Diagnostic methods for initial evaluation of primary gastrointestinal stromal tumors

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ABSTRACT

الأهداف: وصف خصائص تصوير الورم السدوي المعوي المعدي (GISTs) عند التشخيص الأولي مع العلاقة السريرية، والجراحية، والنسيجية و تقييم أهمية التقنيات المختلفة في تشخيص الورم السدوي المعدي المعوي GISTs.

الطريقة: ضمت هذه الدراسة الإسترجاعية 70 مريض ثبت نسيجياً إصابتهم بالورم المعدي المعوي GISTs خلال الفترة من ديسمبر 2004م و مايو 2009م – قسم الجراحة العامة – مستشفى تشونقشان – شنقهاي – الصين. خضع جميع المرضى إلى التصوير المقطعي بالحاسب CT، كما خضع 39 مريض إلى المنظار، و 12 مريض للتصوير فائق الصوت (EUS)، بينما خضع 36 مريض للتخطيط الصوتي لجدار البطن (TAUS). تم تقييم خصائص الورم السدوي المعوي GISTs.

النتائج: أظهر التصوير المقطعي CT ورم غير متمركز في 44 مريض، و مكونات داخل اللمعة في 24 مريض، و توزع عبر الجدار في 2 مريض. تم تشخيص 42 ورم بشكل محصور، و 2 شكل دائري، بينما كان 26 ورم غير منتظم الشكل. كذلك تم تشخيص 43 ورم بكتل منتظمة الشكل، بينما 27 ورم بغشاء غير واضح. أظهر ضعف الطور الشرياني تعزيز متواصل، بينما كان ضعف طور الوريد البابي غير متجانس في 26 مريض، و متجانس في 44 مريض آخر. كانت هنالك علاقة إحصائية بين خصائص التصوير المقطعي بالحاسب CT و خطر احتشاء الورم. وبالتالي يمكننا وصف الورم السدوي المعوي المعدي GISTs في المنظار بأنه شكل أملس و طبيعي و مغطى بالمخاط، و صلب و قليل الصدى في تخطيط الصوتي لجدار البطن(TAUS).

خاتمة: تعد فحوصات الأشعة جوهرية في السيطرة على الورم السدوي المعدي المعوي GISTs. كما أن تصوير الأشعة المقطعية CT مهم في التشخيص، و تصنيف مرحلة الورم، و خطة علاج الورم السدوي المعدي المعوي. يشترك EUS، و المنظار في اكتشاف الآفات المخاطية. تشمل الطرق الأخرى TAUS، و FDG، و PET، و تصوير الأمعاء والمعدة بالتصوير المقطعي CT، و الرنين المغناطيسي MRI في حالات معينة.

Objectives: To describe the imaging features of gastrointestinal stromal tumors (GISTs) at initial presentation with clinical, surgical, and pathologic correlation, and to evaluate values of various techniques in GISTs.

Methods: This retrospective study recruited 70 patients with histologically proved GISTs between December 2004, and May 2009 in the Department of General Surgery, Zhongshan Hospital, Fudan Univeristy, Shanghai, China. Each patient underwent CT scanning, 39 patients underwent simultaneous endoscopy, 12 patients underwent endoscopic ultrasound (EUS), and 36 patients underwent transabdominal ultrasonography (TAUS) simultaneously. Features of GISTs were assessed.

Results: Computerized tomography findings showed an eccentric mass in 44 patients, an intraluminal component in 24, and a transmural distribution in 2. Forty-two tumors were dumbbell-shaped, 2 were round, while 26 were irregular. Forty-three tumors presented with well-defined masses, while 27 with unclear borders. The arterial phase attenuation showed the continuous enhancement. The portal-venous phase attenuation was heterogeneous in 26 and homogeneous in the other 44. There was a significant correlation between certain CT features and tumor risk stratification. Gastrointestinal stromal tumors were characterized by a smooth shape and normal overlying mucosa in endoscopy, hypoechoic, and solid in TAUS.

Conclusion: Imaging examinations are pivotal in the management of GISTs. The CT scan is valuable in the diagnosis, staging, and treatment planning of GISTs. Endoscopy and EUS contribute to the detection of mucosal lesions. Other methods including TAUS, fluorodeoxyglucose positron emission tomography, CT gastrography, and MRI help in specific cases.

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Gastrointestinal stromal tumors (GISTs) are the most common non-epithelial tumors of the gastrointestinal tract, with an estimated annual incidence of 12-14 cases per million population.[1] In earlier medical literatures, GISTs were not distinguished from other mesenchymal neoplasms. However, they are different from the other mesenchymal neoplasms in terms of etiology, immunohistology, and clinical course. With the advancement of immunohistochemical techniques, they were classified as a unique entity. Over the past decade, GISTs have been defined as spindle or epithelioid neoplasms expressing KIT (CD117) and often CD34, which distinguish them from true smooth muscle tumors and neural tumors.[2] Recent availability of KIT-tyrosine kinase inhibitor (STI-571, imatinib [Gleevec], Novartis Pharma, Basel, Switzerland) for successful treatment of GISTs mandates a high level of awareness of diagnosis and therapy of GISTs.[3] Accurate diagnosis is essential for making a reasonable therapeutic regimen. Biopsy is not recommended due to its potential risks of hemorrhage and tumor seeding, and difficulties in making a definite diagnosis with inadequate sampling.[4,5] Currently, pretreatment diagnosis mainly depends on imaging examinations including computed tomography (CT), endoscopy, endoscopic ultrasound (EUS), transabdominal ultrasonography (TAUS), and fluorine 18 fluorodeoxyglucose positron emission tomography (FDG PET), magnetic resonance imaging (MRI), and so forth. The aim of this study was to describe the typical imaging findings of GISTs at initial presentation with clinical, surgical, and pathologic correlation. As CT scan provides important contributions in evaluating GISTs before treatment, we will focus on its value in diagnosis, staging, and treatment planning. Although a number of relevant studies have been published in the past, their interpretations were limited by some intrinsic defects such as small sample size or inconsistent imaging procedures.[6] This study was designed to provide a more accurate interpretation in the diagnosis value of various techniques in GISTs.

