Differentiation of incidental intestinal activities at PET/CT examinations with a new sign: Peristaltic segment sign

Duzgun Yildirim, Muge Oner Tamam, Mutlu Sahin, Baki Ekci, Bengi Gurses

A R T I C L E   I N F O

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A B S T R A C T

Purpose: The aim of this study was to present the effect of the peristaltic segment sign for the differential diagnosis between malignant, physiological and gastrointestinal focal fluorodeoxyglucose (FDG) uptakes as an alternative method to maximum standardized uptake value (SUVmax).

Materials and methods: Gastrointestinal tract (GIT) sections of 823 FDG positron emission tomography/computed tomography (FDG-PET/CT) performed in our center were reviewed retrospectively. Images of these cases that have been reported for positive intestinal focal FDG uptake areas were included. Through the sectional images, any accompanying short segment expanded with air just after or before the uptake area was marked as “positive peristaltism sign”. The cases were confirmed with endoscopy plus biopsy (n:42), endoscopy (n:5), laparotomy (n:1), transabdominal biopsy (n:1), enteroclysis (n:1), CT-colonoscopy (n:5), rectal contrast enhanced CT (n:4). Distinguishing features of the sign were analyzed statistically compared to the conventional method for differentiation of malignancy.

Results: Localized FDG uptake was reported in 59 of 823 cases. A SUVmax greater than 2.5 with intestinal wall thickening allowed the diagnosis of malignity with sensitivity 33%, specificity 65%, positive predictive value 69% and negative predictive value 46%. The peristaltic segment sign, considered as a benign finding, increased the statistical values to 68%, 80%, 82% and 65%, respectively.

Conclusion: In case of gastrointestinal increased focal FDG uptake, the new parameter of peristaltic segment sign may differentiate the physiologic uptakes from the malignant ones more accurately than the conventional SUVmax.
Introduction

Physiological uptakes of $^{18}$F-FDG in the brain, myocardium, muscular tissues, pharyngeal mucosal surfaces and palatine tonsils can be recognized due to their various characteristics defined in the literature.\(^1\)\(^2\) However, activity uptakes in intestinal traces are more heterogeneous and require more information for discrimination. FDG is excreted in part through the gastrointestinal tract (GIT), with uptake in the distal esophagus, stomach, small intestine, and large intestine representing normal patterns of tracer distribution.\(^3\)\(^4\) GIT-originated physiological uptakes, which are frequently encountered on FDG-PET/CT examinations, are likely to cause mistakes during evaluations.\(^1\)\(^–\)\(^8\)

It is difficult to interpret positron emission tomography images in the absence of correlative anatomical images. FDG uptake may occur in some anatomic localization even without malignancy.\(^1\)\(^2\)\(^5\) FDG uptake traces can be localized by the anatomical information obtained from correlative CT sections. Such discriminations can be made more definitely by multimodality advanced evaluations or biopsies, particularly in the oncologic cases.

Diffuse increased FDG uptake in the GIT can be defined as physiologic and unrelated to the malignant process with relatively high certainty. These physiologic or benign sites of FDG uptake may be falsely attributed to a cancerous etiology. A focal, well-circumscribed intra-abdominal area of increased FDG uptake may, however, be interpreted as equivocal or suggestive of malignancy with an unclear location. Also, increased tracer activity in malignant lesions may be erroneously interpreted as unrelated to cancer.\(^3\)\(^4\)

Previous large-scale studies showed no significant difference between FDG uptake rates in terms of SUV\(_{\text{max}}\) of underlying malignant, premalignant and benign lesions in the focal uptakes which occurred in unexpected localizations in GIT.\(^9\) Intense focal uptakes in the intestinal traces are seen by 1.3–3% among the cases that undergo FDG-PET/CT \(^[6–8]\). These uptakes may be physiological or may occur due to the inflammatory, benign, premalignant or malignant lesions as well. Physiological uptakes are those which occur due to peristaltism and originate from the wall composed of smooth muscle, whereas non-peristaltic uptakes may originate particularly from the reactive uptake in the mural lymphatic tissue that spreads over the cecum and ileum traces.\(^3\)\(^4\)\(^6\)

