DOI: 10.7860/JCDR/2024/68803.19175

Original Article

Radiology Section

Prediction of Pathological Risk Stratification using Computed Tomography Features in Gastrointestinal Stromal Tumours: A Retrospective Observational Study

MANALI ARORA[1], ADITYA ABHISHEK[2], NITESH SINGH[3], VISHAL THAKKER[4], SHEENAM AZAD[5], AAKASH GUPTA[6], NAVDEEP SINGH SIDHU[7], RAJIV AZAD[8]

ABSTRACT

Introduction: Gastrointestinal Stromal Tumours (GISTs) are the most common mesenchymal tumours of gastrointestinal tract. A high postsurgical recurrence and metastatic rate have created a need for a presurgical risk profile identification system.

Aim: To assess the association between morphological Computed Tomography (CT) parameters with the pathological risk profile and analyse which CT features can predict the risk grading of GISTs.

Materials and Methods: This was a retrospective cohort study based on imaging and histopathological data of 26 patients with pathologically proven GISTs presenting to the Department of Radiodiagnosis of a tertiary hospital in the northern Indian Himalayan foothills over a period of five years from July 2018 to June 2023. CT imaging features including size, growth pattern, margins, enhancement, calcifications, necrosis, intralesional haemorrhage, enlarged feeding vessels, direct organ invasion, and associations such as ascites and lymphadenopathy were studied. All lesions were classified as per Miettinen risk classification into no risk, very low-risk, low, moderate, and high-risk lesions. Analysis was done by the Chi-square test. Predictive analysis was carried out by computing the odds ratio and performing regression analysis on significantly associated imaging features.

Results: Out of 26 patients, the study group comprised 16 males (61.54%) and 10 females (38.46%). The most common decade of presentation was the 6th decade with the mean age of presentation being 55.81±4.23 years. Twelve patients were grouped under intermediate to high-risk grading. Lesion size >5 cm (p-value=0.0171, OR=19.12), ill-defined margins (p-value=0.0048, OR=18.33), intralesional necrosis (p-value=0.0053, OR=19.8), and enlarged feeding vessels (p-value=0.012, OR=21.27) were identified as imaging features with significant association and predictive ability for high-risk lesions. The strongest predictive ability for a high-risk profile was shown by ill-defined margins (R^2=0.381) and intralesional necrosis (R^2=0.3287).

Conclusion: A preoperative Contrast Enhanced Computed Tomography (CECT) assessment provides a comprehensive imaging profile for GISTs as well as a fair accuracy of risk profile prediction via various singular and clustered morphological parameters.

Keywords: Calcifications, Enhancement, Miettinen risk classification, Necrosis

INTRODUCTION

The GISTs account for 0.1-3% of all gastrointestinal neoplasms [1]. CECT has a paramount importance for the detection, characterisation, staging, and post-treatment surveillance of GISTs, providing accurate information about the primary tumour, presence of distant metastasis, and response to target therapy [2,3]. Postsurgery GISTs have shown recurrence in as many as 50% of cases according to previous literature [4,5]. The risk stratification systems designed for predicting high-risk for recurrent or metastatic disease are based on postoperative parameters of lesion site, size, and histopathological features. Since the recurrence rates are high, a preoperative risk prediction system is desired to better navigate the therapeutic plan [6,7]. While previous literature has studied the role of CT parameters in risk prediction, most such studies have included postoperative specimens only for analysis. In addition, there is no regional literature available on the topic to be used as a reference in the indigenous population. With this background, the present study was conducted with an aim to assess the association between morphological CT parameters with the pathological risk profile and analyse which CT features can predict the risk grading of GISTs.

MATERIALS AND METHODS

This was a retrospective cohort study conducted in the Department of Radiodiagnosis at Shri Guru Ram Rai Institute of Medical and Health Sciences, a tertiary teaching hospital in the northern Indian Himalayan foothills, over a five-year period from July 2018 to June 2023. Following clearance from the Institute's Ethical Committee, as per letter no. SGRR/IEC/01/23, the study utilised imaging and hospital-based pathological data. A consent waiver was obtained as patients had already undergone the necessary investigations for clinical purposes.

Inclusion criteria: All patients with pathologically confirmed GISTs whose CECT images were available for assessment were included in the study.

Exclusion criteria: Patients with prior surgery or Tyrosine Kinase Inhibitor therapy before imaging, patients with a history of another malignancy, inadequate CECT images for lesion evaluation, mitotic index not being included in the histopathological report were excluded from the study.

