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ORIGINAL ARTICLE

Incidental Focal Colonic Uptake of ^{18}F-fluorodeoxyglucose on Positron Emission Tomography/Computed Tomography: Its Incidence and Clinical Significance

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ABSTRACT

Objective: *To determine the incidence and clinical significance of incidental focal colonic ^{18}F-fluorodeoxyglucose (FDG) activity.*

Methods: *A retrospective review of data of 1851 patients who underwent FDG positron emission tomography/computed tomography (PET/CT) imaging in a clinical PET centre, Queen Elizabeth Hospital, from January 2013 to June 2013, was performed. Patients with incidental focal colonic FDG activity mentioned in the PET/CT report with subsequent colonoscopy or surgery within 120 days were included. Patients with uptake corresponding to known colorectal carcinoma were excluded. Using the electronic patient record system, basic demographic information, medical history, and subsequent investigation, as well as endoscopic and histological findings, if any, were reviewed.*

Results: *We found 88 patients (4.8%) with 93 uptake foci. Forty-three of them had subsequent colonoscopy and five of them had undergone surgery. In all, 38 patients with 41 foci had positive endoscopic or surgical findings. Statistically significant differences in maximum standardised uptake values (SUVmax) between benign and malignant groups, and between benign and premalignant groups, were found. The receiver operating characteristic curve of SUVmax for benign versus premalignant lesions had an area under the curve of 0.852, with an optimal cut-off value of 7.5 (sensitivity 78.8%; specificity 87.5%).*

Conclusion: *The incidence of incidental focal colonic FDG activity was 4.8%. The SUVmax for premalignant and malignant lesions was significantly higher than for benign ones. Because of the high positive predictive value, incidental focal colonic FDG uptake should always be reported and investigated without delay, especially with SUVmax ≥7.5.*

Key Words: *Colonic neoplasms; Electronic health records; Fluorodeoxyglucose F18; Incidental findings; Positron-emission tomography*

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Ethics Approval: This study was approved by the Kowloon Central Cluster/Kowloon East Cluster Research Ethics Committee (Ref KCC/KEC-2018-0253). The need for patient consent was waived owing to the retrospective nature of the study.

Declaration: The results of the present study were presented in part at the 23rd Annual Scientific Meeting of the Hong Kong College of Radiologists, Hong Kong on 14-15 November 2015 and the 12th Asia Oceania Congress of Nuclear Medicine and Biology, Yokohama, Japan on 5-7 October 2017.

中文摘要

PET/CT意外探測到直結腸局灶性FDG攝取：發病率和臨床意義

許殷豪、龔本霆、歐陽定勤

目的：研究18氟—脫氧葡萄糖正電子電腦掃描（^{18}F-FDG PET/CT）檢查時意外探測到直結腸局灶性FDG攝取的發病率和臨床意義。

方法：回顧分析2013年1月至2013年6月於伊利沙伯醫院臨床PET中心接受^{18}F-FDG PET/CT檢查的患者共1851例。納入PET/CT檢查時意外探測到直結腸局灶性FDG攝取後120天內進行結腸鏡檢查或手術的患者並排除已知結直腸癌的患者。研究透過醫院的電子病歷系統對基本人口統計信息、病史和後續調查進行回顧分析。部份患者有內鏡和組織學檢查結果。

結果：1851例中確定88例（4.8%）共93個攝取灶，其中43人隨後接受結腸鏡檢查，5人接受手術。38例共41個攝取灶經內鏡或手術檢查診斷為陽性。良性和惡性病變組，以及良性和惡性前期病變組之間的最大標準攝取值（SUVmax）有統計學差異。SUVmax對良性和惡性前期病變的ROC曲線下面積為0.852，最佳臨界值為7.5（敏感性和特異性分別為78.8%和87.5%）。

結論：這項研究顯示意外探測到直結腸局灶性FDG攝取的發病率為4.8%。惡性和惡性前期病變的SUVmax明顯高於良性病變。由於陽性預測值高，當意外探測到直結腸局灶性FDG攝取，尤其當SUVmax為7.5或以上時應盡快作進一步檢查。

