5	19	65.5	10	34.5	7.09	< 0.01	–
	≤ 5	16	100.0	0	0.0			–
% Necrosis	High	8	50.0	8	50.0	11.08	< 0.01	13.50(2.37–76.80)
	Low	27	93.1	2	6.9			1
Shape/ surface	Irregular and lobulated	6	60.0	4	40.0	4.02	0.134	–
	Regular and lobulated	15	75.0	5	25.0			–
	Regular and smooth	14	93.3	1	6.7			–
Adjacent organ infiltration	Present	6	46.2	7	53.8	10.58	< 0.001	11.28(2.25–56.59)
	Absent	29	90.6	3	9.4			1
Mitotic index	High	10	52.6	9	47.4	12.03	< 0.01	22.5(2.51–201.5)
	Low	25	96.2	1	3.8			1

Abbreviations: CI, confidence interval; χ^2, Chi square.

irregular contour, mild-to-moderate heterogenous pattern of enhancement, exophytic growth and necrosis > 30%. The age and sex distribution of our cases as well as the CT morphological parameters were similar to what has been described in several previous studies.[10-12]

At present, risk stratification of GISTs is based on three parameters, namely, tumor size, organ of origin and mitotic rates. There have been numerous studies conducted on GISTs in the past, and more than eight established risk classification systems exist at present. Of these, the classification scores by NIH (Fletcher et al) and The Armed Forces Institute of Pathology (Miettinen and Lasota) are more universally accepted.[13-15]

There are conflicting reports in the available literature as far as the utility of imaging parameters (other than size and organ of origin) in risk assessment is concerned. In our study, we found significant association between percentage of necrosis and risk category. Percentage of necrosis showed fair agreement in predicting risk when cutoff was 50% and moderate agreement when the cutoff was fixed at 30% ($p < 0.01$). None of the cases with < 30% necrosis were in the high-risk category. There was no significant association between percentage of necrosis and MI in our study. Several previous studies too have highlighted the importance of necrosis in risk stratification of GISTs.[16] Liu et al conducted a study on 740 cases of GISTs, which showed that tumor necrosis was significantly associated with large tumor size, higher MI, tumor rupture and nuclear atypia.[17] Gronchi et al have reported that necrosis and adjacent organ infiltration are associated with high risk and high cellularity.[18]

However, there are some studies like the one published by Ahmed et al which failed to show any correlation between radiological appearances such as necrosis, hemorrhage or cyst formation and malignant potential.[19] This is probably due to the very small sample size of 24 cases and the short duration of follow-up.

We found that in our study, all tumors that were predominantly cystic ($n = 7$) belonged to the high-risk category (►**Fig. 8**).

One of these cases was a female patient with history of NF1 who had a large duodenal cystic GIST, which was resistant to Imatinib and developed metastasis on follow-up (►**Fig. 9A-G**). It is well-documented that NF1 associated GISTs are mostly of the wild type and are resistant to Imatinib.[20,21] None of our remaining cases had syndromic association. Wang et al has stated that GISTs with predominant cystic change are seen in high-grade tumors, when they outgrow the blood supply due to aggressive growth and tumor necrosis.[21]

In our study, there was moderate association between GISTs with adjacent organ infiltration and high-risk category (*p*-value of 0.01) as well as with high MI (*p*-value of 0.003). Tumors with lobulated and irregular shape/surface characteristics also showed significant association with risk category (*p*-value of 0.01) and with MI (*p*-value of 0.04). Tateishi et al in their study concluded that the CT features that suggest a high-grade GIST and predict poor outcome include hepatic metastasis, irregular borders, adjacent organ invasion, and lesions larger than 11.1 cm.[22]

When the size cutoff was 5 cm, the accuracy to predict high risk was 82.2%. It is well-documented that large size especially more than 10 cm is a strong predictor of metastasis.[6,22] Among the 10 cases in the study that had metastasis at the time of presentation or on follow-up, 70% were more than 10 cm and all were more than 5 cm. Extent of necrosis more than 30% ($p < 0.01$) and presence of adjacent organ infiltration (*p*-value of 0.001) also showed significant association with development of metastasis. The most common site of metastasis was liver followed by peritoneum/omentum as documented in several previous studies.[12]

The role of a radiologist is limited in predicting risk stratification of GISTs; however, it is important to ascertain the size as well as the organ of origin accurately to guide the clinician and aid in risk stratification.