The clinical and demographic profiles of all patients were obtained from the hospital database. Two radiology consultants, with 10 and 11 years of experience in reporting CT, independently assessed and documented the CT parameters of GISTs. In cases of discordance, the opinion of the senior radiologist prevailed. Accordingly, all lesions were classified based on the Miettinen risk classification into categories of no risk, very low-risk, low-risk, moderate-risk, and high-risk lesions [8]. For this study, lesions were analysed in two groups, where the first three categories were grouped as

low-risk lesions, while moderate and high-risk lesions were grouped into the second group. The associations and predictive ability of individual CT features were studied by comparing them with the lesion risk profile.

Scanning protocol: A predesigned institutional protocol was utilised for triple-phase imaging of abdominal studies, predominantly employing a 128-slice multidetector CT scanner (Philips Ingenuity). The parameters included 120 kVp, 130 mAs, 1.25-mm slice thickness, and 1.25-mm slice interval. Patients were directed to drink 1 litre of oral contrast mixed with water 45 minutes before the examination to ensure adequate bowel and bladder distension. The procedure began with non contrast imaging of the abdomen and pelvis, followed by an arterial phase scan at 25-30 seconds postinjection of 100 mL of non ionic iodinated contrast material at a rate of 3 mL/s. Subsequently, a portal phase scan was conducted at 70-80 seconds postinjection, followed by a venous phase at 180 seconds, and a delayed-phase scan at 3-5 minutes. The scanning range extended from the diaphragm level to the symphysis pubis, with breath-holding instructions provided to minimise motion artifacts. The total radiation exposure was documented for each patient. Images were reconstructed using a standard soft-tissue algorithm with a slice thickness of 5 mm.

Image evaluation and scoring systems: Contrast CT abdomen images were evaluated in all three planes after multiplanar reconstruction. Following the assessment of the lesion's location and identification of the organ of origin, the following imaging features were documented for each lesion: maximum diameter of the lesion in any of the three planes (< or >5 cm), growth pattern (exophytic/endophytic/mixed), margins (well-defined/ill-defined), enhancement pattern (homogeneous/heterogeneous). The degree of enhancement was categorised as mild (an increase of 20-40 HU), moderate (an increase of 41-60 HU), and intense (an increase of >60 HU). The presence or absence of necrosis (hypoattenuating intralesional areas with no enhancement), calcifications, intralesional haemorrhage, direct organ invasion, and surface ulceration were also documented. Enlarged feeding vessels were analysed on maximum intensity projection images. Besides lesion features, associated features such as lymphadenopathy, ascites, and peritoneal seeding were also studied.

STATISTICAL ANALYSIS

Categorical variables were evaluated as percentages. The measures of central tendency in nominal variables were examined as means. Categorical analysis was conducted using the Chi-square test. Predictive analysis was carried out by computing odds ratios and performing regression analysis on significantly associated imaging features. A 95% confidence interval was calculated for all tests. A p-value of <0.05 was considered significant. All statistical analyses were performed using GraphPad Prism Version 10.0.3.

RESULTS

The study group consisted of 26 patients with a male predominance (n=16, 61.54%). The most common decade of presentation was the sixth decade, with a mean age of presentation of 55.81±4.23 years. The most common organ of origin in the study group was the stomach (n=15, 57.69%), followed by the small bowel (n=6, 23.07%) and the duodenum (n=4, 15.38%). One patient presented with GIST of the sigmoid colon.

The CT features analysed included both lesion characteristics and associated features. More than two-thirds of the lesions were over five cm in maximum diameter (n=20, 76.9%) and exhibited an exophytic growth pattern (n=22, 84.6%). A total of 15 lesions (57.69%) showed heterogeneous enhancement, and 13 lesions (50%) had ill-defined margins. Larger lesions greater than five cm (n=12, 46.2%), lesions with ill-defined margins (n=10, 38.4%), heterogeneous enhancement (n=9, 34.61%), along with intralesional haemorrhage (n=4, 15.38%) and necrosis (n=11, 42.30%) were more common in the intermediate to high-risk groups [Table/Fig-1].

