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Original Article

^{18}F-FDG PET/CT에서 저용량 경구용 조영제의 유용성

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Usefulness of Low Dose Oral Contrast Media in ^{18}F-FDG PET/CT

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Purpose: The standard protocol using large volume of oral contrast media may cause gastrointestinal discomfort and contrast-related artifacts in PET/CT. The aim of this study was to evaluate the usefulness of low dose oral contrast in ^{18}F-FDG PET/CT. **Materials and Methods:** We retrospectively reviewed the whole-body PET/CT images in a total of 435 patients. About 200 ml of oral contrast agent (barium sulfate) was administered immediately before injection of ^{18}F-FDG. The FDG uptake of intestines was analyzed by visual and semi- quantitative method on transaxial, coronal and saggital planes. **Results:** Seventy (16%, 113 sites) of 435 images showed high FDG uptake (peak SUV 〉 4); 50 (74%, 84 sites) with diffuse and 20 (26%, 29 sites) with focal uptake. The most commonly delivered site of oral contrast media was small bowel (n=27, 39%). On PET/CT images, FDG uptake coexisted with oral contrast media in 26 patients (54%, 38 sites) with diffuse pattern and 9 (45%, 9 sites) with focal pattern, and by sites, those were 38 (45%) and 9 (31%), respectively. In small bowel regions, the proportion of coexistence reached as high as 61% (29/47 sites). A visual analysis of available non-attenuation corrected PET images of 27 matched regions revealed no contrast-related artifact. **Conclusion:** We concluded that the application of low dose contrast media could be helpful in the evaluation of abdominal uptake in the FDG PET/CT image. (Nucl Med Mol Imaging 2006;40(5):257-262)

Key Words: PET/CT, FDG, oral contrast, artifact, low dose

Introduction

The CT images in combined PET/CT system provide anatomical information as well as shorter total scan time.[1] As non-specific intestinal FDG uptake with high activity and focal pattern in PET image can be confused with pathologic lesions, the anatomical landmark of CT image is needed, especially in the abdominal region.[2,3]

However, the non-contrast enhanced CT has a limitation on discrimination of bowel structures from other abdominal organs, because the CT densities of them are too similar.[4] The administration of oral contrast is a useful method to distinguish intestines from adjacent organs in CT image. For the same reason, the PET/CT with oral contrast may improve diagnostic value on evaluating the abdominal FDG uptake.[5]

Most patients currently receive a large amount (500-1000 mL) of oral contrast media in clinical situations,[6-9] but some of them, especially cancer patients, may have difficulty in having a large volume because of intolerable gastrointestinal side effects such as nausea and vomiting. Moreover, those contrast materials may induce artifacts on CT based attenuation corrected PET images[5,10,11] by attenuating bowel lumen more than other soft tissues. Therefore, a tolerable method for oral contrast with less contrast-related artifact is needed in PET/CT imaging.

In this study, we investigated whether low dose oral contrast protocol, instead of large amount of contrast, could

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be of benefit to interpretation of FDG uptake in gastrointestinal (GI) tracts.

Materials and Methods

Patient population

From March to September 2004, the whole body PET/CT images were performed in a total of 533 patients. Of these, 86 patients were not able to apply oral contrast due to following reasons: 1) nausea and vomiting during administration of low dose oral contrast : 2 cases, 2) refuse because of experience GI discomfort on previous CT scan : 10 cases, 3) the patient's own clinical schedule, such as other medications or examinations on same day, which could be influenced by contrast : 74 cases. Therefore, a total of 435 patients were included in our study and their PET/CT images were retrospectively reviewed. There were 264 men and 171 women, and their mean age was 59 years (range 14-83). Most of patients were referred to evaluate suspected cancers or to screen for malignancy.

PET/CT protocol

After at least 4 hr fasting, all patients received 200 mL of 1.5% diluted barium sulfate suspension followed by 200mL water, immediately before receiving an intravenous administration of 370 MBq ^{18}F-FDG. Patients with gastric cancer were required to have more water (500 mL) immediately before the start of CT scan for the purpose of better visualization of gastric wall. After 1 hr rest, CT data were acquired with the following parameters: tube-rotation time, 1 s per revolution; 120 kV; 70 mA; 7.5 mm per rotation and an acquisition time of 60.9 s for a scan length of 867 mm. Subsequently, 7 or 8 frames (3 min per frame) of emission PET data were acquired in a 2-dimensional mode. PET images were reconstructed using iterative reconstruction (ordered-subsets expectation maximization with 2 iterations and 30 subsets) with a field of view of 600 mm and a 5-mm slice thickness. CT-based attenuation correction was performed and standardized uptake value was calculated for injected dose and body weight.