This analysis included PET studies showing a single site of focally increased abdominal FDG uptake that was more intense than liver uptake and was localized by fused PET/CT to the GIT. The patients had no previous malignant involvement and no clinical or imaging suspicion of abnormalities in the same areas. Different from previous studies,\(^5\)\(^10\) in the present study, we additionally aimed to investigate the efficacy of a special sign, the so-called "intestinal peristaltism sign", in discriminating physiological uptake from malignancy in the focal intestinal uptakes on PET/CT imaging.

This study was initiated by a series of cases in which focal intra-abdominal FDG uptake that had been localized by PET/CT to the GIT, which had no previously known morphologic lesions, was proven on follow-up to be of malignant or premalignant etiology. The purpose of the present study was to evaluate the effect of the peristaltic segment sign in differentiation of the malignant and physiologic localized FDG uptakes through the GIT as a new parameter.

Material and methods

The GIT traces of 823 patients (577 males and 246 females), who had undergone FDG-PET/CT examination because of malignancy in a special health center, were reviewed. The mean age of the cases was 49 years (ranged from 11 to 89 years). Distribution of the tumor types among cases was as follows: 396 pulmonary tumor, 135 lymphoma, 84 colorectal carcinoma, 37 laryngeal tumor, 27 nasopharyngeal tumor, 23 cervical tumor, 13 ovarian tumor, 9 esophageal tumor, 8 melanoma, 6 soft tissue sarcoma, 5 urine bladder tumor, 4 endometrial tumor, 4 non-pulmonary carcinoid tumor, 4 breast tumor, 2 small intestine tumor with reported pathologic FDG uptake and another 66 cases reported to have normal level of FDG uptake thorough the body. On the images of these cases, the foci that FDG uptake had been identified and the reported intestinal foci were retrospectively evaluated. Being aware of the diagnoses of the cases, reviews were performed retrospectively on multi-display workstations with multi-planar reformattting focusing on the GITs that display abnormal uptake on minimum intensity projection. After reviewing the images and reports of all patients, the cases with localized activation in the stomach, duodenum, jejunum, ileum and colon traces were recorded. Focal activities shorter than a segment in the stomach and duodenum, non-longitudinal, nonfocal uptakes in the jejunum and ileum, and focal uptakes limited to maximum one centimeter of the cecum, ascendant colon, hepatic flexure, transverse colon, splenic flexure, descendent colon, sigmoid colon, and rectum segments in the colon were considered as localized activity and included in the study.

Long segmental uptakes, focal or linear uptakes, and the activities that did not show superposition with the intestinal wall on CT fusion images were excluded from the study. The field with increased FDG activity was taken into consideration if it was of a more intense nature than the liver and if the SUV\(_{\text{max}}\) value was higher than 2.5 units.

This low SUV\(_{\text{max}}\) value, although being nonspecific, is selected with the purpose of highly sensitive detection of malignant foci. The "peristaltism sign" was considered positive (for benignity) in the presence of a bowel loop which has been expanded with air and located just proximal or distal to the focused (FDG-affinitive) segment (Fig. 1).

Standard protocol that was applied to all cases investigated for malignancy

- Colon opacification was provided with 1000 ml of 1500 ml oral contrast solution prepared using 40 ml nonionic contrast that was given 12 h before the procedure.
- The stomach and the small intestine were opacified with 500 ml oral contrast solution given an hour before the procedure.
- Intravenous injection of 13–15 mCi FDG 40–60 min before the procedure;
- The patient rested under normal conditions 1 h before the examination.
- CT scan: cranio-caudal, with a section thickness of 3.75 cm, 1.75 pitch, 10 mm collimation, 120 peak kV, and 100–120 mA.
- PET study direction was adjusted as caudo-cranial 2D.