Methods. This study reviewed the patients with histologically proved GISTs who were treated between December 2004 and May 2009 in the Department of General Surgery, Zhongshan Hospital, Shanghai, China. Seventy patients with GISTs were recruited in the study and clinical data were reviewed for patients' age, gender, and presenting signs and symptoms. The pathologic record of each patient was reviewed to assess the histopathology and mitotic activity (number of mitoses per 50 consecutive high-power fields). In all patients, tumor size, cell morphism, and immunoreactivity with KIT and CD34 were detected by a gastrointestinal pathologist. Gastrointestinal stromal tumors were classified into very low-, low-, intermediate-, and high-risk categories according to the consensus statement (**Table 1**).[7,8] Photographs of gross specimens were evaluated for evidence of hemorrhage.[9] The Ethics Committee in Zhongshan Hospital approved this retrospective study and informed consents from patients were not required.

Table 1 - Proposed approach for defining risk of aggressive behavior in gastrointestinal stromal tumors.

Tumors classification	Size* (cm)	Mitotic count (HPF)
Very low risk	<2	<5/50
Low risk	2-5	<5/50
Intermediate risk	<5	6-10/50
	5-10	<5/50
High risk	>5	>5/50
	>10	Any mitotic rate
	Any size	>10/50

*Size represents the single largest dimension. HPF - high power field

Image acquisition. Each patient underwent unenhanced and enhanced CT scanning. The CT scans were performed on a MSCT unit (Philips Mx8000, Armsterdam, The Netherlands) using slices of 5 mm thickness and a 0.875 pitch. An intravenous bolus of contrast medium (120 ml of Omnipaque 300,® GE Healthcare, Milwaukee, Wisconsin, USA) was administered at a rate of 3.0ml/s. Enhanced CT scanning of the portal-venous phase and arterial phase images were performed in each patient. Techniques were standardized since all studies were performed on the same equipment according to the same protocols. Two radiologists reviewed all radiologic studies, respectively, and obtained final interpretations by consensus. In the 70 cases, 39 patients also underwent endoscopic examination and 12 underwent EUS. Electronic gastroscope (Olympus GIF-Q240Z, Tokyo, Japan) and electronic colonoscope (Olympus CF-Q260, Japan) were employed. A miniprobe (Olympus UM-2R, Tokyo, Japan) was introduced through the working channel under an endoscopic ultrasonography system (Olympus EU-M30, Tokyo, Japan). The lesion was evaluated by the location, size, and layer of origin. The TAUS was also performed in 36 patients with the equipment (Acuson 128/XP10, California, USA) using a 3.5MHz vector transducer. Color Doppler ultrasound was used to determine the distribution of vessels. After review of the radiologic studies, correlation with pathology reports in all patients was performed.

Review and evaluation of images. The CT findings were evaluated for the location, size, shape, as well as growth pattern (intraluminal, intramural, or extramural components) of the tumor. They were also

evaluated for evidence of invasion into the adjacent tissues, hemorrhage, calcification, cyst formation, and secondary findings such as nodal metastasis and liver metastasis. The attenuation pattern of the tumors was assessed during the administration of contrast material. Features of GISTs were evaluated using endoscope, ultrasonic endoscope, and TAUS.

Statistical analysis. Spearman's rank correlation test was used to evaluate the correlation between CT features (size, growth pattern, shape, border, ulcer, wall thickening, calcification, arterial phase images, nodal metastasis, and effusion) and risk stratification. Pearson's chi-square test was used to compare the risk of tumor among tumors at various locations. $P<0.05$ was defined as a statistically significance (2-sided). The SPSS version15.0 for Windows software package (SPSS Inc, Chicago, IL, USA) was used for the statistical analysis.

Results. The age range of the study population was 17-80 years (mean, 59 years). There were 33 men and 37 women. Thirty-one (44.28%) patients presented with abdominal pain or distension, each with progressive pain of several months' duration. Twenty-four (34.29%) patients presented with gastrointestinal bleeding, 2 (2.86%) with anorexia, and one (1.43%) with nausea. Twelve (17.14%) patients were diagnosed occasionally by physical examination. Forty-four (62.85%) of these tumors were localized to the stomach, 21 (30%) to the small intestine, one (1.43%) to the pelvic cavity, one (1.43%) to the esophagus, 2 (2.86%) to the rectum, and one (1.43%) to the peritoneum. In 44 cases with gastric GISTs, local resection was performed in 34 and distal or proximal gastrectomy with Billroth 1-2 was conducted in 10. Lymph node dissection was performed together with gastrectomy in 2, and partial hepatectomy was performed together with gastrectomy in one. In 23 cases with small intestine GISTs and 2 with esophageal GISTs, local resection was performed. In one case with rectal GIST, combined abdominoperineal resection (Miles' operation) was performed. In our cohort, 64 cases received targeted therapy with imatinib, 66 received chemotherapy, and one received interventional therapy.

