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BRIEF REPORT – OPEN ACCESS

Potential Use of Integrated Multimodality Imaging ^{18}F-FDG PET-CT in the Evaluation of Inflammatory Bowel Disease: A Brief Report

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ABSTRACT

Inflammatory bowel disease (IBD) significantly increases the risk of colorectal cancer (CRC) due to an inappropriate, aberrant response of the mucosal immune system that can cause chronic irritation and malignant transformation. This prospective study included 8 patients who presented at the Gastroenterology Clinic of Serdang Hospital in Malaysia with a prolonged history of altered bowel habits. Blood tests, endoscopy, tissue biopsy, and whole-body positron emission tomography-computed tomography (PET-CT) using fluorodeoxyglucose F 18 (^{18}F-FDG) as biomarker for tumor imaging were performed. There was a correlation between a high maximum standardized uptake value with contrast-enhanced CT changes, endoscopic, and erythrocyte sedimentation rate findings and clinical presentation. The sensitivity and negative predictive value of ^{18}F-FDG PET-CT were 100%. ^{18}F-FDG PET-CT is a promising, noninvasive method that complements endoscopy in the investigation of IBD and may perhaps play a role as a gatekeeper.

Keywords: Colorectal cancer, fluorodeoxyglucose F 18, inflammatory bowel disease, positron emission tomography-computed tomography

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INTRODUCTION

Inflammatory bowel disease (IBD) is known as a predisposing factor for colorectal cancer (CRC), and the prevalence of IBD is increasing worldwide (1–3). A cascade of inflammatory events can occur due to activated inflammatory cells increasing metabolism in an inappropriate, aberrant response of the mucosal immune system that can lead to chronic irritation and malignant transformation (4–6). Epidemiology studies have shown that CRC mortality increased from 10% to 15% due to IBD, usually as a result of the pro-neoplastic effects of chronic intestinal inflammation. IBD can be diagnosed using methods such as the evaluation of erythrocyte sedimentation rate (ESR), computed tomography (CT), and endoscopy (7, 3). Fluorodeoxyglucose F 18 (^{18}F-FDG) is a nonspecific agent widely used as a biomarker in tumor imaging to detect and assess the staging of tumors. The aim of this study was to evaluate the role of ^{18}F-FDG positron emission tomography-computed tomography (PET-CT) in patients with a high clinical suspicion of IBD (8).

MATERIALS and METHODS

This research was approved by the University of Putra Malaysia Research Ethics Committee.

A prospective study was conducted with 8 patients from the Gastroenterology Clinic of Serdang Hospital, Malaysia, with a prolonged history of altered bowel habits. The inclusion criteria were based on a serum screening for inflammatory parameters, transrectal colonoscopy and tissue biopsy findings, and a whole-body PET-CT scan using ^{18}F-FDG as a surrogate biomarker for bowel inflammation. Prior to the scanning procedure, all of the patients were informed about the risks associated and provided written consent. An endoscopic procedure was performed in all cases for direct visualization of the lesion and a tissue biopsy was obtained for histopathological confirmation. The patients with IBD were diagnosed and selected for the study based on the ^{18}F-FDG PET-CT results that demonstrated a maximum standardized value (SUV_{max}) uptake of more than 2.8; CT scan results revealing contrast enhancement of thick wall of mucosa and muscularis; endoscopy results of mucosal edema, hyperemia, and ulceration; and an ESR result of >12 mm/hour.

Patient Preparation

A standard ^{18}F-FDG PET-CT protocol was observed in all cases. The patients were instructed to fast for at least 6–8 hours prior to the examination. The body weight in kilograms and fasting blood sugar in mmol/L were recorded for the calculation of the semiquantification of FDG-avid lesions expressed as SUV. Patients were encouraged to void their bladder prior to an intravenous injection of 8–10 mCi of ^{18}F-FDG. All of the