CT features	Low grade (n=14)	Moderate to high grade (n=12)	p-value (<0.05)
Size			
< 5 cm	6	0	**0.0171**
> 5 cm	8	12	
Growth pattern			
Endophytic	3	0	0.2246
Exophytic	11	11	
Mixed	0	1	
Margin			
Well-defined	11	2	**0.0048**
Ill-defined	3	10	
Enhancement			
Homogenous	8	3	0.1302
Heterogenous	6	9	
Degree of enhancement			
Mild	7	5	0.7127
Moderate	6	5	
Intense	1	2	
Calcifications			
Present	3	2	1
Absent	11	10	
Necrosis			
Present	5	11	**0.0053**
Absent	9	1	
Lymphadenopathy			
Present	2	5	0.1904
Absent	12	7	
Intralesional haemorrhage			
Present	2	4	0.3652
Absent	12	8	
Enlarged feeding vessels			
Present	0	5	**0.012**
Absent	14	7	
Direct organ invasion			
Present	2	4	0.3652
Absent	12	8	
Ascites			
Present	1	5	0.0652
Absent	13	7	
Peritoneal seeding			
Present	1	3	0.3061
Absent	13	9	
Surface ulceration			
Present	1	4	0.1478
Absent	13	8	

[Table/Fig-1]: CT parameters in comparison to risk stratification of lesions.
Chi-square test was used

It was noted that a size larger than 5 cm (OR=19.12), ill-defined margins (OR=18.33), intralesional necrosis (OR=19.8), and enlarged feeding vessels (OR=21.27) were significantly associated with intermediate to high pathological risk grades [Table/Fig-2].

Ill-defined margins (R^2=0.381) were observed as the strongest individual predictor of higher risk grades in the present study population. This was followed by necrosis (R^2=0.3287), enlarged

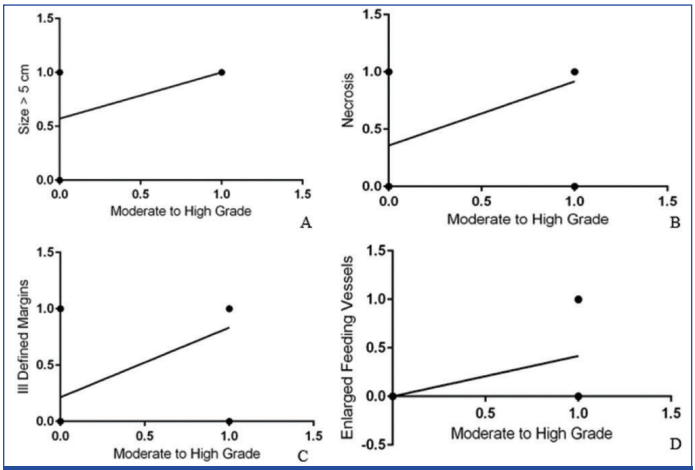
CT parameter	Odds ratio	95% CI	p-value (<0.05)
Size > 5 cm	**19.12**	**0.9465-386.1359**	**0.0543**
Exophytic	3	0.2687- 33.4886	0.3721
Ill-defined margins	**18.33**	**2.5221-133.2645**	**0.0041**
Heterogenous enhancement	4	0.7443-21.4970	0.1061
Moderate-intense enhancement	1.4	0.296-6.6221	0.6713
Calcifications	0.733	1.009-5.3306	0.7593
Necrosis	**19.8**	**1.9443-201.6347**	**0.0117**
Intralesional haemorrhage	0.5	0.0740-3.3778	0.477
Enlarged feeding vessels	**21.27**	**1.0313-438.5596**	**0.0477**

[Table/Fig-2]: Odds ratio of individual CT parameters for prediction of moderate to high-risk grade.

feeding vessels (R^2=0.2778), and lesion size of more than five cm (R^2=0.2571) [Table/Fig-3]. Multivariate regression analysis indicated that combining all the above four CT parameters improved the predictive ability of CT from fair to moderate in delineating intermediate to high-risk GISTs (R^2=0.4906) [Table/Fig-3,4]. A few representative cases are shown in [Table/Fig-5,6].

CT parameters	R Square	95% CI	p-value
Linear regression analysis			
Ill-defined margins	0.381	0.2866-0.9515	0.0008
Necrosis	0.3287	0.2227-0.8964	0.0022
Enlarged feeding vessels	0.2778	0.1336-0.6997	0.0057
Size >5 cm	0.2571	0.1217-0.7355	0.0082
Multivariate regression analysis	**R Square**	**Adjusted R Square**	**p-value**
Ill-defined margins+necrosis+enlarged feeding vessels+Size >5 cm	0.4906	0.3935	0.0052

[Table/Fig-3]: Regression analysis (linear and multivariate) of CT parameters that were significantly associated with moderate to high-risk grading.

