ORIGINAL

Relationship between FDG uptake and the pathological risk category in gastrointestinal stromal tumors

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Abstract : *Purpose.* To evaluate ^{18}F-fluorodeoxyglucose (FDG) uptake and the pathological risk category of gastrointestinal stromal tumors (GISTs), and to investigate the possibility of determining the pathological risk category by positron emission tomography/computed tomography (PET/CT). *Patients and Methods.* We undertook 29 PET/CT studies in 20 patients with GISTs. Eleven of the 20 patients underwent PET/CT prior to therapy, with three of these also undergoing follow-up PET/CT after operation or imatinib therapy. *Results.* All eleven lesions imaged before treatment were FDG-positive on PET/CT. Seven of these eleven primary lesions were categorized as high risk and the other four primary lesions were categorized as low or intermediate risk. There was a significant difference between the maximum standardized uptake value (SUVmax) of the primary lesions categorized as high risk (11.8±3.15) and that of the primary lesions categorized as low and intermediate risk (2.88±0.47) ($p<0.001$). Recurrent tumors were also shown as FDG-positive. *Conclusion.* Primary GISTs and recurrent tumors can be detected by PET/CT. Our study suggests that the degree of FDG uptake is a useful indicator of risk category. In addition, PET/CT is probably useful for follow-up examinations of GIST after operation or imatinib therapy. J. Med. Invest. 57 : 270-274, August, 2010

Keywords **:** *GIST, Risk category, PET/CT*

INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are relatively rare and represent < 3% of all gastrointestinal neoplasms, however, they are the most common mesenchymal tumor of the gastrointestinal tract (1). Approximately 70% of all GISTs are found in the stomach, 20% originate from the small intestine, and 10% are found elsewhere (2).

We retrospectively evaluated ^{18}F-fluorodeoxyglucose (FDG) uptake and pathological risk category. We also evaluated response to therapy with imatinib mesylate. We investigated the possibility of determining the pathological risk category by ^{18}F-FDG positron emission tomography/computed tomography (^{18}F-FDG PET/CT).

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PATIENTS AND METHODS

This retrospective study was approved by the Ethics Committee of the Tokushima University Hospital. We retrospectively reviewed the results of 29 consecutive ^{18}F-FDG PET/CT studies in 20 patients (14 male, 6 female, 44-85 years old) with GISTs between October 2005 and December 2009. ^{18}F-FDG was synthesized by the nucleophilic substitution method using an ^{18}F-FDG-synthesizing

instrument F100 (Sumitomo Heavy Industries, Ltd., Tokyo, Japan) and a cyclotron CYPRIS (Sumitomo Heavy Industries, Ltd.) in our institution. All patients were examined with PET/CT scanner (Aquiduo, Toshiba Medical Systems Corporation, Tochigi, Japan) 1 hour after FDG injection (3.7 MBq/kg). They were imaged from the top of the head to the middle of thigh. The attenuation-corrected PET image, non-attenuation-corrected PET image and CT image were reviewed, and the attenuation-corrected PET and CT image were co-registered using AquariusNET viewer (TeraRecon, Inc.). Eleven of the 20 patients underwent PET/CT prior to therapy. Three of these eleven patients also underwent follow-up PET/CT after operation or imatinib therapy. Nine of the 20 patients underwent PET/CT only after operation. Three of these nine patients had recurrent GIST. Of the eleven patients who underwent PET/CT prior to therapy, the primary tumor was located in the stomach in six patients, in the duodenum in two, and the small intestine in three.

The risk category was determined pathologically by tumor size and the number of mitotic cells (Table 1) (3).

