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Prevalence and Clinical Significance of Incidental Focal ^{18}F-FDG Uptake in Colon on PET/CT Imaging

PET/BT Görüntülemede Kolonda İnsidental Fokal ^{18}F-FDG Tutulumunun Prevalansı ve Klinik Önemi

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Abstract

Objectives: The present study aimed to identify the prevalence of focal uptake in the colon on ^{18}fluorine-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) studies performed for the evaluation of malignancies other than colon, to detect the rate of malignancy in incidental focal ^{18}F-FDG avid colonic lesions and to investigate if any possible role of maximum standardized uptake value (SUV_{max}) values in the discrimination of malignant lesions from premalignant and benign ones exist.

Methods: We retrospectively reviewed the files of 8,017 patients with known or suspected malignancy, who underwent whole-body ^{18}F-FDG PET/CT at our institution during the period November 2017 to November 2019. Patients showing a single site of focally increased colonic ^{18}F-FDG uptake that was more intense compared to liver uptake on ^{18}F-FDG PET studies and referred to colonoscopy were enrolled in the study.

Results: Fifty two patients (83.8%) had at least 1 corresponding lesion on colonoscopy, whereas in 10 patients no lesion was detected. Subsequent histopathological examinations revealed no corresponding lesion in 13 (13.7%), a benign lesion in 18 (18.9%), hyperplastic polyp in 10 (10.5%), low-grade polyp in 16 (16.8%), high-grade polyp in 29 (30.5%) and malignant lesion in 9 (9.5%) of the focal ^{18}F-FDG uptake sites. According to histopathology results, statistically no significant difference was found between the SUV_{max} measurements of malignant and benign cases ($p>0.05$) but the average SUV_{max} measurements of malignant cases were found to be significantly higher than lower + high-grade cases ($p<0.05$) and hyperplastic polyp cases ($p<0.01$).

Conclusion: In conclusion, any unexpected focal ^{18}F-FDG uptake in ^{18}F-FDG PET/CT studies is suspicious for malignancy and should be clarified by colonoscopy. The intensity of ^{18}F-FDG uptake does not preclude the application of colonoscopy and histopathological verification of the lesion if there is any.

Keywords: Gastrointestinal tract, incidentally detected lesions, colon, incidental ^{18}F-FDG uptake

Öz

Amaç: Bu çalışmanın amaçları kolon dışındaki malignitelerin değerlendirilmesi için yapılan ^{18}flor-florodeoksiglukoz (^{18}F-FDG) pozitron emisyon tomografisi/bilgisayarlı tomografi (PET/BT) çalışmalarında kolonda fokal tutulum prevalansını, tesadüfi fokal ^{18}F-FDG avid kolonik lezyonlarda malignite oranını belirlemek ve maksimum standardize alım değeri (SUV_{maks}) değerlerinin, malign lezyonların premalign ve iyi huylu olanlardan ayırt edilmesindeki olası rolünü araştırmaktı.

Yöntem: Kasım 2017-Kasım 2019 döneminde kurumumuzda tüm vücut ^{18}F-FDG PET/BT uygulanan, malignitesi bilinen veya şüphelenilen 8.017 hastanın dosyalarını geriye dönük olarak inceledik. ^{18}F-FDG PET çalışmalarında kolonda, karaciğer tutulumuna göre daha yoğun tek bir fokal ^{18}F-FDG tutulumu gösteren ve kolonoskopiye yönlendirilen hastalar olan çalışmaya alındı.

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Bulgular: Elli iki hastada (%83,8) kolonoskopide buna karşılık gelen en az 1 lezyon bulunurken, 10 hastada lezyon saptanmadı. Sonraki histopatolojik incelemelerde fokal ^{18}F-FDG tutulum bölgelerinin 13'ünde (%13,7) karşılık gelen lezyon izlenmedi, 18'inde (%18,9) benign lezyon, 10'unda hiperplastik polip (%10,5), 16'sında düşük dereceli polip (%16,8), 29'unda (%30,5) yüksek dereceli polip, 9'unda (%9,5) malign lezyon saptandı. Histopatoloji sonuçlarına göre malign ve benign olguların SUV_{maks} ölçümleri arasında istatistiksel olarak anlamlı fark bulunmazken (p>0,05), malign olguların ortalama SUV_{maks} ölçümleri düşük + yüksek gradlı olgulara (p<0,05) ve hiperplastik polip olgularına (p<0,01) göre anlamlı derecede yüksek bulundu.