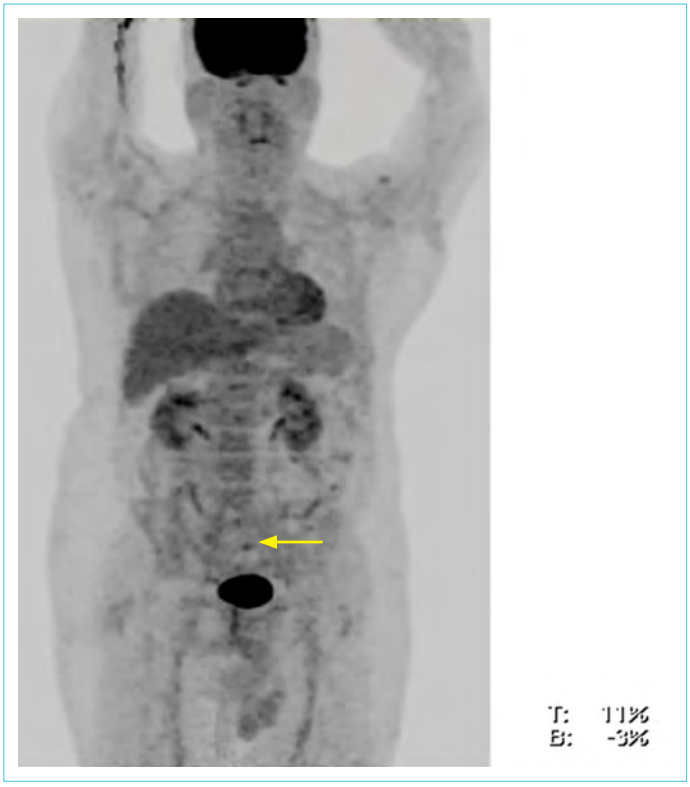

Figure 1. A 71-year-old Indian man who presented with diarrhea ongoing for 6 months. Histopathological examination findings revealed severe pancolitis with malignant transformation. The arrow indicates the positive positron emission tomography-computed tomography findings with a maximum standardized uptake value of >2.8 at the left subclavian artery

patients were given 10 mL of gastroenteral oral contrast solution (Gastrografin; Bracco Imaging S.p.A., Milan, Italy), which contains 1 g of sodium amidotrizoate and 6.6 g of meglumine amitdotrizoate diluted in 500 mL of water. Half was consumed prior to the injection of the isotope and the remaining half just before the patient entered the scanning room. The solution contains 370 mg/mL of iodine and has an osmolality of 2.15 osm/kg H_2O, a viscosity of 8.9 mPa-s, and a density of 1.417 g/mL at 37°C.

PET-CT Method

All of the PET-CT studies were performed using a Siemens Biograph True-V PET-CT device (Siemens AG, Munich, Germany) with 64 slice multi-detector CT capability to provide a 3-dimensional (3-D), whole-body image in 5 different bed positions with 2 minutes per position. In all, 3-D multi-image projection and 2-D multiplanar images in axial, coronal, and sagittal views were obtained for review. The images were transferred from the acquisition console to a remote reporting console using the Siemens radiology information system (Siemens AG, Munich, Germany). The patients were in the supine position on the PET-CT scanner table with the arms above the head throughout the procedure. A scout image was acquired to identify the axial extent of the CT and PET study prior to low-dose CT from the eyes to the thigh using an automated care dose system.

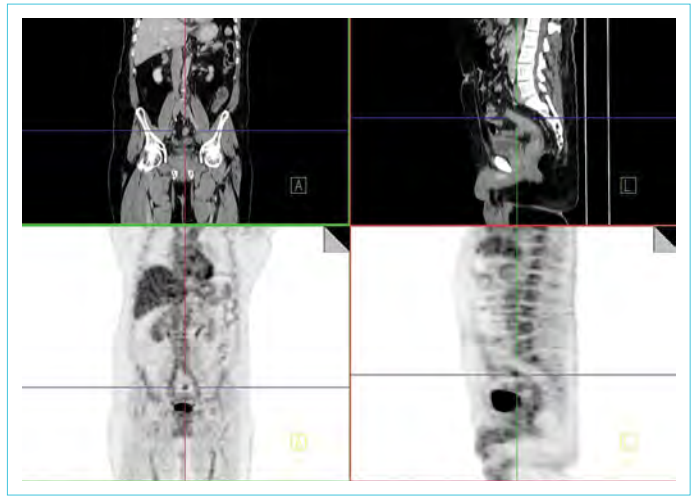

Figure 2. Illustration of severe pancolitis with malignant transformation that was negative on computed tomography but positive on fluorodeoxyglucose F 18 positron emission tomography-computed tomography

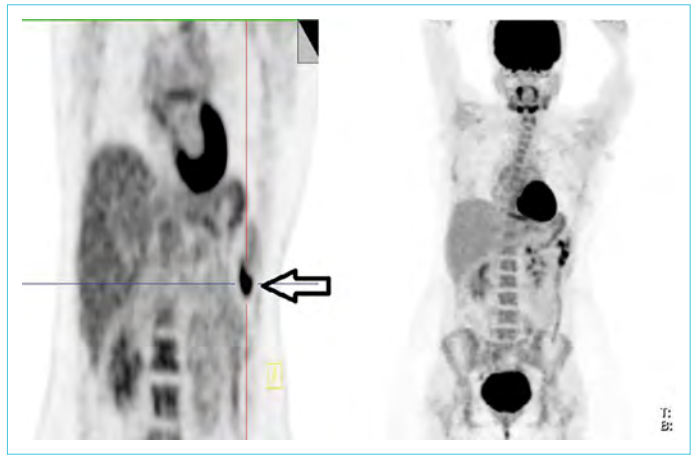

Figure 3. A 32-year-old Indian woman with altered bowel habits present for 2 months. Histopathological examination findings revealed grade 3 ulcerative colitis. Arrow indicates the positive finding of fluorodeoxyglucose F 18 positron emission tomography-computed tomography with a maximum standardized uptake value of 10.24 at the splenic flexure

Statistical Analysis

The underlying relationship analyzed with linear regression models was linear. The standardized uptake values (SUV_{max}, g/dL) of F-18 FDG in the body were obtained from regions of interest. The sensitivity, specificity, false positive and false negative rates of PET-CT were compared with endoscopic and CT findings. All of the statistical analysis was performed using IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY, USA). A p value of <0.05 was considered statistically significant.