Image Analysis

Two reviewers analyzed the whole body PET/CT images visually. The reviewers were blinded to the diagnoses and clinical information. GI tracts were divided into the 6 sections: stomach, small bowel, ascending colon, transverse colon, descending colon, and recto-sigmoid colon. In those sections, we evaluated the pattern of FDG uptake in regions with significant FDG uptake (peak SUV 〉 4.0) and classified these findings as focal and diffuse pattern. Then, we compared the distribution of FDG uptake with that of oral contrast. The regions, which high FDG uptake on PET images coexist with oral contrast media on CT images, was considered as matched, while if high FDG uptake did not coexist with oral contrast media, the regions were considered as mismatched.

All available non-attenuation corrected images (57%, 27/47) were reviewed to evaluate the contrast related artifacts. A contrast-related artifact was defined as the presence of apparently increased glucose metabolism on fused PET/CT compared with non-attenuation corrected images by visual analysis. Increment of FDG uptake on fused PET/CT was determined by comparison with those of adjacent bowels, which was not filled with oral contrast.

We performed the clinical follow-up of patients for 12 months to determine the feature of FDG uptake in the abdomen.

Results

Distribution of FDG uptake by patients

Seventy (16%, 47 men, 23 women; age range = 16-83 years (mean = 55.8)) of 435 patients showed high-intensity FDG uptake in GI tracts. The clinical diagnoses of these patients were as followed: 20 lung cancers, 9

Table 1. Clinical Diagnoses of the 70 Patients

Diagnoses of patients	No. of patients
Lung cancer	20
Lymphoma	9
Stomach cancer	7
Head and neck cancer	5
Breast cancer	3
Rectal cancer	2
Cholangiocarcinoma	1
Prostate cancer	1
Bladder cancer	1
Cervix cancer	1
Screening for malignancy	20

lymphomas, 7 stomach cancers, 5 head and neck cancers (Table 1). In patients who had multiple sites of high-degree FDG uptake, the region with the highest SUV was chosen for analysis.

According to the pattern of FDG uptake, 50 patients (71%, 50/70) were considered to have diffuse FDG uptake and 20 (29%, 20/70) were considered to have focal uptake on PET images (Table 2). Of these, 50% coexisted with oral contrast media (matched regions); 45% for focal pattern and 52% for diffuse pattern (Table 3).

Distribution of FDG uptake by sites

A total of 113 regions showed high-intensity FDG uptake; 84 (74%, 84/113) diffuse and 29 (26%, 29/113) focal pattern (Table 2). Of these, 47 sites (42%, 9/29 for focal and 38/84 for diffuse pattern) were matched regions. Common sites of high FDG uptake were small bowel (n=55, 49%), ascending colon (n=24, 21%), sigmoid colon (n=16, 14%) and descending colon (n=11, 10%) in order of frequency (Table 4).

Table 2. Patterns of ^{18}F-FDG Uptake

	By patients	By sites
Uptake pattern	No (%)	No (%)
Focal	20 (29%)	29 (26%)
Diffuse	50 (71%)	84 (74%)
Total	70 (100%)	113 (100%)

Distribution of oral contrast media by sites

The most common distribution site of oral contrast media was small bowel (n=27, 39%), and others were small bowel with transverse colon (n=6, 8%), and small bowel with ascending and sigmoid colon (n=6, 8%) (Table 5). Of 47 matched regions, the most frequently delivered site was small bowel (n=29, 61%, 29/47) (Table 6).

Results of artifact evaluation

According to evaluation of available non-attenuation corrected images, there was no apparent uptake correlated with oral contrast in gastrointestinal lumen on CT-based attenuation correction image (Fig. 1).