Sonuç: Sonuç olarak, ^{18}F-FDG PET/BT çalışmalarında herhangi bir beklenmeyen fokal ^{18}F-FDG tutulumu malignite açısından şüphelidir ve kolonoskopi ile netleştirilmelidir. ^{18}F-FDG tutulumunun yoğunluğu kolonoskopi yapılmasını ve varsa lezyonun histopatolojik olarak doğrulanmasını engellemez.

Anahtar kelimeler: Gastrointestinal sistem, insidental olarak saptanan lezyonlar, kolon, insidental ^{18}F-FDG tutulumu

Inroduction

In imaging studies, an incidental finding, which is commonly named as "incidentaloma," is a lesion which is detected serendipitously and is of indeterminate clinical significance. ^{18}Fluorine-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) is increasingly being used as an imaging modality in oncology and this has led to an increasing number of focal ^{18}F-FDG-avid lesions in several organs including the thyroid gland, adrenal gland gastrointestinal tract, pituitary gland, prostate gland (1,2,3,4,5). Although identification of some of these findings may provide a chance to treat a secondary primary malignancy, in many cases, further studies done for exploration of these lesions might cause unnecessary anxiety in patients, complications from additional medical interventions and economic burden (6,7).

Physiologic colonic ^{18}F-FDG uptake is a commonly seen variant on PET scans and can be distinguished from malignant processes with its diffuse pattern. Segmental involvement of the colon in ^{18}F-FDG PET studies is suggestive for inflammatory process. Focal involvement of the colon leaves the interpreter with a dilemma since it has the potential for malignancy, while some of the benign lesions also show ^{18}F-FDG uptake. The prevalence of focal colonic incidentalomas detected by ^{18}F-FDG PET or PET/CT was found as 3.6% pooled risk of malignant or premalignant lesions was 68% (8). It can be deduced from all these facts that it is crucial to know the malignancy rates of these lesions and distinguishing features on ^{18}F-FDG PET/CT, in order to make further management properly.

The aims of the present study were to identify the prevalence of focal uptake in the colon on ^{18}F-FDG PET/CT studies done for the evaluation of malignancies other than colon, rate of malignancy in incidental focal ^{18}F-FDG avid colonic lesions and to investigate any possible role of maximum standardized uptake value (SUV_{max}) values in the discrimination of malignant lesions from premalignant and benign ones.

Materials and Methods

Patient Population

We retrospectively reviewed the files of 8,017 patients with known or suspected malignancy, who underwent whole-body ^{18}F-FDG PET/CT at our institution during the period November 2017 to November 2019. Patients with a previous history of colorectal cancer and inflammatory bowel disease, were excluded from our study. Patients showing a single site of focally increased colonic ^{18}F-FDG uptake that was more intense compared to liver uptake on ^{18}F-FDG PET studies and referred to colonoscopy were enrolled in the study. Of the 8,017 patients, 62 (30 men, 32 women; age range, 19-88 y; mean age, 63.66±10.09 y) met these criteria. The type and frequencies of primary malignancies are given in Table 1. Ethical approval was obtained from the Ethics Committee of University of Health Sciences Turkey, Prof. Dr. Cemil Tascioglu City Hospital (protocol number: E-48670771-514.10).

PET/CT Protocol: Imaging and Interpretation

Patients were imaged using an integrated PET/CT scanner that consisted of a full-ring HI-REZ LSO PET and a six-slice CT scanner (Siemens Biograph 6, Chicago, IL, USA).