Pathologic findings. All patients had surgical removal of the tumor and were histologically confirmed GISTs. Grossly, the diameters of tumors ranged from 1.5-25 cm in greatest dimension (mean, 6.5 cm). Forty-four (62.85%) tumors were located in the stomach, 23 (32.86%) in the small intestine, one (1.43%) in the rectum, and 2 (2.86%) in the esophagus. The tumors were extramural in 44 (62.85%) patients, endophytic in 24 (34.29%), and transmurally distributed in 2 (2.86%). Forty-four (62.85%) tumors were oval or round, while 26 (37.15%) exhibited irregular shapes. Forty-three (61.43%) tumors were well-defined, while the other 27 (38.57%) showed unclear borderlines. Forty (57.14%) tumors presented with central areas of hemorrhage, and 6 (8.57%) with calcification. Light microscopy findings showed a pattern of predominantly spindle cells in 60 (85.71%) patients (**Figure 1a**), predominantly epithelioid cells in 7 (10%) (**Figure 1b**), and pleomorphic cells in 3 (4.29%). Immunohistochemical studies were documented in all tumors. There was coexpression of KIT (**Figure 1c**) and CD34 (**Figure 1d**) in 64 (91.43%) tumors. The remaining 6 (8.57%) patients with no CD34 data were included on the basis of the histologic identity with the KIT-positive tumors. Twenty-three (32.86%) patients were classified as high risk, 25 (35.71%) as intermediate risk, 21(30%) as low risk, and one (1.43%) as very low risk.

Imaging findings. Computerized tomography displayed the same anatomical distributions of GISTs as that in the pathologic findings. Forty (57.14%) tumors presented with central areas of hemorrhage, or gas-liquid surface sign (**Figure 2**), and 6 (8.57%) with calcification. Findings in 3 (4.29%) patients showed invasion into the abdominal wall, greater omentum, or spleen, respectively. Two (2.86%) patients presented with ascites, 2 (2.86%) with upper nodal metastasis and one (1.43%) with liver metastasis. The arterial phase attenuation showed continuous enhancement. The portal-venous phase attenuation was heterogeneous in 26 (37.14%) patients, with areas of central low attenuation that corresponded to areas of remote hemorrhage in those patients with photographs of gross specimens, while homogeneous in the other 44 (62.86%).

The areas of low attenuation were evident on unenhanced and enhanced images. The addition of intravenous contrast material made the areas of low attenuation more conspicuous due to the solid portions of the tumor showed enhancement.[9] The 14 (20%) largest tumors (>8.0 cm) had larger areas of central low attenuation on CT (**Figure 3**) when compared with those in the remaining 36 (80%) patients.

Endoscopic and ultrasonic endoscopic findings. Among the 39 patients who underwent endoscopy, 33 tumors were located in the stomach (**Figure 4a**), one in the rectum, while the other 4 were missed. Typically, GISTs were characterized by an oval or smooth shape, normal overlying mucosa with occasional ulceration, and a firm consistency on compression (**Figure 4a**). None of the patients underwent biopsy.

Twelve cases also underwent ultrasonic endoscopy. Among them, 9 tumors were located in the stomach (**Figure 4a**), 2 in the colon, and one in the rectum (**Figure 4b**). The diameters of tumors ranged from 2-11.5 cm in greatest dimension (mean, 5.5 cm). All tumors stem from the muscular layer.

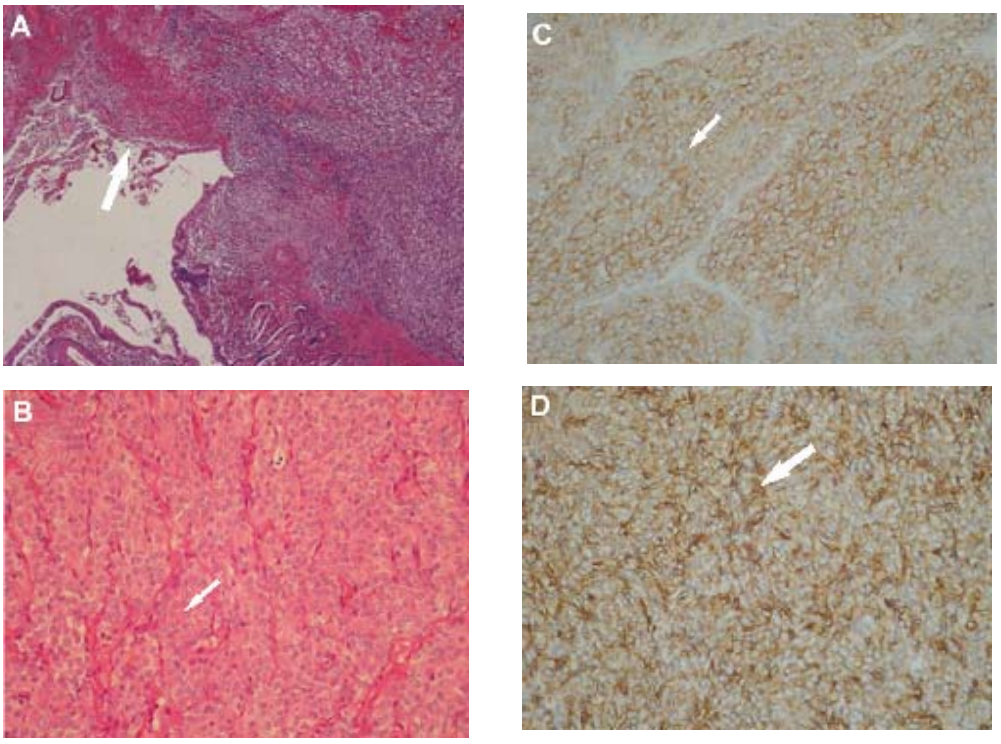

Figure 1 - Gastric spindle cell gastrointestinal stromal tumors showing **a)** mucous invasion and ulcer formation (Hematoxylin and Eosin [H&E], ×100). **b)** The neoplastic cells are arranged into small nests that are deposited in an abundant mucopolysaccharide-rich myxoid stroma (H&E, ×200). **c)** The tumor cells are positive for CD117 in cytoplasm (×200). **d)** The tumor cells are strong positive for CD34 (×200).