INTRODUCTION

Whole-body ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) has been increasingly used for oncologic purposes, including diagnosis, staging, restaging, and treatment monitoring.[1] Incidental bowel FDG uptake is commonly noted.[2,3] These uptakes can represent physiologic, inflammatory or neoplastic changes.[4] Although a diffuse pattern of FDG uptake in bowel is considered physiologic, information on the nature and clinical significance of focal patterns of FDG activity in bowel is limited.[5,6] To date, the incidence of focal colonic FDG activity found on clinical FDG PET/CT in Hong Kong has not been reported. The purpose of this study was to determine the incidence of incidental focal colonic FDG activity and its clinical significance as well as the clinical utility of uptake intensity for discriminating benign from malignant or premalignant pathology.

METHODS

The electronic medical record data of all 1851 consecutive patients who had undergone whole-body FDG PET/CT in Queen Elizabeth Hospital, Hong Kong, during the period January 2013 to June 2013 were retrospectively reviewed. Those patients with incidental focal FDG uptake in the colon mentioned in the PET/CT scan report were included. Incidental focal colonic FDG uptake was defined as focal accumulation of activity greater than the surrounding background in the colon that could not be explained based on the patient's known medical history at the time of scanning. Thus, those foci of increased uptake referring to known colorectal cancers were excluded from the study. The location and intensity in terms of maximum standardised uptake values (SUVmax) of these foci were retrieved from the medical report. The medical records of these patients were then reviewed by a single researcher for demographic information, medical history, and subsequent investigations of the incidental colonic uptake, if any.

Positron Emission Tomography/Computed Tomography Protocol

Imaging was performed with a PET/CT scan system with a spatial resolution of 6.6 mm in the centre of the field of view (Discovery LS, GE Healthcare, Milwaukee [WI], United States). All patients fasted for at least 6 hours before the PET/CT study. 370 MBq of FDG was injected intravenously. Imaging was initiated 60±5 minutes after intravenous FDG injection. Intravenous iodinated contrast medium was used if it was requested by the ordering physicians. Images were acquired from the skull vertex to mid-thigh. Image

acquisition was performed for 3 minutes per bed position. Low-dose CT was performed for attenuation correction and lesion localisation. The examinations were then reported by one of four independent nuclear medicine physicians, each of whom has at least 8 years of PET/CT interpretation experience.

Endoscopic or Surgical Correlation

Findings of subsequent colonoscopy were retrieved from the electronic medical record database for all patients with incidental focal colonic FDG uptake. Colonoscopy was considered diagnostic if it was performed within 120 days of the PET/CT study. For those patients with colonoscopy performed >120 days after the PET/CT study, the focal colonic FDG activity was not further evaluated and excluded from the study. Findings on endoscopy were correlated with the incidental focal colonic FDG activity on the PET/CT report. Whenever a biopsy or polypectomy of the positively correlated endoscopic abnormalities was performed, the subsequent pathological reports were evaluated. If the endoscopic findings were negative, the incidental focal colonic FDG activity was considered as normal/physiologic. The final diagnoses were classified into one of four categories: malignant, premalignant (such as tubular adenoma, villous adenoma, and tubulovillous adenoma), benign (hyperplastic polyps or inflammatory lesions), and normal.

Statistical Analysis

Statistical analysis was performed using SPSS (Windows version 22.0; IBM Corp, Armonk [NY], United States). Descriptive statistics were used to delineate the incidence of incidental focal colonic FDG activity. The non-parametric Mann-Whitney *U* test was used to assess for differences of the SUVmax between groups (malignant vs benign; malignant + premalignant vs benign; and malignant vs premalignant). Statistical significance was assumed for $p<0.05$. Receiver operating characteristic curve (ROC) analysis was performed to determine an optimal cut-off value for SUVmax for differentiating benign from premalignant lesions.

RESULTS

Among the 1851 patients, 93 incidental foci of colonic FDG uptake were reported in 88 patients, giving an incidence of 4.8%. The majority of these patients were men (62 male vs 26 female) with mean age 69 years. Most foci of incidental uptake were located in the sigmoid colon (30 foci, 32%). In total, 22, 19, and 17 foci of increased uptake involved the rectum, ascending colon, and descending colon, respectively. The fewest incidental uptake foci involved the transverse colon, accounting for 5%. Figure 1 shows the flowchart for patient selection.