System

- PET and 16-detector CT (Discovery ST PET/16 slice CT fusion system HPOWER 60; General Electric Medical Systems, Milwaukee, WI).
- A section thickness of 3.75 mm, 2D-PET.
- Multi-display workstations: multiplanar reconstruction (MPR), maximum intensity projection (MIP), PET/CT fused images could be simultaneously evaluated.

The presence or absence of the sign was investigated within the uptake trace in the GITs of 59 cases. Intestinal foci, showing an uptake more intense than the liver localized and measured. And foci with a SUV\(_{\text{max}}\) ≥ 2.5 were included in the study. Endoscopic evaluation (n:47) and endoscopic biopsy (42 of 47 cases) data of the cases were available with gastric-duodenal-colonic uptakes, exploratory laparotomy data of a case diagnosed with small
The GIT is one of the localizations in varying rates. In fact, malignancy was detected in only 5 patients, whereas the activity in the remaining 43 cases was considered as true positive. The cases with increased FDG uptake and malignancy without the peristalsis sign were considered as true negative. The presence of malignancy and the peristalsis sign together throughout the affected FDG-affinitive segment was considered as a false negative. Additionally, the reverse (no malignancy with any sign) was considered as a false positive. Related data were used to identify the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy value for the sign.

Results

In the present study, non-diffuse increased FDG uptake was detected on the localizations consistent with loop traces in 59 (7.2%) of 823 cases. The stomach (n:19, 2.3%), small intestine (n:12, 1.5%), and colon (n:28, 3.4%) represented the focal uptake-related segments in varying rates. In fact, malignancy was detected in only 16 cases, whereas the activity in the remaining 43 cases was recorded as benign (Table 1).

In these 59 cases, separation attempts were made of benign and malignant tissue by measuring the SUVmax values at focal involvement localizations. As a result of this procedure, 43 patients were found to be without malignancy subsequently detected by advanced evaluations. Twenty-three of the 43 had been evaluated with a preliminary diagnosis of malignancy and in 20, follow-up was proposed because of the benign involvement state according to low SUVmax values. In subsequent evaluations, among 16 cases with malignancy, the same conventional measurements were taken. In these cases, 11 were referred with malignancy, and 5 patients were reported as benign (Table 2). This method was estimated with 33% sensitivity, 65% specificity, 69% positive predictive value (PPV), 46% negative predictive value (NPV) and 47% accuracy in discriminating intestinal FDG activity between malignant and benign cases.

The obtained data by testing according to the presence or absence of the “peristaltic segment sign” was used; the sensitivity, specificity, PPV, NPV, and accuracy of the sign in discriminating malignant from benign intestinal uptake by itself were found 68%, 80%, 82%, 65%, and 73% respectively (Table 3).

Discussion

PET/CT imaging provides useful data in detecting malignant diseases and in the discrimination of malignant vs. benign lesions.3,9 It is known that lesions with increased FDG uptakes with high SUVmax values that mimic malignancies are likely to occur in various localizations in the body.2,7,8 The GIT is one of the localizations in which local incidental uptakes are frequently detected.6,8–11 Although the majority of focal gastric and small intestinal uptakes are associated with benign physiological activities, further evaluation is required in colonic focal uptake.6,8,11

In the present study, we tried to discriminate malignant focal FDG uptake from the benign ones, which were retrospectively investigated throughout the entire intestinal system and were well localized via “peristalsis sign” benefiting from the multislice characteristic of the fused CT system. In this context, focal activities throughout the intestinal system were considered as localized activity and included in the study. The “peristalsis sign” was considered positive in the presence of a bowel loop which had been expanded with air and located proximal or distal to the pathologic (FDG-affinitive) intestinal segment.

