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BRIEF ARTICLE

# Incidental focal colorectal <sup>18</sup>F-fluorodeoxyglucose uptake on positron emission tomography/computed tomography

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# Abstract

**AIM:** To assess the clinical significance of incidental focal colorectal <sup>18</sup>F-fluorodeoxyglucose (<sup>18</sup>F-FDG) uptake on <sup>18</sup>F-FDG-positron emission tomography/computed tomography (PET/CT).

**METHODS:** The records of all the cases which had undergone colonoscopy after PET/CT within a two weeks interval were reviewed. Adenomas were considered advanced when they were villous,  $\geq$  10 mm in size, or had high-grade dysplasia. Colorectal cancers and advanced adenomas are collectively referred to as advanced colorectal neoplasms. Receiver-operating characteristic curve analysis was used to determine the significant predictive maximum standardized uptake value (SUVmax) cutoff value for advanced colorectal neoplasms and cancer.

**RESULTS:** Ninety-five colorectal lesions matched the site of incidental focal colorectal <sup>18</sup>F-FDG uptake on PET/CT and 146 did not. Colonoscopy showed advanced colorectal neoplasms corresponding to the site of <sup>18</sup>F-FDG uptake in 49 of the 95 (51.5%) lesions with incidental uptake. Of the lesions without incidental uptake, only 6 of 146 (4.1%) had advanced colorectal neoplasms on colonoscopy, indicating a statistically significant difference between the two groups (P <0.001). The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of incidental focal <sup>18</sup>F-FDG uptake in identifying advanced colorectal neoplasms were 89.1%, 75.3%, 51.6%, 95.9%, and 78.4%, respectively. In detecting only CRC, these values were 89.2%, 69.6%, 34.7%, 97.3%, and 72.6%, respectively. The significant SU-Vmax cutoff value for advanced colorectal neoplasms (area under the curve 0.755, *P* < 0.001) was 4.35, with a sensitivity, specificity, PPV, NPV, and accuracy of 75.5%, 65.2%, 69.8%, 71.4% and 70.5%, respectively. For CRC, 5.05 was the significant SUVmax cutoff value (area under the curve 0.817, P < 0.001), with a sensitivity, specificity, PPV, NPV, and accuracy of 84.8%, 71.0%, 80.9%, 89.8%, and 75.8%, respectively.

**CONCLUSION:** The presence of incidental focal colorectal <sup>18</sup>F-FDG uptake on PET/CT with a SUVmax  $\geq$  4.35 increases the likelihood of an advanced colorectal neoplasm.

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Key words: Positron emission tomography; Adenomas; Computed tomography; Colorectal cancer; Colonoscopy



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**Core tip:** Increased focal uptake of <sup>18</sup>F-fluorodeoxyglucose (<sup>18</sup>F-FDG) in the colon and rectum can be found incidentally during <sup>18</sup>F-FDG-positron emission tomography/computed tomography (PET/CT). The presence of incidental focal colorectal <sup>18</sup>F-FDG uptake on PET/CT indicated advanced colorectal neoplasms in more than half of the cases. Our study confirms the necessity of colonoscopy when incidental FDG uptake is detected on PET/CT to allow the early diagnosis and management of advanced colorectal neoplasms.

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# INTRODUCTION

<sup>18</sup>F-fluorodeoxyglucose (<sup>18</sup>F-FDG)-positron emission tomography/computed tomography (PET/CT) is a technique used to reduce false-positive findings by combining two imaging modalities, and can distinguish physiological activity from pathology more readily than PET or CT alone. PET/CT is commonly used during the evaluation of malignant tumors, and an increased focal colorectal uptake of <sup>18</sup>F-FDG can be observed incidentally because of the capacity of PET/CT to detect the foci of tumors, which display increased glycolysis<sup>[11]</sup>.

Several previous studies have shown that not only is a high incidence of unexpected gastrointestinal malignancies associated with incidental <sup>18</sup>F-FDG avidity<sup>[2]</sup>, but also that the presence of these lesions can change patient management in up to 28% of cases<sup>[3]</sup>. And in symptomatic patients with proven or suspected colorectal cancer (CRC) recurrence PET detected additional sites of disease in up to 48.4% of patients<sup>[4]</sup>.