Patients were instructed to fast, for 4-6 h before the injection of 370-555 MBq (10-15 mCi) of ^{18}F-FDG. All patients were administered oral contrast starting 4 h before the study. Blood glucose levels were measured before the study and ^{18}F-FDG was injected only when the blood glucose level was below 11.11 mmol/L. At 60 min post-injection, PET/CT scan was conducted with an emission time of 3 min per bed position from the vertex to the upper thigh. Before emission images, a low-dose CT scan was performed for attenuation correction and anatomical localization with the following parameters: 50 mA, 140 kV, and 5 mm section thickness. Image analysis was carried out on the Esoft multimodality computer platform (Siemens Medical Solutions, Erlangen, Germany). All images were reassessed by two experienced nuclear medicine physicians who were unaware of the endoscopic and histopathologic results.

Table 1. Baseline features of the patients and their incidental lesions

		n (%)
Age (year)	Min-max	19-88 (64.5)
	Mean ± SD	62.84±11.54
Sex (n=62)	Male	32 (51.6)
	Female	30 (48.4)
Location in colon	Rectum	24 (25.3)
	Sigmoid colon	22 (23.2)
	Descending colon	13 (13.7)
	Transverse colon	12 (12.6)
	Ascending colon	13 (13.7)
	Cecum	7 (7.4)
	Anal region	4 (4.2)
SUV_{max}	Min-max	0-49.8
	Mean ± SD	7.51±8.05
Histopathology	Physiologic	13 (13.7)
	Benign	18 (18.9)
	Hyperplastic polyp	10 (10.5)
	Low grade	16 (16.8)
	High grade	29 (30.5)
	Malignant	9 (9.5)
Size	<1 cm	25 (26.3)
	1-3 cm	37 (38.9)
	3-5 cm	4 (4.2)
	>5 cm	18 (18.9)
	N/A	11 (11.6)
Primary malignancy	Endometrium carcinoma	6 (9.7)
	Breast carcinoma	12 (19.4)
	Carcinoma of unknown primary	9 (14.5)
	Lymphoma	6 (9.7)
	Lung cancer	9 (14.5)
	Neuroendocrine tumor	1 (1.6)
	Testis carcinoma	2 (3.2)
	Gastric carcinoma	2 (3.2)
	Renal cell carcinoma	1 (1.6)
	Pancreas carcinoma	3 (4.8)
	Cholangiocarcinoma	1 (1.6)
	Larynx carcinoma	2 (3.2)
	Cervix carcinoma	2 (3.2)
	Ovarian carcinoma	1 (1.6)
	Skin cancer	4 (6.4)
	Multiple myeloma	1 (1.6)

Min: Minimum, Max: Maximum, SD: Standard deviation, SUV_{max}: Maximum standardized uptake value

Focal suspicious colorectal ^{18}F-FDG uptake sites showing intense activity compared with the liver were recorded, whereas diffuse and segmental uptake sites were excluded.

Regions of interest were manually drawn in transaxial slices encircling the focal activity to measure the SUV_{max} as a semiquantitative index. The colon was divided into 7 anatomical segments as the rectum, sigmoid colon, descending colon, transverse colon, ascending colon, cecum, anal region. The lesions are classified according to their locations in these segments by using the body low-dose CT component.

We accepted a findings in PET/CT results as true-positive when focal ^{18}F-FDG uptake corresponded to a certain lesion in endoscopic or surgical evaluation. When no solid lesion was detected with these evaluations, the cause of the ^{18}F-FDG uptake was attributed to physiologic accumulation of activity and the result was interpreted as false-positive. The true-positive lesions were further categorized as benign, premalignant and malignant.

Colonoscopic and Histopathological Evaluation

Histopathologic evaluation of the lesions following colonoscopy was used as the gold standard and performed in all patients within 60 days of the PET/CT scan. Biopsy or excision of the 95 lesions corresponding to the focal ^{18}F-FDG uptake sites was performed. The descriptions of the lesions were also done morphologically during colonoscopy and the lesions were reported as polyp, mass lesion, diverticulum, hemorrhoid, ulcerovegetative mass, radiation colitis, rectovaginal fistula and ulcer. Any ^{18}F-FDG uptake focus without a corresponding lesion on colonoscopy and negative histopathological result was considered as physiological.