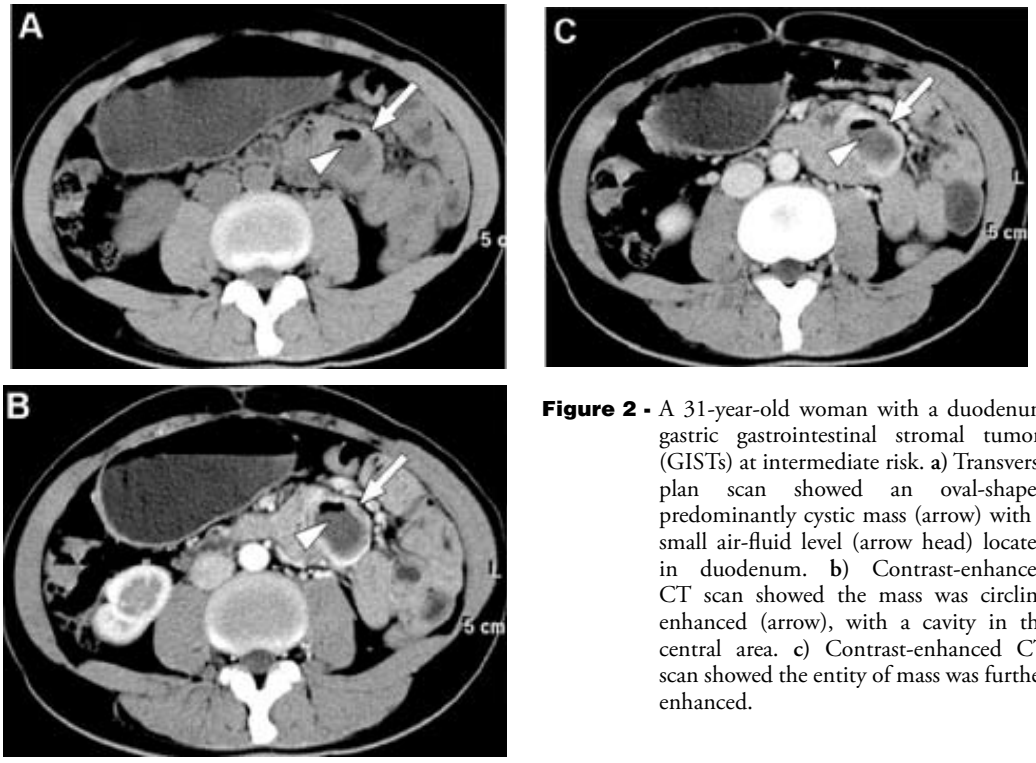

Figure 2 - A 31-year-old woman with a duodenum gastric gastrointestinal stromal tumors (GISTs) at intermediate risk. **a)** Transverse plan scan showed an oval-shaped predominantly cystic mass (arrow) with a small air-fluid level (arrow head) located in duodenum. **b)** Contrast-enhanced CT scan showed the mass was circling enhanced (arrow), with a cavity in the central area. **c)** Contrast-enhanced CT scan showed the entity of mass was further enhanced.

Ultrasonic findings. Among the 36 patients who underwent TAUS examination, 17 (47.22%) tumors were detected and 19 (52.78%) were missed. Sixteen (94.11%) GISTs were hypoechoic and one (5.89%) hyperechoic. Fourteen (82.35%) were solid and 3 (17.65%) cystic. Color Doppler flow imaging (CDFI) in 5 (29.41%) patients showed punctate, linear, or branch flow. Correlation between CT features and tumor risk Spearman's rank correlation test demonstrated a significant correlation between size, shape, border, arterial phase images, and tumor risk (rs=737, p=0.000; rs=0.318, p=0.007; rs=0.245, p=0.041; rs=0.399, p=0.001; rs=0.414, p=0.001). Pearson's chi-square test illustrated a significant difference of tumor risk among tumors at various locations (p=0.034).

Discussion. Gastrointestinal stromal tumors are the most common non-epithelial tumors of the gastrointestinal tract, which are now thought to derive from interstitial cells of Cajal, clearly distinct from other mesenchymal tumors. Gastrointestinal stromal tumors can occur anywhere in the gastrointestinal tract.[9,10] Tumor sites in the current study are, in order of frequency, stomach, small bowel, rectum, esophagus, pelvic cavity, and peritoneum.[10] Mean patients' age in our study was 59 years, and only 5 (7.1%) patients were below the age of 40, which was in consistent with the previous findings.[11] Although GISTs are reported asymptomatic in most cases, such symptoms as abdominal pain, bloating, and gastrointestinal bleeding are common in our series, which might be due to the delayed discovery of tumors, indicating the significant importance of early detection. Due to the non-specific symptoms and the extramural growth of the tumors,[12] small GISTs are often incidentally detected during surgery, or by endoscopy or barium studies, for other clinical indications, while most tumors have not been detected until late-stage. Over the past decade, with the increasing recognition of GISTs and the development of Gleevec, early diagnosis has become extremely important for planning appropriate treatment and improving prognosis.[13] Currently, CT scan is the imaging modality of choice in detecting GISTs due to its panoramic capability and accurate visualization of the visceral wall. In this study, CT