CT morphological parameters of significance in risk stratification as per our study include tumor necrosis, predominant cystic change, irregular and lobulated shape/surface characteristics and adjacent organ infiltration.

Those parameters that predicted high MI were large size, irregular or lobulated shape/surface, endophytic growth pattern and adjacent organ infiltration.

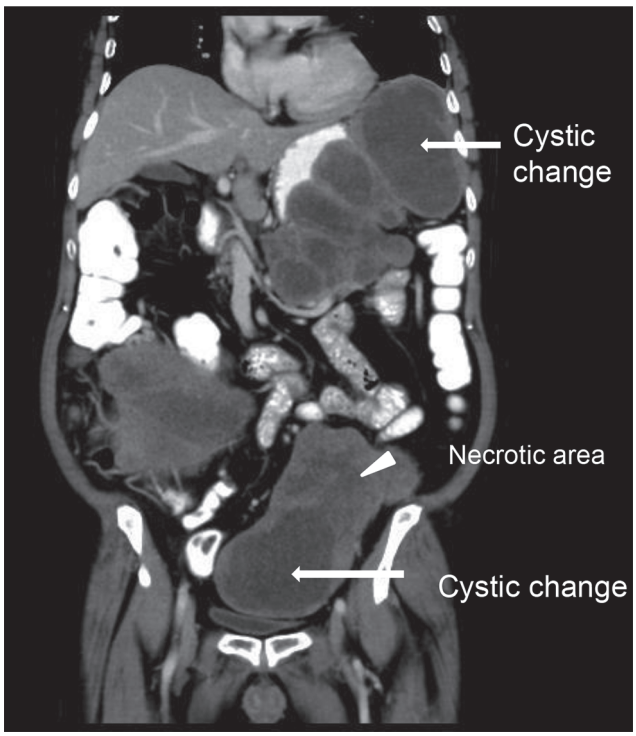

Fig. 8 Coronal contrast-enhanced CT image showing large exophytic gastric gastrointestinal stromal tumor (GIST) with predominant cystic change and multiple peritoneal deposits. Pelvic metastatic deposit shows necrotic area as well as cystic change. High risk. Mitotic index (MI): > 5/50 HPF. Size 19.1 cm (white arrows point to cystic change and white arrowhead points to necrotic area).

The parameters which were associated with development of metastasis were size > 5 cm, necrosis > 30% and the presence of adjacent organ infiltration. None of the low-risk cases in our study, or those with < 30% necrosis, developed metastasis during follow-up. Only one (10%) small bowel GIST with low MI had metastasis. Burkill et al in their study have reported the imaging features and metastatic pattern of GIST, but they have not correlated the imaging features with metastatic potential of GIST.[23]

Pitfalls

Our study had several limitations, the major factor being the relatively limited sample size. Among the 45 cases in the study, only 33 could be followed-up. We did not carry out separate assessment for gastric and nongastric GISTs. Only very few of our cases had PET CT evaluation and therefore we have not assessed its role in risk stratification. Due to the very small number of cases that had MRI evaluation in our study (n = 4), it was not feasible to ascertain the usefulness of this modality in GIST risk assessment or prediction of metastasis. We have not done a prospective study to verify the analysis.

Conclusion

The role of the radiologist is limited in predicting risk category of GISTs. However, if there are certain imaging morphological parameters which can predict risk category/predisposition to develop metastasis, then it is of great value to the clinician in prognostication and treatment planning.

CT morphological parameters of significance in risk stratification, as per our study, include tumor necrosis > 30%, predominant cystic change, irregular/lobulated shape/surface characteristics and presence of adjacent organ infiltration.