However, the significance of incidental focal colorectal <sup>18</sup>F-FDG uptake observed on PET/CT has not yet been fully clarified. Only one previous prospective study has demonstrated a requirement for colonoscopy when incidental FDG uptake was found with PET/CT imaging<sup>[5]</sup>. However, those researchers could not determine the statistically significant maximum standardized uptake value (SUVmax) with which to detect advanced colorectal adenoma and cancer because of the broad overlapping SUV values among the patient groups.

As far as we know, we have evaluated the largest number of cases yet assessed to determine the value of colonoscopy when incidental FDG uptake is observed on PET/CT images. In this study, we investigated the clinical significance of incidental focal colorectal <sup>18</sup>F-FDG uptake detected on PET/CT, and determined the SUVmax for detecting advanced adenoma and cancer.

# MATERIALS AND METHODS

#### Patients

We analyzed the records of 583 consecutive colonoscopic lesions examined over a three-year period, from those who had undergone colonoscopy after PET/CT within a two weeks interval.

The exclusion criteria were an incomplete colonoscopic examination, insufficient biopsy specimen for pathological diagnosis, diffuse colorectal <sup>18</sup>F-FDG uptake on PET/CT, and proven or suspected CRC in a previous study. A surveillance PET/CT examination performed for clinical assessment after curative CRC resection was not an exclusion criterion. Based on these criteria, 342 lesions were excluded.

A total of 241 colonoscopic lesions (88 from women and 153 from men) were eligible for the study. The median age was 62 years (range: 29-86 years). The study was approved by the Institutional Review Board of Seoul St Mary's Hospital, Catholic University of Korea College of Medicine.

## **PET/CT** acquisition

The subjects were fasted for at least 6 h before the FDG injection. Their blood glucose levels were determined in capillary blood samples before the intravenous injection of FDG. At our institution, a cutoff blood glucose level of 8 mmol/L contraindicates FDG injection. PET/CT images were acquired 1 h after the injection of 370-570 MBq of <sup>18</sup>F-FDG. The subjects were scanned from the base of the skull to the upper thighs, with their arms raised above their heads.

The PET/CT scans (dual-section helical CT) were performed on a Biograph Duo scanner (Siemens Medical Solutions, Knoxville, TN, United Statets) with an axial spatial resolution of 6.5 mm. Neither intravenous contrast medium nor bowel preparations were used for the CT scan.

The PET/CT images were reviewed on a workstation with fusion software (Syngo, Siemens, Knoxville, TN, United Statets). An experienced nuclear medicine physician reviewed the PET/CT images. PET, CT, and fused whole-body images displayed in the axial, coronal, and sagittal planes were available for review. The PET data were also displayed in a rotating maximum-intensity projection. The intensity of the <sup>18</sup>F-FDG uptake can be analysed qualitatively and semiquantitatively by measuring the standardized uptake value, which is usually expressed as its maximum. The SUV is defined as the ratio of activity within the tissue (Bq/mL) and decay-corrected total activity injected divided by body weight (Bq/g)and it is calculated using the software provided by the workstation manufacturer. Abnormal FDG uptake, the SUVmax of the primary tumor, and distant metastases were evaluated.

## PET/CT interpretation and analysis

PET studies showing focal, well-circumscribed foci of



Table 1Baseline characteristics and pathologic diagnoses of the 241 elegible colorectal lesions $n$ (%)						
Variables	Total ( <i>n</i> = 241)	Focal FDG uptake $(+)$ (n = 95)	Focal FDG uptake (-) (n = 146)	<i>P</i> value		
Baseline characteristics						
Age, yr <sup>1</sup> (range)	62 (29-86)	64 (31-86)	59.5 (29-84)	0.068		
Males	153 (64)	57 (60)	96 (65)	0.366		
Overweight or obesity (BMI > $25 \text{ kg/m}^2$ )	22 (9.1)	9 (9.5)	13 (8.9)	0.367		
F/U after complete CRC resection	67 (28.2)	16 (17.9)	51 (34.9)	0.006		
Pathologic diagnoses						
Non specific	140 (58.1)	26 (27.5)	114 (78.1)	< 0.001		
Inflammation	24 (9.9)	18 (18.9)	6 (4.1)	< 0.001		
Adenoma (any size)	40 (16.6)	18 (18.9)	22 (15.1)	0.430		
Advanced adenoma	18 (7.5)	16 (16.8)	2 (1.4)	< 0.001		
Cancer	37 (15.4)	33 (34.7)	4 (2.7)	< 0.001		
Advanced colorectal neoplasms	55 (22.9)	49/95 (51.5)	6/146 (4.1)	< 0.001		

<sup>1</sup>Median (range). FDG: <sup>18</sup>F-Fluorodeoxyglucose; BMI: Body mass index; F/U: Follow up; CRC: Colorectal cancer.