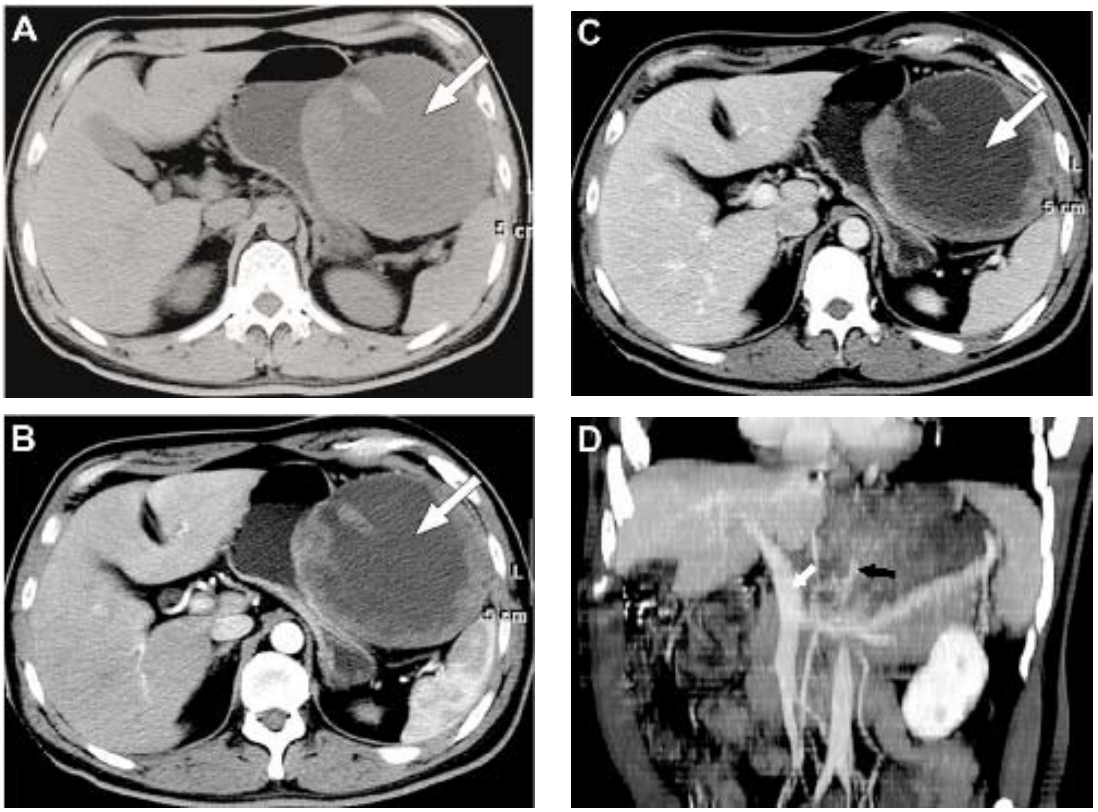

Figure 3 - A 48-year-old man with a gastric gastrointestinal stromal tumors (GISTs) at high risk. **a)** Transverse plan scan showed an oval-shaped predominantly cystic mass (arrow) with a small air-fluid level (arrow head) located in duodenum. **b)** Contrast-enhanced CT scan showed the mass was circling enhanced (arrow), with a large necrosis area in the central area. **c)** Contrast-enhanced CT scan showed the entity of mass was further enhanced in venous phase. **d)** Multi planar reconstruction showed portal vein (black arrow) and celiac trunk (white arrow) are not invaded.

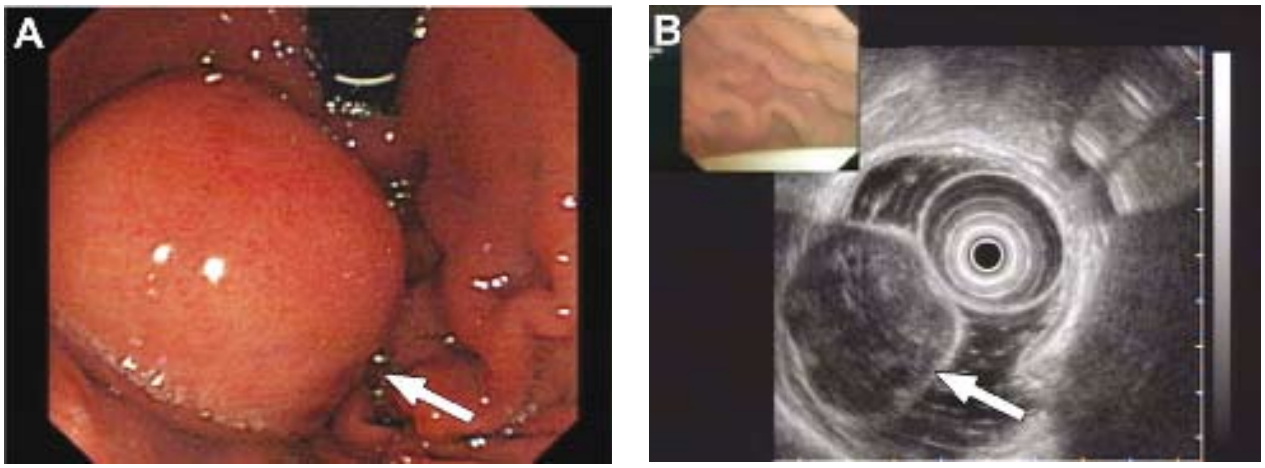

Figure 4 - A 49-year-old man with a gastric gastrointestinal stromal tumors (GISTs) at intermediate risk **a)** Ultrasonic endoscope **b)** shows endolominal mass in stomach, which stems from the muscular layer (arrow).