RESULTS

Tumor size, primary site, maximum standardized uptake value (SUVmax), and risk category of 20 patients who underwent PET/CT are presented in Table 2. All eleven lesions were FDG-positive upon pre-treatment PET/CT (SUVmax 2.2-15.7,

Table 1. Risk category

	Tumor size (cm)	Number of mitotic cells per 50 high-power fields
Very low	<2	<5
Low	2-5	<5
Intermediate	<5 5-10	6-10 <5
High	>5 >10 Any size	>5 Any mitotic rate >10

Table 2. Primary site, tumor size, SUVmax, risk category and treatment outcome of 20 GIST patients

Pt. no.	Age (y)/ gender	Primary site	Size (cm)	SUVmax		Risk category	Treatment	Follow-up period (mo)	Outcome
				PET/CT Prior to therapy	Follow-up PET/CT after operation or chemotherapy				
1	62/M	stomach	3.5x3	3.0	-	low	op	1	rec (-)
2	72/F	stomach	5x3.5	3.0	abnormal uptake (-)	low	op	23	rec (-)
3	72/M	small intestine	5x4	2.2	-	low	op	24	rec (-)
4	62/F	stomach	5.4x5.2	3.3	abnormal uptake (-)	intermediate	op	38	rec (-)
5	54/M	stomach	21x5.5	10.0	-	high	neoadjuvant+op+adjuvant	27	rec (-)
6	65/M	stomach	7x4	14.3	-	high	op+adjuvant chemo	12	rec (-)
7	49/M	stomach	11x7.4	15.7	-	high	chemo	3	PR
8	50/M	duodenum	11x10	8.0	→5.0→10.0	high	chemo	32*	PR→PD
9	66/M	duodenum	14x7.5	10.7	-	high	op	1	rec (-)
10	57/M	small intestine	12x6.5	8.8	-	high	op	29	rec (-)
11	71/M	small intestine	7x4.5	15.0	-	high	op+adjuvant chemo	25*	rec (+)
12	61/M	stomach	-	-	8.7 (liver meta.)	unknown	op+adjuvant chemo	40	rec (+)
13	85/M	duodenum	-	-	5.5 (abdominal mass)	unknown	op+adjuvant chemo	28	rec (+)
14	73/M	rectum	-	-	2.5 (pelvic mass)	high	neoadjuvant+op+adjuvant	66	rec (+)
15	59/M	stomach	-	-	abnormal uptake (-)	unknown	op+adjuvant chemo	67	rec (+)→CR
16	62/F	stomach	-	-	abnormal uptake (-)	unknown	op+adjuvant chemo	85	rec (+)→CR
17	79/F	stomach	-	-	abnormal uptake (-)	high	op+adjuvant chemo	68	rec (-)
18	58/M	stomach	-	-	abnormal uptake (-)	unknown	op+adjuvant chemo	175	CR→rec (+)
19	44/F	sigmoid colon	-	-	abnormal uptake (-)	high	op	50	rec (-)
20	52/F	unknown	-	-	abnormal uptake (-)	unknown	op+adjuvant chemo	84	rec (+)→CR

*Patient died.
Pt. no. 10 underwent PET/CT once after therapy. Pt. nos. 8, 17 underwent PET/CT twice after therapy. Pt. nos. 4, 19 underwent PET/CT three times after therapy.
SUVmax : maximum standardized uptake value
GIST : gastrointestinal stromal tumor
PET/CT : positron emission tomography/computed tomography

average 8.5). Seven of eleven primary lesions were categorized as high risk, and showed intense FDG uptake with SUVmax of 8.0, 8.8, 10.0, 10.7, 14.3, 15.0 and 15.7. Four of eleven primary lesions were categorized as low and intermediate risk and showed much lower FDG uptake (low risk : SUVmax 2.2, 3.0 and 3.0 ; intermediate risk : SUVmax 3.3). There was a significant difference between the SUVmax of the primary lesions categorized as high risk (11.8± 3.15) and that of the primary lesions categorized as low and intermediate risk (2.88± 0.47) ($p< 0.001$) (Fig. 1). All recurrent tumors showed high FDG uptake except for one case. The recurrent tumor of this case, confirmed high-risk at initial diagnosis, showed relatively low uptake (SUVmax 2.5). Six of the nine patients who underwent PET/CT only after operation had no abnormal FDG uptake on PET/CT.