Of 45 patients undergoing subsequent endoscopies and five patients undergoing surgery ≤120 days after the PET/CT study, the histological specimens of one of the patients were considered necrotic by the pathologists and the nature of the lesion could not be determined. Another patient, with two foci of FDG uptake on the PET/CT study, underwent endoscopy at another location, and detailed pathological reports were not available. Thus, these two patients were excluded from further histopathologic analysis.

After these exclusions, 48 patients remained: 33 of them (35 foci of increased uptake) had true-positive colonoscopies; five patients (six foci of uptake) underwent surgery directly; and the remaining 10 patients had normal colonoscopy. Of the 38 patients with positive findings, nine patients (10 foci of uptake) had adenocarcinoma, 21 patients (23 foci of uptake) had

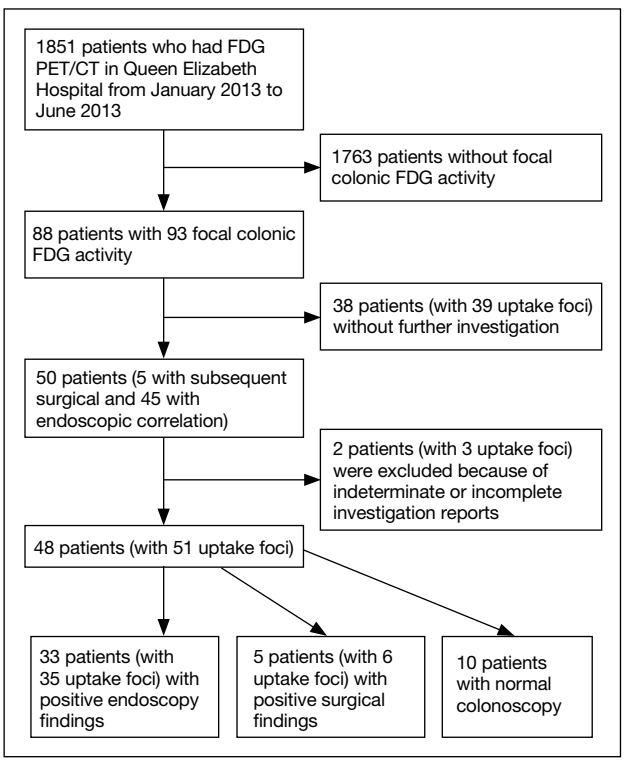

Figure 1. Flowchart for patient selection.
Abbreviations: FDG = ^{18}F-fluorodeoxyglucose; PET/CT = positron emission tomography/computed tomography.

premalignant lesions, and the remaining eight patients (8 foci of uptake) had benign pathology on histological findings. The mean, median and interquartile range of these uptakes are given in the Table. Figure 2 shows one of the patients with positive colonoscopy findings. A statistically significant difference of SUVmax was found between the benign and malignant groups (p = 0.001) as well as between the benign and premalignant/malignant groups (p = 0.002). There was no statistically significant difference in SUVmax between the premalignant and malignant groups when analysed with the Mann-Whitney *U* test (p = 0.066). According to ROC analysis, the optimal diagnostic cut-off value to discriminate between benign and premalignant/malignant lesions was an SUVmax of 7.5 (sensitivity 78.8%; specificity 87.5%; area under curve 0.852). Figure 3 shows the ROC.

Table. Correlation with focal colonic uptake intensity and findings/histopathology. Statistically significant differences are found in maximum standardised uptake values (SUVmax) between benign and malignant groups (p = 0.001), between premalignant/malignant and benign groups (p = 0.002), as well as between normal and all positive findings (including benign, premalignant and malignant [p = 0.006]). No statistically significant difference was noted between the SUVmax of premalignant and malignant lesions (p = 0.066).