Colonoscopies of the cases with incidental, focal colonic FDG activity revealed organic pathologies (mucosal abnormalities, adenoma, or carcinoma) in various rates ranging from 71% to 95%6–8. Increments in localized peristalsism due to partial obstruction caused by the lesion may be responsible for the focal uptake in the colon and concurrent peristalsism sign. Kamel et al. evaluated the probability of an organic pathology in overall incidental focal uptakes of the GIT, which could change the future diagnostic and therapeutic steps. He found organic pathology in 28% of the cases with intestinal focal uptake detected on PET/CT.7 The rate was also consistent with the rate (27%) defined in our study. In literature, there are studies about the efficacy of SUVmax measurements in the differentiation of etiological factors of focal uptake,6,12 whereas there are also studies emphasizing that discrimination of malignant vs. benign lesions could not be made properly by
measuring uptake value alone and that further evaluation is required. Moreover, Isreal et al. in their review displayed that there was no statistically significant difference between physiological uptake and incidental uptake occurring due to premalignant-malignant lesions in terms of SUVmax values of incidental uptake in the intestinal tract. This has shown that SUVmax has no efficacy in discriminating malignancy in a focal incidental uptake. The number of the cases with benign lesions that have substantially high SUVmax is not low at all. In the present study, substantially low SUVmax values were included. Matched sections of peristalsis sign were found, superposed, and accordingly, the definite discrimination of intestinal vs. non-intestinal uptakes has been made.

It is known that intestinal uptakes exist in a wide spectrum including diffuse, segmental and focal uptake. Unifocal uptakes are seen mostly in Barret’s esophagus and tubulovillous adenomas, whereas multifocal, segmental or diffuse intestinal uptake is seen in inflammatory bowel diseases.14–18 Several studies emphasized that long segmental uptakes are caused by benign entities (physiological or inflammatory or post RT colitis). Therefore, recent studies have been targeted to discriminate malignancy via new parameters taking the cases with focal uptakes into consideration. Gluecker et al. reported that dependent intestinal mucosal-mural FDG uptake occurs frequently due to contact with stool and irritation. The same study emphasized that nondependent incidental focal intestinal uptakes are more meaningful and require further evaluation. Because discrimination of dependent vs. nondependent methods might be unable to define the origin of an FDG shining focus in the presence of uptake in the collapsed small intestine or in colonic loop trace, we did not use it as a criterion.

Artefactual uptakes in the GIT may be reduced by lowering the amount of swallowing and providing colon cleansing with iso-osmotic solution. In order to eliminate luminal or mural pathology of the colon, methods that discriminate the wall from the lumen are required. For this procedure, the lumen and the wall can be clearly exposed with a rectal contrast enema that would expand the entire colon. Otherwise, peristaltic segments or the segments with insufficient filling might not be visualized optimally. Since rectal contrast use is unlikely during PET/CT imaging, it can be used just in the suspected cases, if required, as the next evaluation step. Additional late phase imaging protocols may be needed especially for gastric lesions. Gastric focal uptakes could not be differentiated from the activities in the same lodge such as pancreatic tile uptake and lymph node uptake of the splenic medial pole.

The present study revealed an underlying malignancy by a high rate such as 27% at these incidental intestinal uptake foci, and discriminated the malignancies more sensitively than the conventional method (33% vs. 68%). In general, literature revealed that endoscopic correlation is required to eliminate malignancy in the cases of esophageal uptakes. As a result, histopathological sampling is in question to eliminate premalignant lesions even for benign activities, in which uptake occurs at Barret’s point.24,25 We already have excluded the esophagus for the indicator of sign, since an active peristalsis would not be in question except for nutrition.

In the present study, we investigated the presence of a peristaltic segment sign for the stomach and duodenum considering the existence of low-grade adenocarcinomas, which are likely to have low SUVmax rates. We had high rates of false negativity (approximately 60%) in the cardia. This was attributed to the point’s being the Barret’s point, and peristalsis-associated changes’ being unable to be visualized on CT sections, despite the presence of premalignant and malignant lesions. Since neither the cardia nor the distal segment of the esophagus could be evaluated in terms of presence or absence of peristalsism because of the same problem, such a high false negativity has been considered as directive, rather than a handicap, for endoscopy to eliminate the premalignant lesions.