On histopathological evaluation, the lesions are categorized as physiological; benign; hyperplastic polyp; low-grade polyp; high-grade polyp and malignant. The lesions were also categorized according to their dimensions as 1 cm >; 1-3 cm; 3-5 cm; 5 cm <.

Statistical Analysis

Number Cruncher Statistical System 2007 & PASS (Power Analysis and Sample Size) 2008 Statistical Software (Utah, USA) program was used for statistical analysis. While evaluating the study data, in addition to descriptive statistical methods (mean, standard deviation, median, frequency, ratio), Shapiro-Wilk test and box plot graphs were used for the normal distribution of variables. Mann-Whitney U test was used for intergroup comparisons of parameters not showing normal distribution. Spearman's correlation analysis was used to evaluate the relationships between variables. Receiver operating characteristic (ROC)

curve analysis and diagnostic screening tests were used to determine the cut off for the SUV_{max} value. Significance was evaluated at the $p<0.05$ level.

Results

Of the 8,017 PET/CT scans performed during the study period, 95 focally increased colonic ^{18}F-FDG uptake was found in 62 (0.77%) patients. Among these 62 patients showing focal ^{18}F-FDG uptake, 52 patients (83.8%) had at least 1 corresponding lesion in colonoscopy, whereas in 10 patients no lesion was detected. Of the 95 hypermetabolic foci, 7 were in the cecum, 13 in the ascending colon, 12 in the transverse colon, 13 in the descending colon, 22 in the sigmoid colon, 24 in the rectum and 4 in the anal region. Subsequent histopathological examinations revealed no corresponding lesion in 13 (13.7%), a benign lesion in 18 (18.9%), hyperplastic polyp in 10 (10.5%), low-grade polyp in 16 (16.8%), high-grade polyp in 29 (30.5%) and malignant lesion in 9 (9.5%) of the focal ^{18}F-FDG uptake sites. So a premalignant lesion (high grade polyp + low grade polyp) and a malignant lesion were detected in totally 54 (56.8%) of the suspicious hypermetabolic foci.

Malignant and Premalignant Lesions

The malignant lesions were found in the descending colon in 3 (33.3%), transverse colon in 3 (33.3%), rectum in 2 (22.2%) and the sigmoid colon in 1 (11.1%) cases (Figure 1). SUV_{max} in malignant lesions was 14.41±14.4 (0-49.8) on average. The size of the malignant lesions was 4.56±1.32 (2.5-5.5) cm on average. The distribution of 45 premalignant lesions detected on colonoscopy were 14 in sigmoid (31.1%), 7 in the rectum (15.5%), 8 in the ascending colon (17.7%), 7 in the descending colon (15.5%), 6 in transverse colon (13.3%), 3 in the cecum (6.6%). Histopathologic examination revealed 29 high-grade and 16 low-grade polyps (n=24 tubuler adenoma; n=21 tubulovillous adenoma) showing ^{18}F-FDG uptake with an average SUV_{max} of 6.54±7.87 (0-27) and size of 1.41±1.13 (0.5-5.5) (Figure 2).

Hyperplastic Polyps

The distribution of 10 hyperplastic polyps among the colon segments was as follows: 5 lesions in the rectum (50%), 2 in the ascending colon (20%), 1 in the cecum (10%), one in the descending colon (10%) and 1 in sigmoid (10%). SUV_{max} in hyperplastic polyps was 2.76±5.12 (0-16.3) on average.