Discussions

The physiologic FDG uptakes in GI tract, which can be caused by intestinal peristaltic movement or secretion from mucosal, glandular structures,[4,6] are often misinterpreted as the pathologic lesions of intestine or other abdominal organs in PET image. By introducing combined PET/CT system, it becomes easier to interpret those FDG uptakes compared with conventional PET system. However, CT also has a limitation on discrimination of intestinal structure from adjacent organs without the aid of contrast agents. Therefore, the use of oral contrast is accepted as essential

Table 3. Proportions of Matched and Mismatched Regions

	By patients		By sites	
Uptake pattern	Matched*	Mismatched†	Matched*	Mismatched†
Focal	9 (45%)	11 (55%)	9 (31%)	20(69%)
Diffuse	26 (52%)	24 (48%)	38 (45%)	46(55%)
Total	35	35	47	66

*Matched: high ^{18}F FDG uptake coexisted with oral contrast media
† Mismatched: high ^{18}F FDG uptake without oral contrast media

Table 4. Distribution of ^{18}F-FDG Uptake in Gastrointestinal Tract

Gastrointestinal sections	No. of regions		
	Focal	Diffuse	Total
Small bowel	16	39	55 (49%)
Ascending colon	4	20	24 (21%)
Sigmoid colon	4	12	16 (14%)
Descending colon	2	9	11 (10%)
Transverse colon	3	4	7 (6%)
Total	29	84	113 (100%)

Table 5. Distribution of Bowel Opacification by Oral Contrasts

Gastrointestinal sections	No. of regions (%)	Gastrointestinal sections	No. of regions (%)
SB	27 (39%)	Stomach-SB	2 (3%)
SB-T	6 (8%)	Sig	1 (1%)
SB-A-Sig	6 (8%)	Stomach-A-T	1 (1%)
SB-A	4 (6%)	SB-A-D-Sig	1 (1%)
Stomach-SB	3 (5%)	Stomach-SB-D	1 (1%)
SB-Sig	2 (3%)	SB-D-Sig	1 (1%)
Stomach-SB-A	2 (3%)	T-D	1 (1%)
SB-D	2 (3%)	Stomach-SB-Sig	1 (1%)
SB-A-D	2 (3%)	SB-A-T	1 (1%)
SB-A-T-D	2 (3%)	Stomach-SB-A-T-Sig	1 (1%)
Stomach-SB-T	2 (3%)	SB-A-T-Sig	1 (1%)

SB, small bowel; A, ascending colon; T, transverse colon; D, descending colon; Sig, sigmoid colon

Table 6. Distribution of Matched Regions in Gastrointestinal Tract

Gastrointestinal sections	No. of regions		
	Focal	Diffuse	Total
Small bowel	6	23	29 (61%)
Ascending colon	3	7	10 (21%)
Descending colon	0	4	4 (8%)
Sigmoid colon	0	3	3 (6%)
Transverse colon	0	1	1 (4%)
Total	9	38	47 (100%)