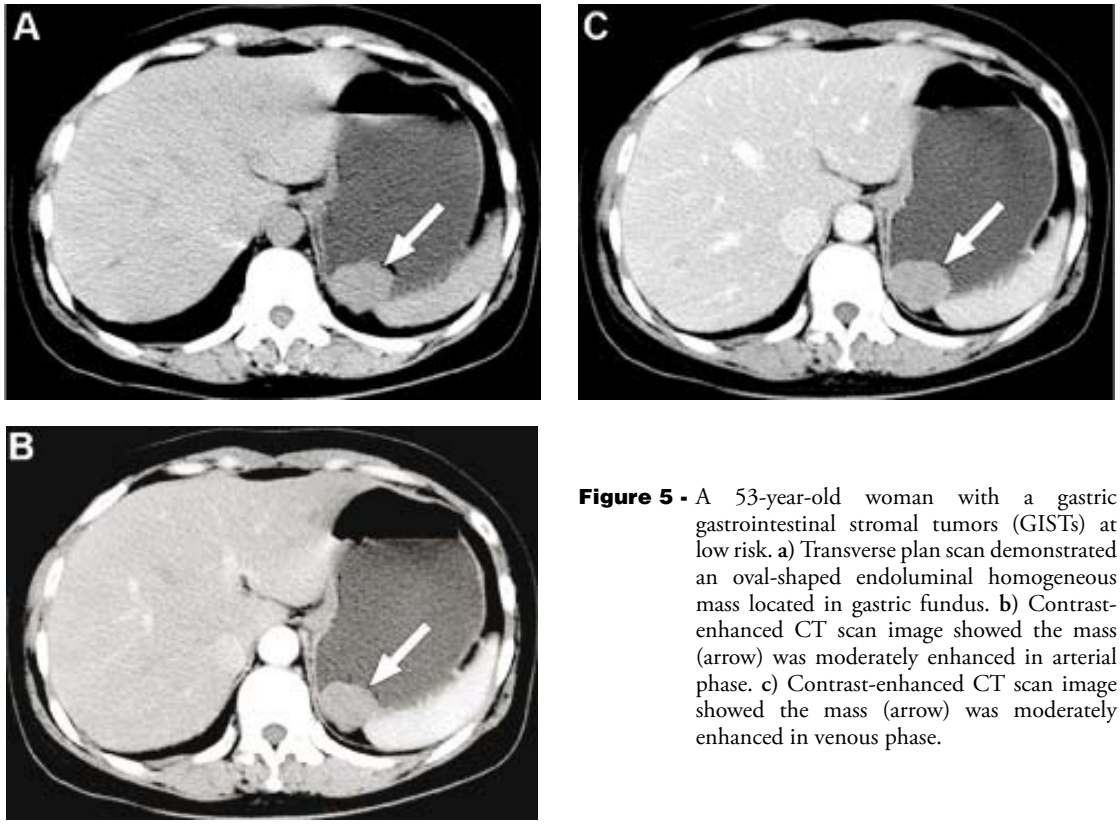

Figure 5 - A 53-year-old woman with a gastric gastrointestinal stromal tumors (GISTs) at low risk. **a)** Transverse plan scan demonstrated an oval-shaped endoluminal homogeneous mass located in gastric fundus. **b)** Contrast-enhanced CT scan image showed the mass (arrow) was moderately enhanced in arterial phase. **c)** Contrast-enhanced CT scan image showed the mass (arrow) was moderately enhanced in venous phase.

features of GISTs varied greatly. On contrast-enhanced CT scans, primary GISTs were typically characterized by lesions with irregular margins, extraluminal growth patterns, and in homogenous density (**Figures 2 & 3**). By contrast, small GISTs (diameter <5 cm) usually had distinct margins, an intraluminal growth pattern, and a homogenous density (**Figure 4**). Special CT features such as ulceration, fistula, intratumoral gas and fluid, ascites, and calcification were commonly observed in large GISTs (**Figures 3 & 5**). These CT signs confirmed the previous reports and provided useful information in distinguishing GISTs from other mesenchymal tumors, mainly including gastrointestinal carcinomas, lymphomas, and schwannomas.[14-16]

Computerized tomography scans also provide clues to risk stratification. Currently, GISTs are classified into very low-, low-, intermediate-, and high-risk categories based on tumor size and mitotic rate.[7] Staging criteria