Table 2 Positron emission tomography/computed tomographindications of the eligible colorectal lesions						
Initial cancer staging (n = 99)	After complete cancer resection (n = 87)	After cancer chemotherapy (n = 12)	Health screening $(n = 31)$	Others $(n = 12)$		
Stomach: 33 MUO: 19 OBGY: 12 Lung: 10 Hepatobiliary: 9 Others: 16	Colorectum: 67 Stomach: 8 Others: 12	Stomach: 2 OBGY: 2 Others: 8				

MUO: Metastasis of unknown origin; OBGY: Obstetrics and gynecology.

increased abdominopelvic <sup>18</sup>F-FDG uptake, localized by PET/CT images to the colorectum, and distinguishable from the background colonic uptake, were reviewed for interpretation<sup>[6]</sup>. The incidence of incidental focally increased <sup>18</sup>F-FDG uptake in the colorectum was calculated and the intensity of the uptake was measured by calculating SUVmax from the attenuation-corrected PET data, using the software provided by the workstation manufacturer. Lesion size on PET/CT was not part of the inclusion criteria. The PET/CT findings were correlated with the various colonoscopic and histopathological results.

## Colonoscopy and surgery

Two hundred forty-one colorectal pathological specimens obtained from 212 subjects who had undergone a total colonoscopy were studied. All colorectal lesions that appeared to be of neoplastic origin were biopsied and removed by polypectomy and/or surgery. Colonoscopy with a pathological examination was considered the gold standard diagnostic method.

Adenomas were considered advanced when they were villous,  $\geq 10$  mm in size, or had high-grade dysplasia. Colorectal cancers and advanced adenomas are collectively referred to as advanced colorectal neoplasms. If a subject had more than one detectable colorectal lesion, then each lesion was analyzed individually.

## Statistical analysis

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of the incidental focal <sup>18</sup>F-FDG uptake in predicting advanced colorectal neoplasms and CRC were calculated. Receiver-operating characteristic (ROC) curve analysis was used to determine the significant predictive SUVmax cutoff value for advanced colorectal neoplasms and cancer. For all tests, a *P* value < 0.05 was considered statistically significant. All statistical analyses were performed with SPSS, version 16 (SPSS, Chicago, IL, United States).

# RESULTS

## Patient characteristics

Two hundred forty-one eligible colonoscopic lesions were obtained from 212 individual subjects. Of these, 95 lesions showed incidental focal colorectal <sup>18</sup>F-FDG uptake on PET/CT and 146 did not. The characteristics of the 241 colonoscopic lesions evaluated in this study are shown in Table 1. Of these, 153 were male and the mean age was 62 years (range: 29-86 years). The sex, age, and body mass index did not differ significantly between the <sup>18</sup>F-FDG positive and negative groups. The indications for PET/CT were as part of the initial staging of malignancies other than CRC in 99 cases, after the complete resection of malignancies other than CRC in 87 cases, and after chemotherapy for malignancies other than CRC in 12 cases. Thirty-one scanned cases were performed during health screening and 12 during screening for other purposes (Table 2).

The pathological diagnoses were 37 cancers, 24 acute or chronic inflammation, 140 non specific, and 18 advanced adenomatous lesions among a total of 40 adenomatous lesions (Table 1).