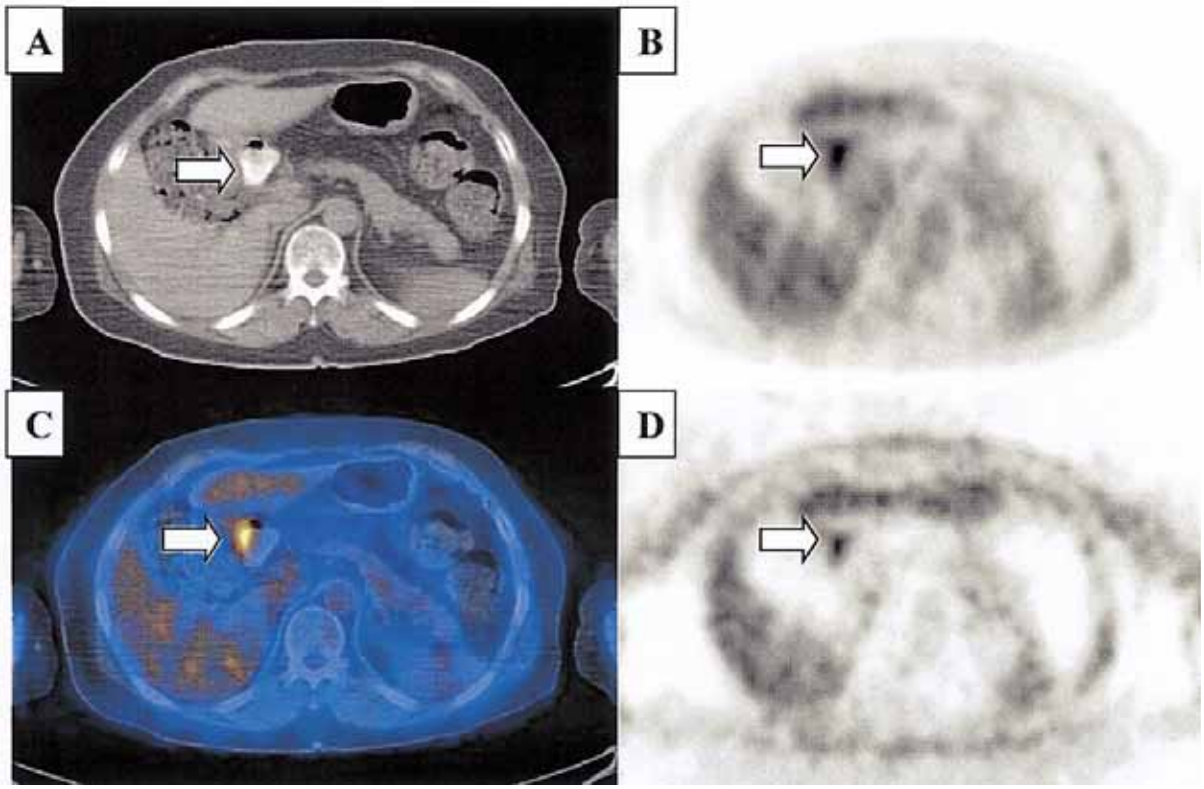

Fig. 1. The presence of oral contrast is observed in small bowel on CT image (Fig 1A, arrow) and there is apparently focal increased glucose metabolism on corrected PET image (Fig 1B, arrow). On fused PET/CT image, this focal FDG uptake is coexisted with oral contrast (Fig 1C, arrow). Non-attenuation corrected PET image demonstrates also increased FDG uptake in same area (Fig 1D, arrow) and we can conclude this uptake is not due to contrast-induced artifact.

procedure in abdominal CT and it may be necessary in PET/CT for the same reason.[7)]

In previous studies, they usually used 500-1000 mL of diluted oral contrast solutions,[4,12,13)] but that may cause GI discomfort and contrast-related artifacts on attenuation-corrected PET images.[4,5,14)] Christian et al.[5)] showed that the artifactual foci appeared above a certain level of concentration in a dose-dependent manner and dropped after a peak activity. In another study, oral contrast agent on CT led to overestimation of PET attenuation coefficient from 2.5% to 26.2%, and their SUV error induced by CT-based attenuation correction ranged up to 11.3%.[4)] For these reasons, we used only 200 mL diluted barium sulfate (= 3 g) with additional 200 mL water in this study.

As a result, our low dose protocol was well tolerable by cancer patients. During this study period, only a few patients (12/533, 2.2%), refused to take the oral contrast media or vomited because of GI discomfort, which was less than that in routine volume of contrast (overall 12% according to previous studies[15,16)]).

In this study, we reviewed the non-attenuation corrected images as well as attenuation-corrected images to identify the expected artifacts of oral contrast agent. However, there was no contrast-filled region showing more prominent FDG uptake after CT- based attenuation correction, which confirmed the lack of artifacts. Although only 27 non-attenuation corrected emission PET images of 47 matched cases were available because of earlier technical problem with data storage, we could conclude that low dose oral contrast agent was safe method in technical aspect at routine PET/CT. While there are a lot of experimental or clinical evidences that FDG uptake can be increased regularly or irregularly in the contrast-filled bowels, their clinical significance seems minimal. Similar to this result, a few previous investigations supported the use of oral contrast in PET/CT in that it did not cause clinically significant artifacts.[4,6,12)]

Water-based negative contrast agents (not used in this study) can be alternative method in differentiating bowel loops from surrounding structures. Their advantage over positive oral contrast agents is that they do not effect on FDG uptake by increasing CT attenuation.[10)] A few recent studies[17,18)] revealed that negative oral contrast provided excellent bowel distention without increasing FDG uptake, as was expected.