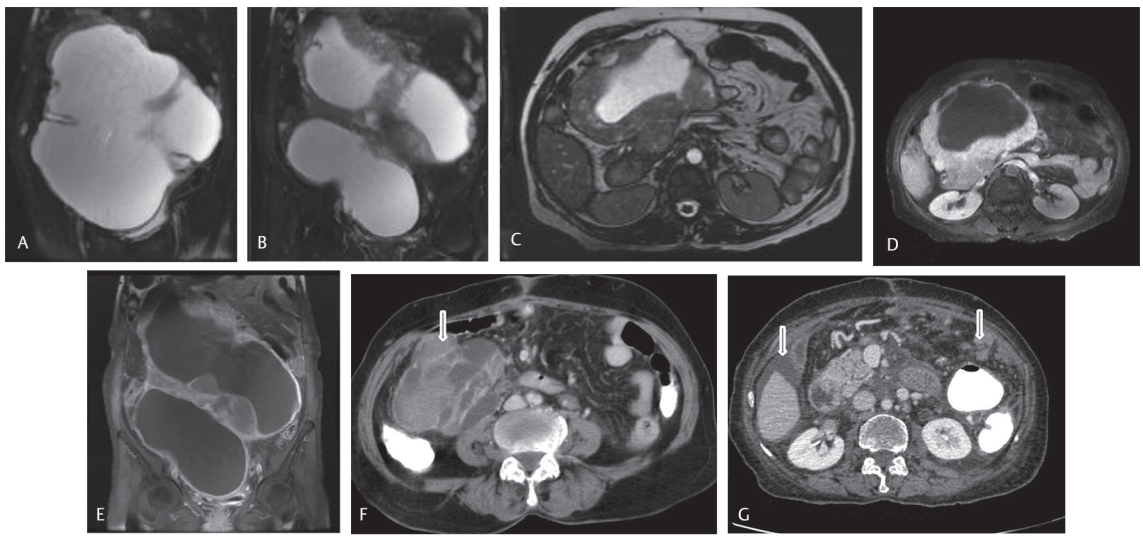

Fig. 9 Correlative MRI scan–Coronal T2WI images (**A, B**) of a known case of neurofibromatosis type I (NF1), showing large complex solid cystic lesion filling almost the whole abdomen. Axial FIESTA image (**C**) shows the superior end of the lesion indenting the 3rd segment of duodenum. Central cystic and peripheral solid components of lesion appreciable. Postcontrast axial (**D**) and coronal (**E**) T1W images show moderate to marked enhancement of the peripheral solid components. Postsurgical, follow-up contrast-enhanced CT axial images (**F, G**) after 6 months show recurrence in the right iliac fossa (solid cystic mass) along with ascites and multiple omental deposits (white arrows). High risk tumor with predominant cystic changes and size > 20 cm and mitotic index (MI) > 5/50 HPF arising from duodenum with recurrence on follow-up.

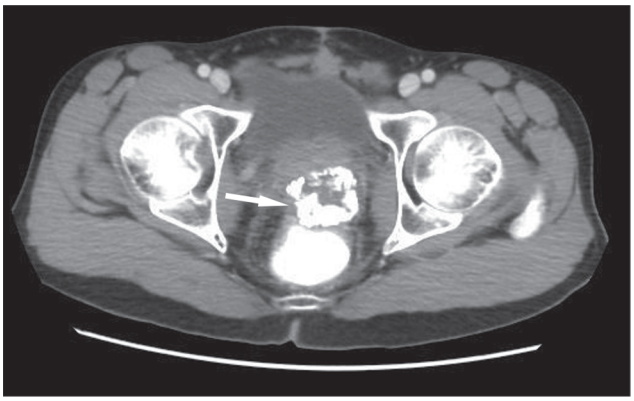

Fig. 10 Axial contrast-enhanced CT image showing partially calcified rectal gastrointestinal stromal tumor (white arrow). High risk. Mitotic index (MI) > 5/ 50 HPF. Size: 5 cm.

Size > 5 cm, along with irregular/lobulated contour, adjacent organ infiltration and endophytic growth pattern favored high MI.

The parameters which were associated with development of metastasis were size > 5 cm, necrosis > 30% and the presence of adjacent organ infiltration. None of the patients with less than 30% necrosis developed metastasis in our study.

The radiologist also plays an important role in ascertaining the size of tumor and the organ of origin accurately to guide the clinician in risk calculation and subsequent prognostication.

Size and organ of origin are already known to have a significant role in risk stratification, and this was reinstated in our study. However, as these two parameters are already incorporated in risk classification, it is inappropriate to assess their association with risk. Nevertheless, the increased risk of extragastric GIST when compared with gastric GIST was reaffirmed. All four rectal GISTs in our study were in the high-risk category (►**Fig. 10**).

Conflict of Interest

None declared.

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