RESULTS

The gender distribution was 5:3 (male:female) with a mean age of 45.7±0.32 years. There was a correlation between a high

Table 1. The correlation between ESR, CECT changes, ^{18}F-FDG PET-CT, endoscopic findings, and clinical presentation

No	PET-CT findings SUV_{max}	Endoscopic findings	HPE findings	ESR (mm/hr)	Clinical presentation
1	Marked morphology change	Colon carcinoma	Tubulovillous adenoma	20	Altered bowel habits
2	No change	Dysplastic polyps	Tubulovillous adenoma	10	Altered bowel habits
3	Thickened wall	Mild colitis	Ulcerative colitis, grade 3	24	Anemia, mucus in stool, abdominal cramps
4	Thickened wall	Moderate colitis	Ulcerative colitis, grade 3	76	Anemia, lethargy, diarrhea
5	No change	Mild colitis	Ulcerative colitis, grade 2	16	Lethargy, loose stools
6	No change	Severe colitis	Ulcerative colitis, grade 3	15	Diarrhea, rectal bleed, mucus in stool
7	No change	Mild colitis	Non-specific colitis	6	Backache with altered bowel habits
8	No change	GIST	No malignancy	4	Altered bowel habits

^{18}F-FDG: Fluorodeoxyglucose F 18; CECT: Contrast-enhanced computed tomography; ESR: Erythrocyte sedimentation rate; GIST: Gastrointestinal stromal tumor; HPE: Histopathological examination; PET-CT: Positron emission tomography-computed tomography

SUV_{max} uptake and contrast-enhanced computed tomography changes, endoscopic findings, and ESR results, and the clinical presentation and comorbidities of hypertension, anemia, and altered bowel habits. (Fig. 1–3). ^{18}F-FDG PET-CT showed very promising results when compared with endoscopy study, CT, and histopathological findings (Table 1). The sensitivity and negative predictive value (NPV) of ^{18}F-FDG PET-CT were each 100%. The sensitivity of the endoscopic procedure and CT was 75% and 50%, respectively; however, these methods demonstrated greater specificity (75%) with a low false positive rate (FPR) of 25% compared with the specificity of ^{18}F-FDG PET-CT (75%). The accuracy of ^{18}F-FDG PET-CT in signaling IBD lesions was similar to that of CT (62.5%), but less than that of an endoscopic procedure (75%) or ESR evaluation (88%).

DISCUSSION

Invasive endoscopic procedures that demonstrate histopathological results such as ulcerative colitis (UC) are required to ascertain the specific IBD subtype and to evaluate the progression of the disease (9, 10) (Fig. 1–3). However, the alternative of using the radioactive glucose analogue ^{18}F-FDG and a PET-CT scan is a new and non-invasive diagnostic tool for suspected IBD (11). The ^{18}F-FDG PET-CT combination provided a more precise evaluation of the extent of disease and the involvement of the gut wall, which is very important in the diagnosis of the specific IBD subtype and involvement of progressive carcinoma. The FDG tracer that was injected for use with PET/CT imaging is a glucose analogue taken up by cells in proportion to their metabolic activity; IBD disease demonstrates hypermetabolic features (12). This high metabolic activity is due to an up-regulation of glucose transporters to meet increased metabolic demands in the inflamed state. The 100% sensitivity and NPV of ^{18}F-FDG PET-CT were very encouraging when compared with endoscopy, CT, and histopathological findings. PET can also be instrumental in detecting disease activity in UC, with a sensitivity of 96%. The findings suggest that there is significant potential for the use of ^{18}F-FDG PET-CT to detect IBD based on the specificity and sensitivity achieved as well as the ability to perform both functional and morphological visualization of the whole structure of the gastrointestinal tract and detection of extra-intestinal areas of inflammation and the progression of cancer (13, 14).

CONCLUSION

The favorable results seen using ^{18}F-FDG PET-CT suggest that it may be a useful, noninvasive modality to complement endoscopy in the investigation of IBD, and may perhaps serve as a gatekeeper.

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Ethics Committee Approval: The UPM Ethics Committee granted approval for this study (date: 21.11.2014, number: UPM/TNCPI/RMC/1.4.18.1(JKEUPM)/F2).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – AJN, SS; Design – SS; Supervision – AJN; Resource – AJN; Materials – FF; Data Collection and/or Processing – SS; Analysis and/or Interpretation – AJN; Literature Search – FF; Writing – SS, AJN; Critical Reviews – FF.

Conflict of Interest: The authors have no conflict of interest to declare.

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