	No. of lesions	Median SUVmax	Mean SUVmax	Interquartile range (SUVmax)
Benign	8	5.9	6.3	5.0-7.1
Premalignant	23	9.1	11.5	6.8-14.3
Malignant	10	12.8	13.6	10.3-16.6
Normal	10	6.1	6.4	5.5-7.5

DISCUSSION

Because of the increased application of PET/CT for oncological management, incidental FDG activity in the gastrointestinal tract is encountered more frequently. In the present study, incidental focal colonic FDG uptake was found in 4.8% of our patients. The incidence of incidental focal colonic FDG activity varies among studies, ranging from 1.1% to 28%.[7-9] This wide range of incidence may be related to the variation in the definition of focal FDG uptake.

Unfortunately, nearly half of the uptake foci (44%) did not have subsequent correlative surgery or endoscopy in our study. One of the reasons for not undergoing subsequent correlative investigation for these patients

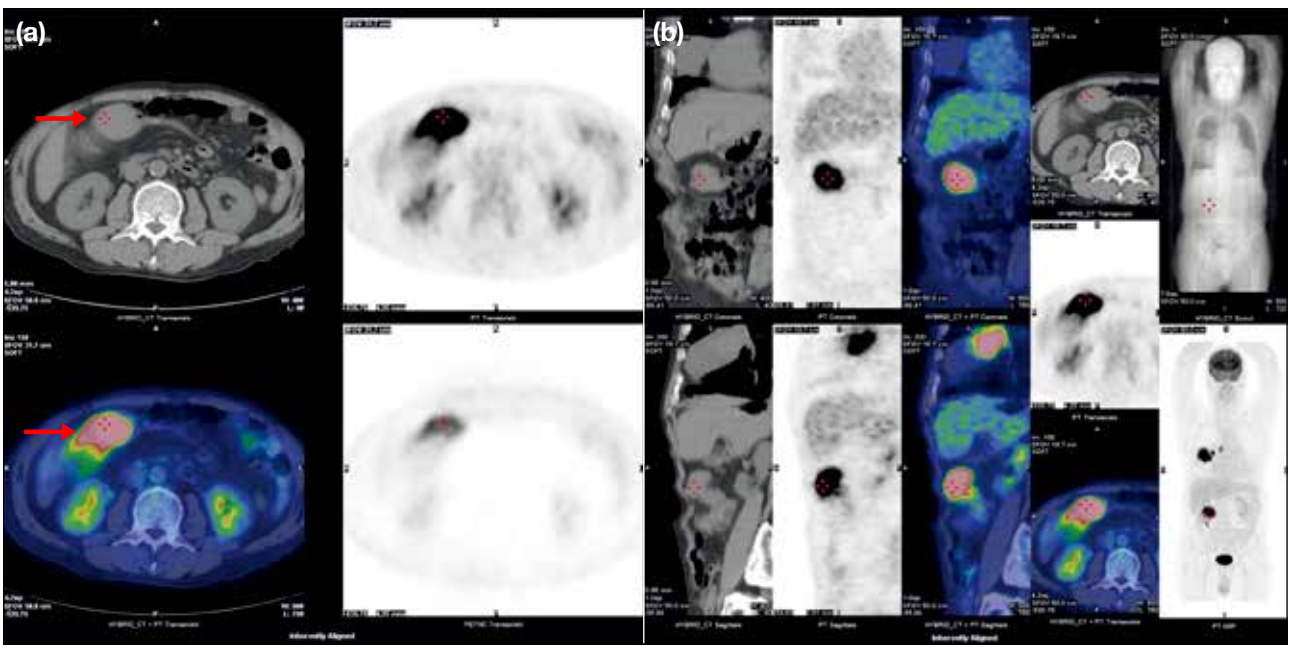

Figure 2. (a) Transaxial view of non-contrast ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT). This patient was a 67-year-old man undergoing PET/CT for staging of right lung carcinoma. Incidental findings of a hypermetabolic mass (red arrows), maximum standardised uptake value 13.7, in the transverse colon near the hepatic flexure. Subsequent colonoscopy revealed a circumferential mass at hepatic flexure with biopsy confirming to be adenocarcinoma of colon. (b) Three plane views of non-contrast PET/CT showing the focal colonic uptake at transverse colon. Also seen in the maximum intensity projection image are hypermetabolic foci in the right lung corresponding to right lung cancer and the hilar nodal metastasis.