Physiologic Uptake and Benign Lesions

Histopathologic examinations revealed benign inflammatory pathologies in 18 of the lesions. Activated ulcerative colitis was the cause in 2 lesions (11.1%). Granulation was detected in the ulcerous ground in 5 lesions (27.7%). In 2 patients who had undergone radiotherapy for gynecological malignancies, radiation colitis was detected (11.1%). Diverticula was detected in the descending colons of 2 patients (11.1%). Hemorrhoids in the lower rectum was seen in 4 patients and rectovaginal fistulas in 1 patient (5.5%). Tuberculous ulcers were the cause in two incidental ^{18}F-FDG uptake sites (11.1%) (Figure 3). SUV_{max} in

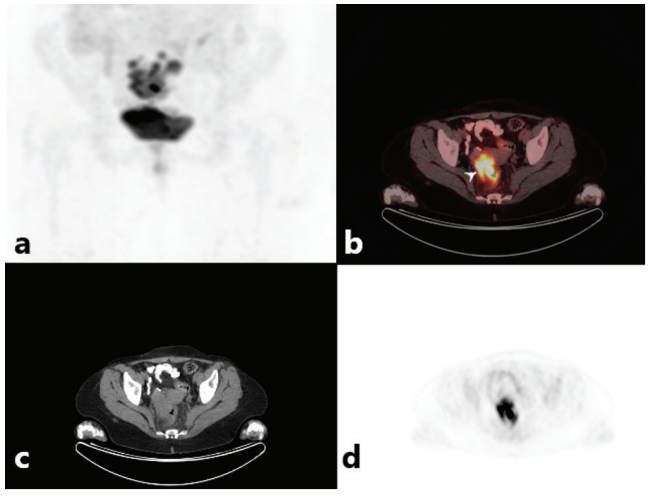

Figure 1. MIP (a), axial fusion, CT and PET (b, c, d) images of a 31-year-old female patient who underwent ^{18}F-FDG PET/CT scanning for breast cancer revealed intense ^{18}F-FDG avid mass (SUV_{max}: 12.7) in sigmoid colon (arrow head) which turned out to be an adenocarcinoma of the colon
CT: Computed tomography, PET: Positron emission tomography, ^{18}F-FDG: ^{18}Fluorine-fluorodeoxyglucose, SUV_{max}: Maximum standardized uptake value

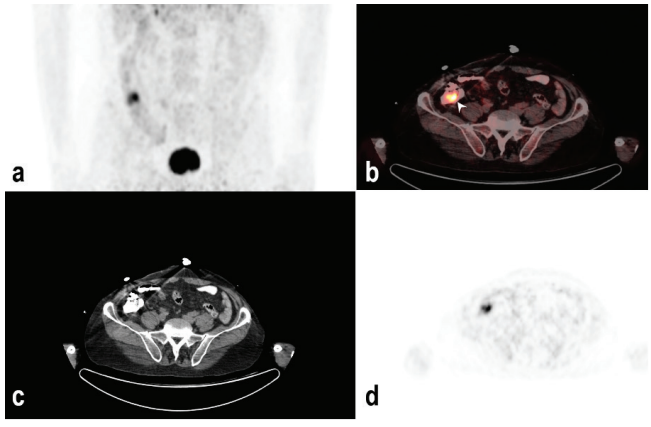

Figure 2. MIP (a), axial fusion, CT and PET (b, c, d) images of a 61-year-old male patient who underwent ^{18}F-FDG PET/CT scanning for malignant melanoma, revealed incidental focal ^{18}F-FDG uptake (SUV_{max}: 8.1) in ascending colon (arrow head). It was a polyp 4 cm in diameter and after excision histopathology of the lesion turned out to be a polyp with high grade dysplasia
CT: Computed tomography, PET: Positron emission tomography, ^{18}F-FDG: ^{18}Fluorine-fluorodeoxyglucose, SUV_{max}: Maximum standardized uptake value

these benign lesions was 7.88±5.09 (2.9-24.6) on average. In 13 of the hypermetabolic foci, colonoscopy revealed no corresponding lesions and the activity accumulations at these sites are attributed to physiologic uptake. The average SUV_{max} values at these false positive uptake sites were 9.22±4.88 (3.8-18.4). The average SUV_{max} in all lesions was 7.51±8.05 (0-49.8) (Figure 4).

According to histopathology results, statistically no significant difference was found between the SUV_{max} measurements of malignant and benign cases ($p>0.05$). The average SUV_{max} measurements of malignant cases were found to be significantly higher than low + high-grade cases ($p<0.05$) and hyperplastic polyp cases ($p<0.01$).