Concerning with the timing of contrast enhancement, while we used single administration at immediately before injection of ^{18}F-FDG, they used 2 or 3 split administration including smaller volume on scanning table to enhance multiple segments of GI tract in other studies[12,13)]. However, split administration does not always guarantee whole intestinal enhancement. In this study, though we used single administration in all patients, oral contrast was seen through multiple segments (not whole intestines) in most images. In the images showing oral contrast in recto-sigmoid colon, stomach and duodenum were rarely enhanced, and vice versa.

In evaluating the usefulness of low dose oral contrast, we were interested in the focal pattern of FDG uptake in bowel regions, because focal physiologic uptake is more difficult to distinguish from pathologic one than diffuse uptake. As an example, focal FDG uptake is usually confused with lymph nodes in mesentery or other organs. The present study revealed that 20 patients (26%, 29 sites) had focal significant FDG uptake. If FDG uptakes were coexisted with oral contrast in CT image (matched), we could determine clearly that the lesions were in the lumen of the GI tract. In our study, the proportion of matched regions was 45% (9/20) for focal uptake pattern by patients, and 31% (9/29) by sites. This result sufficiently supported that it was well worth using small volume of oral contrast.

The most commonly delivered site of oral contrast media was small bowel (39%), which also was the most common matched region (61%) in this study. Therefore, we can conclude that low dose contrast protocol may facilitate identification of small bowels and interpretation of its FDG uptake in PET/CT. This result is also in accordance with that of Christian et al.[5)], which suggested that well enhancement in the small bowel is more valuable than other GI region, because of especially difficulty to evaluate anatomical boundary in small bowel regions.

The limitation of this study is that clinical follow-up was the only way to confirm those significant FDG uptakes. Corresponding radiographic images or pathologic evaluations were rare because we reported all of those

uptakes as benign according to the location and pattern. On clinical follow-up, at least 12 month, there was no malignant or other pathologic lesion identified.

As a conclusion, low dose oral contrast protocol has been implemented in PET/CT and it appeared safe from contrast-induced artifact on PET images and helpful in interpreting abdominal FDG uptake, so it could be acceptable method as a routine clinical use.

요 약

목적: 기존의 CT 영상 촬영에서 이용되고 있는 고용량의 경구용 조영제는 복용과정에서 위장계통의 불편함이 나타나고 또한 PET/CT에 이용할 경우에는 이로 인해 인공물(artifact)이 생길 우려가 있다. 본 연구의 목적은 ^{18}F-FDG PET/CT에서 저용량의 경구용 조영제 사용의 유용성에 대해 알아보고자 한다. **대상 및 방법:** 총 435명의 전신 PET/CT 영상을 후향적으로 분석하였다. 모든 환자들은 ^{18}F-FDG. 주사 직전에 200 ml의 경구용 조영제(barium sulfate)를 복용하였다. 장에서의 FDG 섭취양상을 가로단면, 관상면, 시상면에서 시각적으로 판독하였고, 섭취양상을 반정량화하였다. **결과:** 435명의 영상 중 70명(16%, 113부위)에서 높은 FDG섭취(peak SUV 〉 4)를 보였으며, 이 중 미만성 섭취를 보인 경우가 50명(74%, 84부위), 국소적 섭취를 보인 것은 20명(26%, 29부위)이였다. 경구용 조영제가 가장 흔하게 분포된 부위는 소장(n=27, 39%)이었다. PET/CT 영상에서 FDG 섭취부위와 조영제 분포 부위가 일치하는 경우 중에서 미만성 섭취를 보인 것은 26명(54%, 38부위), 국소적 섭취를 보인 것은 9명(45%, 9부위)이였다. 이들을 부위별로 보면 미만성 섭취를 보인 것은 38개(45%), 국소적 섭취를 보인 것이 9개(31%)였다. FDG 섭취와 조영제의 분포가 일치하는 부위는 소장에서 61% (29/47부위)로 가장 많이 관찰되었다. 감쇠 보정을 하지 않은 PET 영상을 본 결과, 검토가 가능했던 27개의 섭취 일치 부위에서 조영제로 인한 인공물(artifact) 영향은 관찰되지 않았다. **결론:** 저용량 경구용 조영제는 FDG PET/CT 영상에서 인공물 영향 없이 복부의 FDG 섭취를 판별하는데 도움을 줄 수 있다.

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