CASE 1

A 72-year-old woman had a mass behind the stomach, which measured 5.0×3.5 cm, and showed mild FDG uptake with an SUVmax of 3.0 on PET/CT (Fig. 2). The abdominal mass was resected and

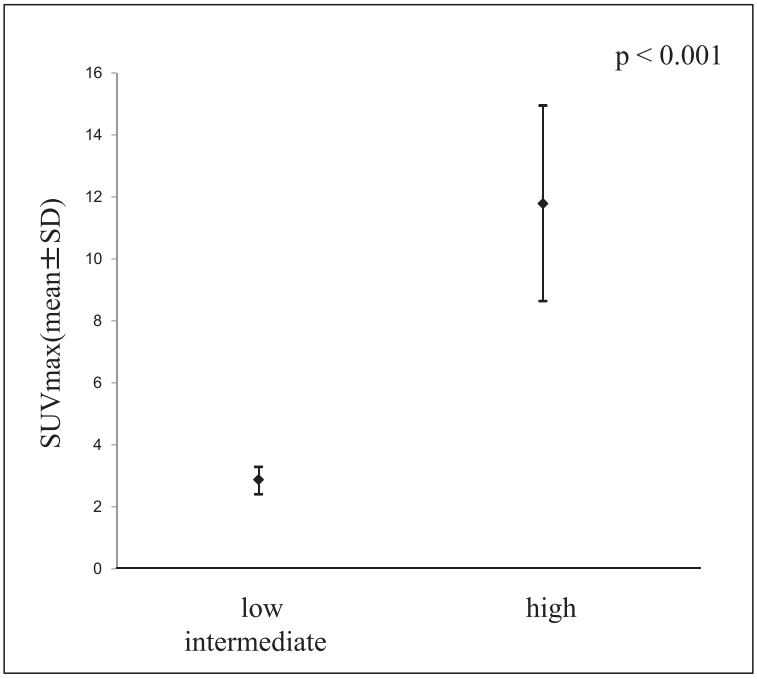

Fig. 1. Comparison of SUVmax (mean±SD) of the primary lesions categorized as high risk and that of the primary lesions categorized as low and intermediate risk. The SUVmax of the primary lesions categorized as high risk was significantly higher than that of the primary lesions categorized as low and intermediate risk (11.8±3.15 vs 2.88±0.47 ; $p< 0.01$).

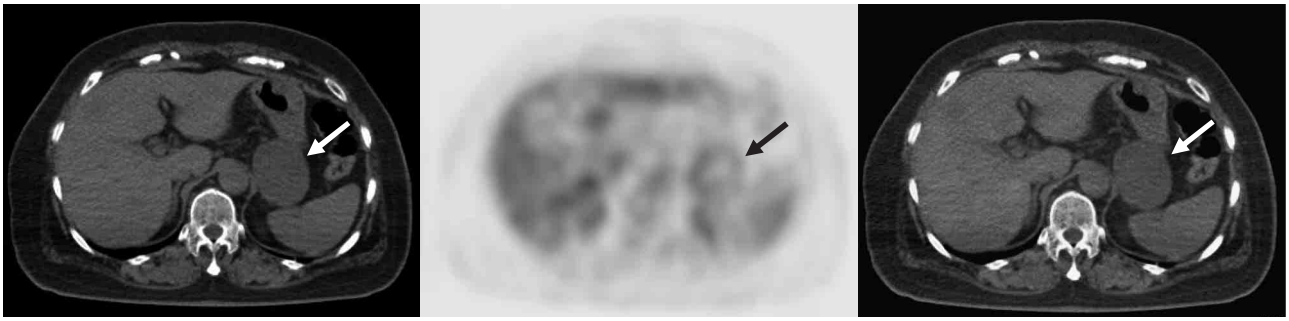

Fig. 2. Transaxial CT (left), FDG-PET (middle), and fusion (right) images of the abdomen in a 72-year-old woman with GIST categorized as low risk. The tumor was behind the stomach, measured 5.0×3.5 cm, and showed mild FDG uptake with an SUVmax of 3.0 (arrow).

confirmed pathologically as GIST of the stomach, and categorized as low risk. No recurrence and metastasis were detected on follow-up PET/CT performed 3.5 months after the operation.