Based on this significance, it was considered to determine the cut-off point for SUV_{max} in detecting malignant cases. ROC analysis was used to determine the cut off point according to the groups.

For the 5.2 cut-off value of SUV_{max} measurement; sensitivity, specificity, positive predictive value (PPV), negative predictive value and accuracy in the discrimination between malignant and low + high-grade groups were 88.9%, 62.2%, 32%, 96.6%, 85.2% respectively. The ODDS rate for SUV_{max} measurement is 12.00 [95% confidance interval (CI): 1.38-104.3] that means that the risk of malignancy is 12 times higher in patients with SUV_{max} level of 5.2 and above.

When discrimination between malignant and hyperplastic polyp groups was concerned, for the 5.2 cut-off value of SUV_{max} measurement; sensitivity, specificity, PPV, negative predictive value and accuracy were 88.9%, 90%, 88.9%, 90%, 84.2% respectively.

A statistically significant difference was found between SUV_{max} measurements according to lesion size ($p<0.01$). SUV_{max} measurement of cases with a lesion size less than 1 cm was found to be statistically significantly lower than other dimensions.

According to histopathology results, size measurements of malignant cases were found to be significantly higher than premalignant cases ($p<0.05$).

Discussion

Focal incidental ^{18}F-FDG uptake is a commonly encountered finding in PET/CT studies done of various oncologic diseases. Sone et al. (9) reported that in 6.7% of the PET/CT studies incidental finding is seen and in 2.2% of all patients, histopathology revealed malignancy in incidental lesions. The most commonly detected sites for these incidental lesions were the colon, lung and stomach (9).

In patients with more than one malignancies, although the prognosis becomes poorer, early detection of the second primary cancer improves the overall outcome (10,11). Adams et al. (6) reported that at least 1 incidental finding was reported in the findings section of 74.9% of PET/CT reports, resulting in a substantial additional cost per PET/CT study. So it becomes crucial to decide when to make suggestions for further investigations in the evaluation of incidental findings instead of follow-up and this requires knowledge of its differential diagnosis, the possibility of malignancy and other PET/CT criteria, which can be used in the characterization of the finding (12).

In our study, incidental colorectal uptake of ^{18}F-FDG was found in 62 of 8,017 patients who underwent ^{18}F-FDG PET/CT studies. In a meta-analysis comprising 32 studies,

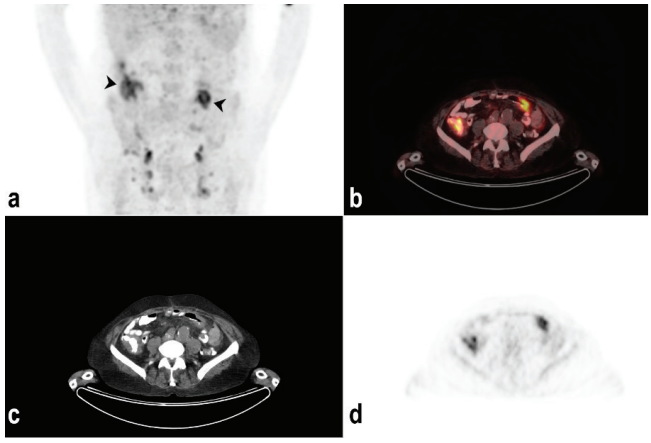

Figure 3. MIP (a), axial fusion, CT and PET (b, c, d) images of a 74-year-old male patient who underwent ^{18}F-FDG PET/CT scanning for search of carcinoma of unknown primary, revealed focal ^{18}F-FDG uptake in walls of cecum (SUV_{max}: 6.6) and transverse colon (SUV_{max}: 7.5) (arrow heads). Histopathological evaluation done following endoscopy showed that the lesions were tuberculous ulcers

CT: Computed tomography, PET: Positron emission tomography, ^{18}F-FDG: ^{18}Fluorine-fluorodeoxyglucose, SUV_{max}: Maximum standardized uptake value