by CT are still in debate since previous studies were limited by such intrinsic defects as small sample size or inconsistent imaging procedures. Previous study[9] reported no correlation between malignant potentiality and CT features, while others[17,18] found a link between some CT features and mitotic index of GISTs. Our study established a correlation between the risk stratification of GISTs and CT features including lesion, size, location, shape, border, and arterial phase images. Appropriate initial evaluation by CT was crucial for selecting the appropriate management strategy. At present, standard treatment options for GISTs include surgery and targeted therapy. Targeted therapy with imatinib has revolutionized the outcomes in cases with metastatic and unresectable tumors, and can be considered in an attempt to render the tumor resectable, whereas surgical resection of the local lesion remains a vital role.[19] Once the diagnosis of GISTs is made, operability should be assessed. If no CT evidence of adjacent organ invasion or distant metastasis exists, complete excision may serve as the original treatment. Information on correct growth pattern, tumor size, location, and signs of infiltration by CT scan helps to determine the optimal operative approach. Generally, local excision is favored since nodal metastasis is rare.[20,21] It is interesting that nodal metastasis, although described extremely rare, was also found in our series. In this subset of patients, lymph node dissection should be performed to achieve better prognosis. In cases of gastric GISTs, local resection, whether open or laparoscopic, is the most frequently performed. Distal or proximal gastrectomy with Billroth one or 2 was reserved for lesions adjacent to the pylorus or gastroesophageal (GE) junction to prevent functional impairment, in which cases information on the distance from the tumor to the GE junction or pylorus is crucial. For GISTs of the duodenum, partial resection or pancreaticoduodenectomy may be required where the sign of infiltration by CT is crucial for the selection of the correct type of surgical intervention.

Endoscopy is another standard preoperative work-up for suspected GISTs, which is sensitive in detecting mucosal lesions. Typically, GISTs were characterized by a smooth shape, normal overlying mucosa with occasional ulceration, and a consistency on compression (**Figure 4a**). However, visibility with endoscopy is limited to smaller tumors, in which case CT should further be performed. None of our patients underwent biopsy since the results of endoscopic biopsy often can be non-diagnostic due to insufficient tissue collection. The 4 missed diagnosis in our study by endoscopy occurred in the routine physical examination, indicating its limitation in the detection of extraluminal tumors. Our study confirmed the valuable information provided by EUS for therapeutic planning in accurately detecting the location, size and layers of origin of submucosal GISTs (**Figure 4b**).[22] Recently, EUS has been suggested to predict malignancy. Nevertheless, predictive accuracy of this methodology has not been well defined.[23] In addition, EUS-guided fine-needle aspiration (EUS-FNA) was recently suggested for the diagnosis of subepithelial gastrointestinal tumors.[24,25] The clinical role of such testing in GISTs needs further investigation. There were few studies assessing the appearance of GISTs on TAUS. Varied patterns of GISTs were displayed on TAUS in the current study, and the typical images of GISTs were hypoechoic and solid masses, in accordance with a recent investigation.[26] Special flow images may aid in the differential diagnosis. As a first-line diagnostic tool, TAUS may identify large GISTs, so that other imaging tests can be performed to confirm the diagnosis. Besides, it is important in screening liver metastatic lesions. Our study showed a high rate of missed diagnosis by TAUS, which mainly occurred in those with insidious symptoms.

Several other imaging techniques, such as FDG PET, CT gastrography, and MRI, can be employed in certain settings. The FDG PET is highly sensitive,[5] however, due to the limited access and high cost, it has played more of a role in the early assessment of treatment response.[15,27] The CT gastrography using MDCT provides comprehensive information, allowing the performance of preoperative mapping (**Figure 3**).[28] Magnetic resonance imaging is indicated for surgical planning, and for cases in which CT is contraindicated. This is the first time that records of radiology, pathology, and operation were reviewed to obtain an objective interpretation of the diagnosis value for GISTs by using various approaches. Standardization of imaging techniques enabled us to accurately analyze the enhancement pattern of the tumors. As a retrospective review, a natural selection bias in referred patients limits the approximation of our study population to a natural population of patients. Only one patient in our series presented with liver involvement, and 3 displayed initial evidence of peritoneal dissemination in our cohort, although as many as half of the patients were reported having distant metastases at presentation. It was reasonable in the specific settings of the surgical department, since patients with advanced stage will probably be recommended for targeted therapy as the original treatment, rather than surgery.

In conclusion, imaging examinations play a pivotal role in the management of GISTs. The CT scan is the most valuable technique for the diagnosis, staging, and treatment planning of GISTs. Endoscopy and EUS contribute to the evaluation of mucosal lesions. Transabdominal ultrasonography may serve as the first-line examination. Other methods such as MRI, CT gastrography, and FDG PET help in specific cases.