In the small-intestine-related uptakes, the peristalsism sign was used efficiently in 12 cases where the focal uptake in the jejunoileal segments have been evaluated, except for a case with false positive and another case with false negative, for the discrimination of malignant vs. benign conditions.

### Table 1

<table>
<thead>
<tr>
<th>Gastro-Duodenal (n=19)</th>
<th>Small intestine (n=12)</th>
<th>Colon (n=28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardio-esophageal junction (n=5)</td>
<td>Jejunum (n=2)</td>
<td>Cecal apex (n=7)</td>
</tr>
<tr>
<td>Antrum (n=11)</td>
<td>Ileum (n=4)</td>
<td>Hepatic flexure (n=4)</td>
</tr>
<tr>
<td>Duodenal bulbus (n=2)</td>
<td>Ileocecal valve (n=6)</td>
<td>Sigmoid colon (n=11)</td>
</tr>
<tr>
<td>2nd duodenal segment (n=1)</td>
<td></td>
<td>Rectum-anorectal sphincter (n=6)</td>
</tr>
<tr>
<td>Malignant: 7 (Adenocarcinoma)</td>
<td>Malignant: 2 (Lymphoma)</td>
<td>Malignant-premalignant: 7 (5 Adenocarcinoma, 1 tubulovillous adenoma, 1 anorectal junction squamous cell carcinoma)</td>
</tr>
<tr>
<td>Benign: gastritis, duodenitis, hypertrophic rugae</td>
<td>Benign: Crohn’s disease in one of the cases via enteroclysis, no underlying pathology in the other cases</td>
<td>Benign: Diverticulitis (n=1), tubular adenoma (n=1), normal (n=19)</td>
</tr>
</tbody>
</table>

### Table 2

Data obtained from the evaluation by measuring the SUVmax levels (conventional method).

<table>
<thead>
<tr>
<th>Suspicious malignity and advices for further evaluation in case of measuring &gt; 2.5 SUVmax values</th>
<th>In endoscopically verified normal cases (physiological uptake) (n=43)</th>
<th>Maliganity verified with biopsy (pathological uptake) (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prediagnoses</td>
<td>Malignant: 23 Benign: 20</td>
<td>Malignant: 11 Benign: 5</td>
</tr>
</tbody>
</table>

### Table 3

Sensitivity values of the special sign (peristalsism sign), which has been used in the discrimination of malignant vs. benign uptakes.

<table>
<thead>
<tr>
<th>False positive</th>
<th>False negative</th>
<th>True positive</th>
<th>True negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>11</td>
<td>23</td>
<td>20</td>
</tr>
<tr>
<td>Special peristalsism sign</td>
<td>Antrum (n=1)</td>
<td>Jejunum (n=1)</td>
<td>Antrum (n=1)</td>
</tr>
<tr>
<td></td>
<td>Ileocecal valve (n=1)</td>
<td>Colon (n=6)</td>
<td>Jejunum (n=1)</td>
</tr>
</tbody>
</table>
FDG activity within the colon is typically heterogeneous. There is higher uptake within the cecum and right colon due to the higher concentration of lymphoid tissue in this region. Diffuse uptake is usually associated with infectious or inflammatory colitis. Focally increased FDG uptake within the bowel has been described for both malignant and benign processes. PET-CT findings in these cases may be diagnostic, since the CT manifestations of these entities are well described in the literature as appendicitis, diverticulitis or nonspecific uptake. On the other hand, although FDG-PET has been shown to be highly sensitive in detecting colorectal cancer it has low specificity because of physiological uptakes as well as inflammatory causes.

Conflict of interest

The authors have no conflict of interest to declare.

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