# Diagnostic accuracy of focal incidental uptake on PET/CT

In those lesions showing incidental uptake on PET/CT, 49 of 95 (51.5%) had advanced colorectal neoplasms on colonoscopy corresponding to the site of <sup>18</sup>F-FDG uptake, whereas in those lesions without uptake, only 6



of 146 (4.1%) were found to have advanced colorectal neoplasms on colonoscopy. This indicates a statistically significant difference between the two groups (P < 0.001). Overall, the sensitivity, specificity, PPV, NPV, and accuracy of incidental focal <sup>18</sup>F-FDG uptake in predicting advanced colorectal neoplasms were 89.1%, 75.3%, 51.6%, 95.9%, and 78.4%, respectively. For detecting only CRC, the sensitivity, specificity, PPV, NPV, and accuracy of incidental focal <sup>18</sup>F-FDG uptake were 89.2%, 69.6%, 34.7%, 97.3%, and 72.6%, respectively.

## SUVmax and colorectal neoplastic lesions

The statistically significant SUVmax cutoff value that allowed the discrimination of advanced colorectal neoplasms from non advanced neoplastic and non neoplastic lesions was 4.35 (area under the ROC curve 0.755, P < 0.001), with a sensitivity, specificity, PPV, NPV, and accuracy of 75.5%, 65.2%, 69.8%, 71.4%, and 70.5%, respectively. For CRC, 5.05 was the statistically significant SUVmax cutoff value (area under the curve 0.817, P < 0.001), with a sensitivity, specificity, PPV, NPV, and accuracy of 84.8%, 71.0%, 80.9%, 89.8%, and 75.8%, respectively.

## DISCUSSION

PET/CT is a well-accepted technique for the diagnosis and staging of several malignancies because it provides more accurate functional and anatomical assessments than CT or other conventional imaging modalities<sup>[6]</sup>. Some researchers demonstrated that multidetector CT colonography has excellent sensitivity and specificity for lesions < 10 mm. In fact, one study reported superior sensitivity compared to conventional colonoscopy for the detection of adenomas 10 mm or larger (93.8% *vs* 85.5%)<sup>[7]</sup>. A recent study looking at the feasibility of FDG-PET/CT colonography in patients with high clinical suspicion of colorectal carcinoma showed promising results in being an "all-in-one" staging modality, but was practically challenging and still required a formal colonoscopy for histopathological confirmation<sup>[8]</sup>.

Physiological <sup>18</sup>F-FDG uptake within the gastrointestinal tract, with variable intensities and localization patterns, has previously been described. Focal tracer uptake is frequently seen at the gastroesophageal junction, moderate uptake in the stomach, low-intensity uptake in the small bowel, and diffuse or focal uptake in the colon<sup>[9]</sup>. The mechanisms underlying this physiological activity are unclear. Muscular peristaltic activity, the presence of lymphoid tissue in the cecum, high concentrations of white blood cells in the bowel wall, and/or the presence within the bowel wall of cells secreting <sup>18</sup>F-FDG, especially in cases of cecum distention, have been hypothesized<sup>[10]</sup>. Increased FDG uptake can also be associated with inflammation, such as enterocolitis<sup>[11]</sup> or inflammatory bowel disease<sup>[12]</sup>. In our study, only focal or multifocal FDG findings were considered significant because diffuse uptake is considered to have a physiological origin.

Focal colorectal <sup>18</sup>F-FDG uptake indicates a high (70%-80%) probability of corresponding abnormal histopathological findings<sup>[13-15]</sup>. Despite this increase in confidence and reduction in the number of suggestive or equivocal lesions, the precise localization of increased <sup>18</sup>F-FDG foci using PET/CT cannot at present resolve the diagnostic dilemma of abnormal tracer uptake in the colorectum. For this reason, we assessed the clinical significance of incidental focal colorectal <sup>18</sup>F-FDG uptake on PET/CT and also determined a clinically useful SUVmax cutoff value for the detection of advanced adenoma and cancer. Our results are consistent with two large studies that showed that PET/CT is a sensitive tool with which to detect premalignant lesions<sup>[15,16]</sup>. In another previous study, PET/CT had a sensitivity of 74% and a specificity of 84% in the detection of colonic abnormalities<sup>[17]</sup>. However, that study was limited by its small sample size (39 patients).

Although previous studies have evaluated the etiology of incidental PET/CT findings in the colon<sup>[15,18]</sup>, we believe that our study contributes to the clinician' s perspective by providing a SUVmax cutoff value that discriminates advanced colorectal neoplasms from non advanced lesions.