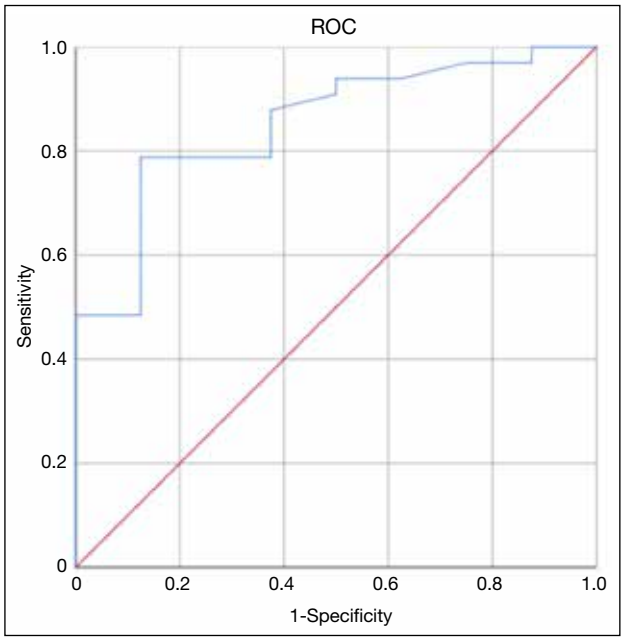

Figure 3. Receiver operating characteristic curve (ROC) of maximum standardised uptake values to discriminate benign from malignant/premalignant lesions (area under the curve = 0.852).

was related to the advanced stage or metastatic nature of their diseases (34%). As a result, we have no idea of the nature of the lesions these foci represent. Among the 48 patients (with 51 foci of increased uptake) having subsequent correlative investigations, 38 of them (with 41 uptake foci) had a positive endoscopy or surgery, giving positive predictive value (PPV) of 80.4%. Our findings are similar to previous studies concerning focal colonic FDG uptake. Gutman et al reported that 15 of 20 patients with focal colonic FDG uptake had positive endoscopic findings.[10] van Hoeij et al,[11] Treglia et al,[7] Garrido Durán et al[12] and Putora et al[13] reported a PPV of 62% to 86%. In view of the high likelihood of identifying a polypoid lesion, our study supports previous suggestions of performing endoscopy for further investigations of incidental focal colonic activity.[14]

In our study, the SUVmax for malignant and premalignant lesions were significantly higher than those for benign lesions, but not significantly different between malignant and premalignant lesions. In the retrospective study done by Luboldt et al,[15] high-grade adenomas and malignancies demonstrated significantly higher SUVmax. Similar findings were also reported in a retrospective study done by van Hoeij et al.[11] However, some other previous studies had been unable to demonstrate these differences among the different groups assessed.[16] In our study according to ROC analysis, an optimal cut-off value to discriminate premalignant/malignant from benign lesions is SUVmax ≥7.5. With colorectal cancer known to be arising from adenomatous polyps, it is a common practice to remove these polyps to prevent future development of malignancy.[17] Thus we believe including precancerous lesions to be of utmost importance in cancer prevention.

Our study has some limitations. First of all, up to 40% of the patients with incidental focal colonic FDG activity did not undergo further endoscopic correlation. As a result, we were unable to know the nature of these uptakes. Secondly, our data are limited to a single, tertiary referral centre. Lastly, our study was a retrospective review of PET/CT reports that have been reported by several nuclear medicine physicians; hence inter-observer variations in reporting were expected.

CONCLUSION

The incidence of incidental foci of colonic FDG uptake identified in our institution was 4.8%. These incidental foci had a high PPV for polypoid growths. Thus, all incidental focal hotspots in the colon should be further investigated. Malignant and premalignant lesions have significantly higher SUVmax than benign lesions. The SUVmax may be helpful in distinguishing premalignant/malignant from benign lesions, with an optimal cut-off of ≥7.5. Thus, SUVmax may have a role in assisting prioritisation of incidental foci of increased uptake for endoscopic investigation.

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