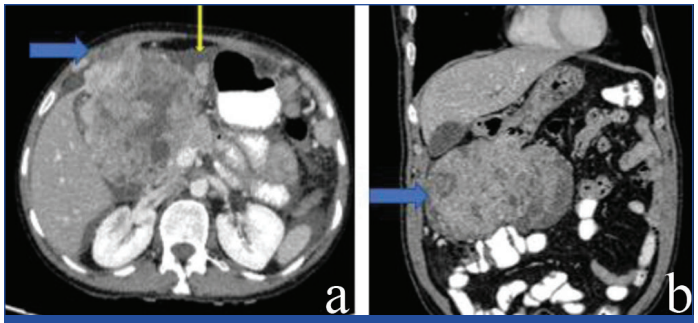


[Table/Fig-4]: Linear regression analysis graphs for: a) Size > 5 cm; b) Necrosis; c) Ill-defined margins; and d) Enlarged feeding vessels in prediction for moderate to high-risk grades.

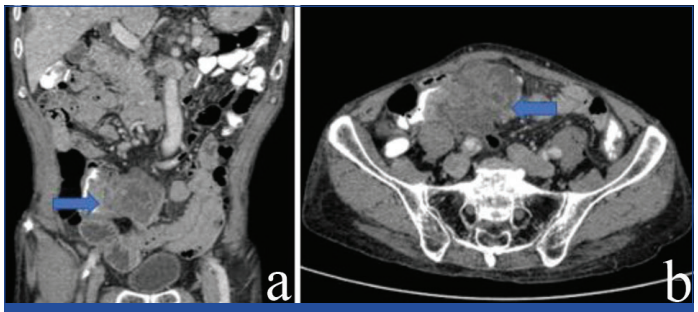
DISCUSSION

CECT is the standard preoperative imaging modality for GISTs. Two out of three parameters required by Miettinen's pathological system of risk stratification, i.e., lesion location and size, can be comfortably evaluated by CECT [8,9].

In the present study, it was observed that lesion size >5 cm, ill-defined margins, presence of necrosis, and enlarged feeding vessels were significantly associated with intermediate to high-risk grades of GIST. Conversely, lesion growth pattern, enhancement patterns, and intralesional haemorrhage did not show any significant association with the risk profile. Although lymphadenopathy, direct organ invasion,



[Table/Fig-5]: Contrast enhanced a) axial CT image and b) Coronal CT image shows large heterogenous, multilobulated, irregular mass arising from greater curvature of stomach with intralesional hypodense non enhancing areas suggestive of necrosis (blue arrow) with adjacent free fluid (yellow arrorw). This lesion was graded as high-risk lesion on Miettinen risk stratification.



[Table/Fig-6]: Contrast enhanced CT images a) Coronal and b) Axial image shows a lobulated partially exophytic lesion (blue arrow) arising from distal ileal loops, which shows irregular margins, heterogenous enhancement and internal areas of necrosis. The lesion was demarked high-risk on risk stratification grading.

and ascites were more frequently seen in the intermediate to high-risk group, no statistically significant associations were observed. This lack of significance may be attributed to a lower sample size, as these features were present in only a few patients.

Lesion size is a crucial factor for pathological risk stratification according to the pathological risk grading system [8]. Larger lesions often exhibit malignant features or pose a high-risk for postoperative recurrence and metastasis [10]. Zhou C et al., during the analysis of predictive CT features in 129 patients with histopathologically confirmed GISTs, observed that lesion size was linked to high-risk GISTs and could serve as a predictor for risk grading as well [11]. Kim HC et al., reported that lesion size was the sole CT feature that could significantly predict the mitotic rate [12]. Similar findings were noted by Tateishi U et al., who associated lesions larger than 11.1 cm with high-grade GISTs and poor outcomes [13].

Smooth lesion margins are seen in smaller lesions with lower-risk grading. Conversely, lobulated to ill-defined margins are seen in high-risk lesions [14,15]. In the present study population, a large proportion of high-risk lesions, i.e., 83.33%, show ill-defined margins. This association was significant with an odds ratio of 18.33 for ill-defined margins. In the study by Grazzini G et al., lesion margins were significantly associated with the Miettinen stratified risk category. However, it could not be established as a predictor of the risk category [7]. Cannela R et al., while studying morphological CT features for risk stratification in 88 patients, observed that lesions with ill-defined margins were associated with a shorter disease-free interval. Additionally, an additional haemorrhage with ill-defined margins could predict an overall shorter survival [10]. Intralesional necrosis was found to be significantly associated with patients in the intermediate to high-risk group, similar to the observations of Maldonado FJ et al., and Ianicelli E et al., [16,17]. Enlarged feeding vessels were seen in five patients, all of whom had intermediate to high-risk lesions, thereby marking a significant association. Similar observations were made by Grazzini G et al., while studying 54 patients with GIST, where 92.3% of lesions with enlarged feeding vessels were demarked as high-risk [7].