Larger series, with 3210 and 2000 patients, identified 20 (12 villous adenomas, six carcinomas, and two tubular adenomas) and 13 abnormalities (seven adenomatous polyps and six carcinomas), respectively, with colonoscopy<sup>[5,19]</sup>. However, they failed to determine a significant SUVmax cutoff value that would be clinically useful in discriminating advanced colorectal neoplasms from malignant carcinomas. In our study, the cutoff SUVmax value was higher in the CRC group than in the advanced neoplasms group (5.05 vs 4.35, respectively). We showed that the intensity of FDG uptake correlated with the severity of the lesion. This is consistent with the results of previous studies, although in those, the cutoff SUVmax value that allowed advanced and non advanced neoplasms to be distinguished was not determined, whereas this was one of the main goals of our study<sup>[3,20]</sup>. In the present study, a SUVmax  $\geq$  4.35 increased the likelihood of advanced colorectal neoplasms and a SUVmax  $\geq$  5.05 increased the likelihood of CRC.

One limitation of our study was a potential selection bias because we included those cases which had undergone PET/CT for the initial staging of a non colorectal malignancy and those in whom surveillance PET/CT had been performed for clinical assessments after curative CRC resection. However, we believe that our study more accurately reflects the real-life clinical situation by including them. The prevalence of focal colonic lesions in our study is also similar to that in previous studies that have used PET to detect colonic lesions<sup>[19,21,22]</sup>.

In conclusion, our study shows that advanced colorectal adenomas and malignant carcinomas should be suspected when focal <sup>18</sup>F-FDG uptake is detected by PET/CT and that this is clinically significant in most cases. Incidental focal colorectal <sup>18</sup>F-FDG uptake detected on PET/CT with a SUVmax  $\geq$  4.35 and a SUVmax



 $\geq$  5.05 increases the likelihood of advanced colorectal neoplasms and CRC, respectively.

Our study confirms the necessity of colonoscopy when incidental FDG uptake is detected on PET/CT to allow the early diagnosis and management of advanced colorectal neoplasms.

# COMMENTS

#### Background

Positron emission tomography (PET)/computed tomography (CT) is commonly used during the evaluation of malignant tumors. Increased focal uptake of <sup>18</sup>F-fluorodeoxyglucose (<sup>18</sup>F-FDG) in the colon and rectum can be found incidentally during FDG-PET/CT.

#### Research frontiers

Several previous studies have shown that not only is a high incidence of unexpected gastrointestinal malignancies associated with incidental <sup>18</sup>F-FDG avidity, but also that the presence of these lesions can change patient management. However, the significance of incidental focal colorectal <sup>18</sup>F-FDG uptake observed on PET/CT has not yet been fully clarified.

#### Innovations and breakthroughs

The authors have evaluated the largest number of cases yet assessed to determine the value of colonoscopy when incidental FDG uptake is observed on PET/CT images. In this study, the authors investigated the clinical significance of incidental focal colorectal <sup>18</sup>F-FDG uptake detected on PET/CT, and determined the maximal standardized uptake value (SUVmax) for detecting advanced adenoma and cancer.

#### Applications

This study shows that advanced colorectal adenomas and malignant carcinomas should be suspected when focal <sup>10</sup>F-FDG uptake is detected by PET/CT and that this is clinically significant in most cases. This study confirms the necessity of colonoscopy when incidental FDG uptake is detected on PET/CT to allow the early diagnosis and management of advanced colorectal neoplasms.

#### Terminology

FDG-PET/CT display increased sites of glycolysis and by increased focal colorectal uptake of <sup>18</sup>F-FDG and is capable to detect the foci of tumors. The SUVmax of <sup>18</sup>F-FDG is a way to measure the intensity of the <sup>18</sup>F-FDG uptake during FDG-PET/CT. It is measured using the software provided by the FDG-PET/CT workstation manufacturer.

#### Peer review

The authors assessed the clinical significance of incidental focal colorectal <sup>18</sup>F-FDG uptake on FDG-PET/CT. The accuracy of incidental focal <sup>18</sup>F-FDG uptake in identifying advanced colorectal neoplasms and colorectal cancer (CRC) were 78.4% and 72.6%, respectively. In addition, they demonstrated higher cutoff SUVmax value in the CRC group than in the advanced neoplasms group (5.05 vs 4.35, respectively).

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