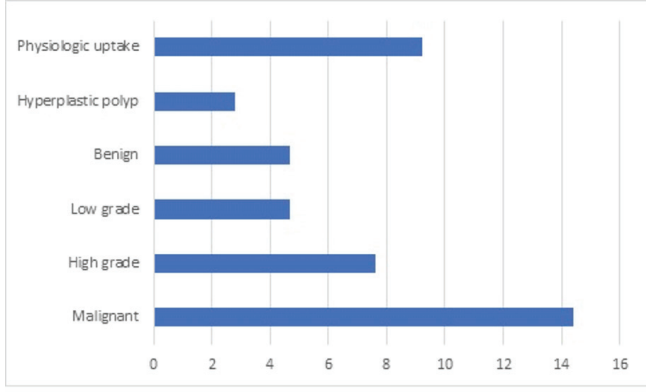

Figure 4. Distribution of SUV_{max} values according to histopathology

SUV_{max}: Maximum standardized uptake value

a pooled prevalence of 3.6% (0.4-16.3%) was reported for focal incidental colonic uptake (8). Initial detection rate of incidental colonic findings might be as high as 10% due to the high mean age of the patients included (13). Lower levels of incidental detection rate of 1.17% was also reported, which is attributed to the inclusion criteria of the study that restricted patients only to meet the strict criteria for focal colonic uptake (14).

In our study, among the patients showing focal ^{18}F-FDG uptake, 83.8% had at least 1 corresponding lesion in colonoscopy, either benign or malign, whereas in 10 patients (16.2%) no lesion was detected. On lesion-based analysis 13 of the 95 (13.7%) focal uptake sites represented physiologic accumulation with no corresponding lesion. Although physiological activities are generally seen in diffuse pattern and therefore not included in studies on incidental ^{18}F-FDG uptake, they can also be seen as a focal involvement. In the past studies, no correlative lesions were detected at endoscopy in 13.7-56% of patients with focal colorectal uptake of ^{18}F-FDG who underwent colonoscopy (13,15,16,17,18). Although the mechanisms of this physiologic intestinal activity are not established clearly, several studies have suggested that the gut microbiota, peristaltic activity in muscles, presence of lymphoid tissue, high concentration of WBCs in the bowel wall, ^{18}F-FDG secreting cells in the wall of the intestines, is responsible (18,19,20,21,22).

A premalignant lesion (high grade polyp + low grade polyp) and a malignant lesion were detected in totally 54 (56.8%) of suspicious hypermetabolic foci. This finding was consistent with the literature; Treglia et al. (8) conducted a systematic review and meta-analysis of incidental focal colonic uptake among 89,061 patients evaluated by ^{18}F-FDG PET or PET/CT and they found the pooled risk of malignant or premalignant lesions as 68% [95% CI (60-75%)]. Another study conducted by Treglia et al. (17), reported malignant or premalignant lesions in 64% of the patients who underwent further investigations. The rate of false positivity can be related to the reference activity chosen for comparison to accept a lesion as positive. Liu et al. (23) reported colon cancer in 10 out of 24 (PPV: 42%) patients who showed incidental focal ^{18}F-FDG uptake in ^{18}F-FDG PET/CT studies, which means that 58% of lesions were false positive. They explained this relatively high false positivity by taking the comparison of focal ^{18}F-FDG activity with blood pool activity as criteria for positive focal ^{18}F-FDG (23). The authors compared their results with Cho et al.'s (24) study in which also low levels of PPV were reported (51.6%) and they attributed this to the definition of a positive criterion on imaging findings with SUV_{max} >3.5.

In our study, focal suspicious colorectal ^{18}F-FDG uptake sites showing intense activity compared with the liver were accepted as positive focal ^{18}F-FDG. So given that mean SUV_{max} value of liver is 2.89±1.26 (1.30-5.2) in our study, we can postulate that the false positivity rate (43.2%) could be lower if we accepted a higher reference SUV_{max} value.