While analysing overall risk predictors, Wang TT et al., studied Gastric GISTs for their CT features and observed that tumour size, margins,

and growth pattern were predictors of pathological risk grades [18]. Jovanic MM et al., assessed 79 patients to determine the role of CT morphological and texture analysis parameters of suspected GISTs for pathological risk prediction [19]. They found that, along with tumour size, margins, and growth pattern, mucosal continuity, enlarged peri- and intra-tumoural Feeding Or Draining Vessel (EFDV) were also significant predictive factors for high-risk GISTs. Similarly, Wang Y et al., observed that tumour size, EFDV, enlarged lymph nodes, and enhancement were independent predictors of the biological risk of GIST [20]. In agreement with recent literature, the overall analysis of risk prediction in the study inferred that all four associated features-lesion size > 5 cm, ill-defined margins, necrosis, and enlarged feeding vessels-showed a linear correlation with lesion risk profile, thus serving as risk predictors.

The strength of the study lies in the potential preoperative evaluation through basic CT morphological features for risk prediction. Such features can be easily assessed on CT machines of varied caliber set-up in different centres. The learning curve for such evaluation also remains shorter. This can provide a stronger and earlier prediction of lesion activity, thereby shaping a management plan in the early stages. However, it is recommended that more multicentre trials be conducted with research support to yield more plausible results with less variation and higher accuracy.

Limitation(s)

The major limitation of the present study was its moderate sample size and retrospective design. Additionally, the comparison was made with a risk stratification score rather than actual clinical recurrence and metastasis. Since the scans observed were taken over a five-year period, the scanning protocol was not uniformly the same for all cases. However, the image quality for lesion character assessment was at the discretion of the observer. Despite these limitations, the limited and varied literary evidence for preoperative risk prediction for GISTs justifies the present study and its observations.

CONCLUSION(S)

Multiple CT features, such as size, margins, necrosis, and enlarged vessels, were associated with high-risk GISTs. These features have shown the ability to predict lesion risk profiles when assessed individually as well as in a cluster. The fair prediction ability of morphological features, along with a comprehensive evaluation for gastrointestinal tumours, makes CT a desirable preoperative assessment tool for profiling risk.

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PARTICULARS OF CONTRIBUTORS:
1. Associate Professor, Department of Radiodiagnosis, Shri Guru Ram Rai Institute of Medical and Health Sciences, Dehradun, Uttarakhand, India.
2. Senior Resident, Department of Radiodiagnosis, Shri Guru Ram Rai Institute of Medical and Health Sciences, Dehradun, Uttarakhand, India.
3. Assistant Professor, Department of Radiodiagnosis, Naraina Medical College and Research Centre, Kanpur, Uttar Pradesh, India.
4. Associate Professor, Department of Radiodiagnosis, Shri Guru Ram Rai Institute of Medical and Health Sciences, Dehradun, Uttarakhand, India.
5. Professor, Department of Pathology, Shri Guru Ram Rai Institute of Medical and Health Sciences, Dehradun, Uttarakhand, India.
6. Postgraduate Resident, Department of Radiodiagnosis, Shri Guru Ram Rai Institute of Medical and Health Sciences, Dehradun, Uttarakhand, India.
7. Postgraduate Resident, Department of Radiodiagnosis, Shri Guru Ram Rai Institute of Medical and Health Sciences, Dehradun, Uttarakhand, India.
8. Professor, Department of Radiodiagnosis, Shri Guru Ram Rai Institute of Medical and Health Sciences, Dehradun, Uttarakhand, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Vishal Thakker,
Associate Professor, Department of Radiodiagnosis, SGRRIM&HS,
Dehradun-248001, Uttarakhand, India.
E-mail: docvdt@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Nov 30, 2023
- Manual Googling: Jan 18, 2024
- iThenticate Software: Jan 23, 2024 (6%)

ETYMOLOGY: Author Origin

EMENDATIONS: 5

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Consent waived (as declared)
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Nov 27, 2023**
Date of Peer Review: **Jan 17, 2024**
Date of Acceptance: **Jan 27, 2024**
Date of Publishing: **Mar 01, 2024**