CASE 2

A 50-year-old man had an abdominal mass near the pancreatic body, which showed intense FDG uptake (SUVmax 8.0) (Fig. 3a). Tumor with ulcer formation was detected in the horizontal part of the duodenum at endoscopy. For biopsy, the mass was confirmed pathologically as GIST of the duodenum and categorized as high risk. Systemic chemotherapy with imatinib mesylate was started as neoadjuvant therapy. Follow-up PET/CT was performed 4 months after chemotherapy showed a reduction in tumor size and decreased FDG uptake (SUVmax 5.0) (Fig. 3b). However, follow-up PET/CT at 10 months after chemotherapy showed tumor enlargement and increased FDG uptake (SUVmax 10.0) (Fig. 3c).

DISCUSSION

All primary GISTs and recurrent tumors can be detected by ^{18}F-FDG PET/CT. GIST can be shown to be FDG-positive, with a varying degree of uptake. Isis G et al. reported the sensitivity of GISTs including metastatic lesions by FDG-PET was 86% (1). Kamiyama et al. reported that the sensitivity of GISTs by FDG-PET was 100% (4). FDG uptake and pathological risk category may have some relationship. It has been reported that a high rate of FDG uptake in GIST indicates high metabolism and malignant potential (4). There have been many reports that FDG accumulation and grade of malignancy are correlated with each other (4, 5). Kamiyama et al. reported that there was a significant difference between the SUV of the primary lesions categorized as high and intermediate risk (6.52± 1.15) and that of the primary lesions categorized as low risk (2.18± 0.06) ($p< 0.01$) (4, 5). In our study, all the primary high-risk GISTs showed intense FDG uptake (SUVmax 11.8± 3.15). The low- and intermediate-risk GISTs also showed FDG uptake (SUVmax