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References

1. Saleem TB, Ahmed I. Gastrointestinal stromal tumour-evolving concepts. ***Surgeon*** 2009; 7: 36-41.
2. Koay MH, Goh YW, Iacopetta B, Grieu F, Segal A, Sterrett GF, et al. Gastrointestinal stromal tumours (GISTs): a clinicopathological and molecular study of 66 cases. ***Pathology*** 2005; 37: 22-31.
3. Verweij J, Casali PG, Zalcberg J, LeCesne A, Reichardt P, Blay JY, et al. Progression-free survival in gastrointestinal stromal tumours with high-dose imatinib: randomised trial. ***Lancet*** 2004; 364: 1127-1134.
4. Kimura H, Shima Y, Kinoshita S, Takahashi I, Okai T. Endosonographic misdiagnosis of tumor recurrence after surgery for malignant GIST. ***Endoscopy*** 2002; 34: 238.
5. Stroobants S, Goeminne J, Seegers M, Dimitrijevic S, Dupont P, Nuyts J, et al. 18FDG-Positron emission tomography for the early prediction of response in advanced soft tissue sarcoma treated with imatinib mesylate (Glivec). ***Eur J Cancer*** 2003; 39: 2012-2020.
6. Miettinen M, Furlong M, Sarlomo-Rikala M, Burke A, Sobin LH, Lasota J. Gastrointestinal stromal tumors, intramural leiomyomas, and leiomyosarcomas in the rectum and anus: a clinicopathologic, immunohistochemical, and molecular genetic study of 144 cases. ***Am J Surg Pathol*** 2001; 25: 1121-1133.
7. Fletcher CD, Berman JJ, Corless C, Gorstein F, Lasota J, Longley BJ, et al. Diagnosis of gastrointestinal stromal tumors: A consensus approach. ***Hum Pathol*** 2002; 33: 459-465.
8. Miettinen M, Lasota J. Gastrointestinal stromal tumors: pathology and prognosis at different sites. ***Semin Diagn Pathol*** 2006; 23: 70-83.
9. Levy AD, Remotti HE, Thompson WM, Sobin LH, Miettinen M. Gastrointestinal stromal tumors: radiologic features with pathologic correlation. ***Radiographics*** 2003; 23: 283-304.
10. Agaimy A, Wunsch PH. Gastrointestinal stromal tumours: a regular origin in the muscularis propria, but an extremely diverse gross presentation. A review of 200 cases to critically re-evaluate the concept of so-called extra-gastrointestinal stromal tumours. ***Langenbecks Arch Surg*** 2006; 391: 322-329.
11. Horton KM, Juluru K, Montogomery E, Fishman EK. Computed tomography imaging of gastrointestinal stromal tumors with pathology correlation. ***J Comput Assist Tomogr*** 2004; 28: 811-817.
12. Scarpa M, Bertin M, Ruffolo C, Polese L, D'Amico DF, Angriman I. A systematic review on the clinical diagnosis of gastrointestinal stromal tumors. ***J Surg Oncol*** 2008; 98: 384-392.
13. Ye YJ, Gao ZD, Poston GJ, Wang S. Diagnosis and multi-disciplinary management of hepatic metastases from gastrointestinal stromal tumour (GIST). ***Eur J Surg Oncol*** 2009; 35: 787-792.
14. Burkill GJ, Badran M, Al-Muderis O, Meirion Thomas J, Judson IR, Fisher C, et al. Malignant gastrointestinal stromal tumor: distribution, imaging features, and pattern of metastatic spread. ***Radiology*** 2003; 226: 527-532.
15. Choi H, Charnsangavej C, de Castro Faria S, Tamm EP, Benjamin RS, Johnson MM, et al. CT evaluation of the response of gastrointestinal stromal tumors after imatinib mesylate treatment: a quantitative analysis correlated with FDG PET findings. ***AJR Am J Roentgenol*** 2004; 183: 1619-1628.
16. Levy AD, Quiles AM, Miettinen M, Sobin LH. Gastrointestinal schwannomas: CT features with clinicopathologic correlation. ***AJR Am J Roentgenol*** 2005; 184: 797-802.
17. Kim HC, Lee JM, Kim KW, Park SH, Kim SH, Lee JY, et al. Gastrointestinal stromal tumors of the stomach: CT findings and prediction of malignancy. ***AJR Am J Roentgenol*** 2004; 183: 893-898.
18. Ulusan S, Koc Z, Kayaselcuk F. Gastrointestinal stromal tumours: CT findings. ***Br J Radiol*** 2008; 81: 618-623.
19. Demetri GD, Benjamin RS, Blanke CD, Blay JY, Casali P, Choi H, et al. NCCN Task Force report: management of patients with gastrointestinal stromal tumor (GIST)--update of the NCCN clinical practice guidelines. ***J Natl Compr Canc Netw*** 2007; 5 Suppl 2: S1-29.
20. Iwahashi M, Takifuji K, Ojima T, Nakamura M, Nakamori M, Nakatani Y, et al. Surgical management of small gastrointestinal stromal tumors of the stomach. ***World J Surg*** 2006; 30: 28-35.
21. Agaimy A, Wunsch PH. Lymph node metastasis in gastrointestinal stromal tumours (GIST) occurs preferentially in young patients < or = 40 years: an overview based on our case material and the literature. ***Langenbecks Arch Surg*** 2009; 394: 375-381.
22. Martinez-Ares D, Martinez Cadilla J, Caceres Alvarado N, Gonzalez Carrero-Fojon J, Martin-Granizo Barrenechea I, Pallares Peral A. [Intermediate-risk gastrointestinal stromal tumor: diagnosis through hydrogastric ultrasonography]. ***Gastroenterol Hepatol*** 2006; 29: 622-624.
23. Shah P, Gao F, Edmundowicz SA, Azar RR, Early DS. Predicting malignant potential of gastrointestinal stromal tumors using endoscopic ultrasound. ***Dig Dis Sci*** 2009; 54: 1265-1269.
24. Chen VK, Eloubeidi MA. Endoscopic ultrasound-guided fine-needle aspiration of intramural and extraintestinal mass lesions: diagnostic accuracy, complication assessment, and impact on management. ***Endoscopy*** 2005; 37: 984-989.
25. Chhieng DC, Jhala D, Jhala N, Eltoum I, Chen VK, Vickers S, et al. Endoscopic ultrasound-guided fine-needle aspiration biopsy: a study of 103 cases. ***Cancer*** 2002; 96: 232-239.
26. Wronski M, Cebulski W, Slodkowski M, Krasnodebski IW. Gastrointestinal stromal tumors: ultrasonographic spectrum of the disease. ***J Ultrasound Med*** 2009; 28: 941-948.
27. Prior JO, Montemurro M, Orcurto MV, Michielin O, Luthi F, Benhattar J, et al. Early prediction of response to sunitinib after imatinib failure by 18F-fluorodeoxyglucose positron emission tomography in patients with gastrointestinal stromal tumor. ***J Clin Oncol*** 2009; 27: 439-445.
28. Kim JH, Park SH, Hong HS, Auh YH. CT gastrography. ***Abdom Imaging*** 2005; 30: 509-517.