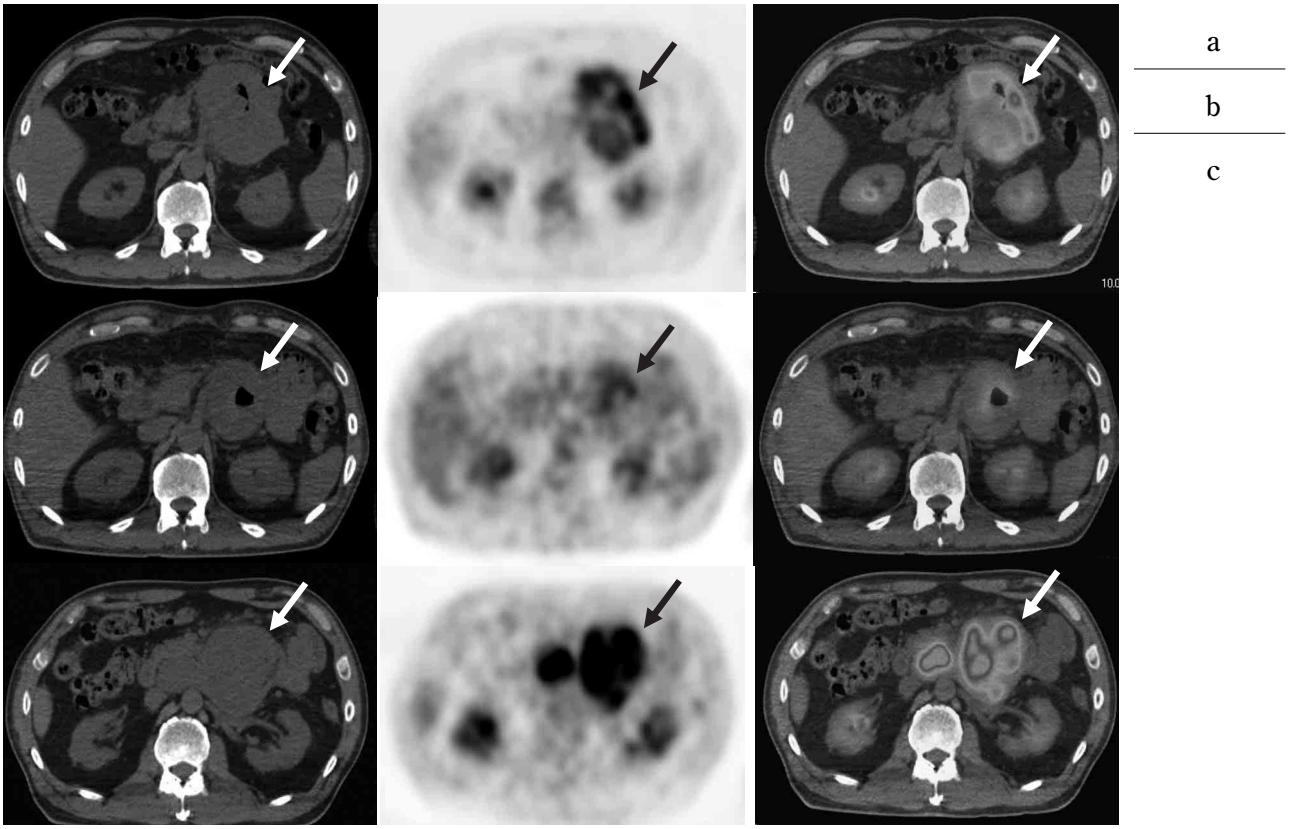

Fig. 3. Transaxial CT (left), FDG-PET (middle), and fusion (right) images of the abdomen in a 50-year-old man with GIST categorized as high risk. The abdominal tumor showed intense FDG uptake (SUVmax 8.0) (a, arrow). Reduction in tumor size and lower FDG uptake (SUVmax 5.0) were observed on a PET/CT image (b, arrow) performed 4 months after chemotherapy with imatinib mesylate, but tumor enlargement and increased FDG uptake (SUVmax 10.0) were observed on a PET/CT image (c, arrow) performed 10 months after chemotherapy.

2.88± 0.47). The SUVmax of the primary lesions categorized as high risk was significantly higher than that of the primary lesions categorized as low and intermediate risk. This observation suggested that the degree of FDG uptake may be a useful indicator of risk category. The size of the recurrent tumor in patient No.14 was small (about 1 cm). FDG uptake depends on spatial resolution of the PET/CT system and a partial volume effect may decrease FDG uptake, which leads to low SUV in a small tumor (6). Therefore, this recurrent tumor showed relatively low uptake (SUVmax 2.5) in spite of being high-risk.

The patients of GIST post operation showing no abnormal FDG uptake on PET/CT are clinically considered as no recurrence and no metastasis. PET/CT is useful for follow-up examinations of GIST post operation.

In case 2, follow-up PET/CT performed 4 months after chemotherapy showed a reduction in tumor size and lower FDG uptake. Imatinib mesylate was considered to be effective, but follow-up PET/CT performed 10 months after chemotherapy showed tumor enlargement and increased FDG uptake. This was considered to be indicative of resistance to imatinib mesylate (7). It has been reported that many GISTs may not change significantly in size during early response to imatinib mesylate administration (8). PET has been shown to be highly sensitive in detecting early response to imatinib mesylate therapy (8, 9). It has been reported that density reduction on CT reflects necrotic changes in the tumor and is a predictor of early response to imatinib mesylate therapy. However, it is relatively difficult to evaluate early response to imatinib mesylate therapy by CT alone (8, 10). If a tumor temporarily grew larger as an early response to imatinib mesylate therapy, it might be evaluated as showing a lack of response to imatinib mesylate therapy (10). By means of PET/CT, we can evaluate response to imatinib mesylate therapy before tumor shrinkage.

It may be that GISTs in pathologically high-risk patients have high glucose metabolism (4). Since ^{18}F-FDG PET/CT can evaluate glucose metabolism, it may be a useful tool for determining GIST risk category.

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