As an indicator of metabolic activity, SUV_{max} value of lesions has been proposed as a semiquantitative index that can be helpful in the discrimination of benign and malignant lesions in oncologic PET/CT studies. When the colonic incidentalomas concerned, previous studies report that SUV_{max} value is unreliable enough to be used in the differentiation of malignant, premalignant and benign lesions because of significant overlap between SUV_{max} of benign and malignant lesions. Indeed, some of these previous studies have reported differences in SUV_{max} measurements between malignant and benign lesions or physiologic uptake, but none of them claimed that this difference in SUV_{max} precludes colonoscopy (18,25,26,27,28). Several studies have shown no statistical differences in SUV_{max} between true and false positive uptake sites (17,29,30). There have been made to determine a certain cut-off value for SUV_{max} in the discrimination of malignant and benign lesions; Luboldt et al. (28) proposed optimal SUV_{max} threshold of 5. However, their results were not confirmed by a study by Rigault et al. (31) in which they reported 14 advanced neoplasias with SUV_{max} values ≤5.

Hoeij et al. (25) reported sensitivity 80%, specificity 82%, PPV 34%, negative predictive value 98% in the discrimination of malignant and benign incidental colonic lesions when the optimal cut-off value was taken as 11.4. Although the authors stated that all incidental focal lesions showing ^{18}F-FDG uptake with a SUV_{max} ≥11.4 should be examined by colonoscopy without delay, they concluded that SUV_{max} alone is not sufficiently discriminative to differentiate malignant, premalignant and benign lesions (25).

We could not find any significant difference between the SUV_{max} measurements of malignant and benign cases. When these benign lesions were overviewed; activated ulcerative colitis was the cause in 2 lesions of a patient, radiation colitis was detected in two patients who had undergone radiotherapy for gynecological malignancies and diverticula were detected in the descending colon of 2 patients. Although these lesions are not discriminated from malignancies due to their metabolic activity, when the morbidity of these lesions is regarded, early detection of them with ^{18}F-FDG PET/CT becomes crucial (32).

Depending on the statistically significant high values of SUV_{max} in malignant cases compared with low + high grade cases and hyperplastic polyp cases, we tried assessing the threshold of SUV_{max} to differentiate the malignant cases and we found that above 5.2 the malignancy is detected with a sensitivity and specificity of 88.9% and 62.2% compared with low + high grade groups and 88.9% and 90%, when compared with hyperplastic polyp groups. Although these values seem to be high, given that 12 out of 18 benign lesions and 10 out of 13 physiologic uptake sites exhibit SUVmax values more than 5.2, in line with the literature, this cut-off value cannot be set as a strict threshold for the discrimination of malignant lesions.

Study Limitations

Our study has some limitations. First, it was limited by its retrospective and single center design. We couldn't detect the sensitivity of ^{18}F-FDG PET/CT in the identification of colonic neoplasms since whole lesions found in colonoscopy whether they were ^{18}F-FDG avid or not are not recorded. All patients were administered oral contrast before the study as a part of routine applications in our PET/CT studies in our department. This might be mentioned as a limitation since it might have caused artefacts in the PET images, but these artefacts were distinguished from unusual focal ^{18}F-FDG uptake with their diffuse patterns, and any misinterpretations were avoided. Administration of negative contrast material like water to improve bowel distention might have been more appropriate in this kind of study.

Conclusion

In conclusion, any unexpected focal ^{18}F-FDG uptake in ^{18}F-FDG PET/CT studies is suspicious for malignancy and should be clarified by colonoscopy. The intensity of ^{18}F-FDG uptake does not preclude the application of colonoscopy and histopathological verification of the lesion if there is any. SUV_{max} values more than 5.2 might only alert the physician to the higher risk of malignancy and force for urgent intervention.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Ethics Committee of University of Health Sciences Turkey, Prof. Dr. Cemil Tascioglu City Hospital (protocol number: E-48670771-514.10).

Informed Consent: Retrospective study.

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Authorship Contributions

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References

1. Kamakshi K, Krishnamurthy A, Karthik V, Vinodkumar P, Kumar RK, Lakshmipathy KM. Positron emission tomography-computed tomography-associated incidental neoplasms of the thyroid gland. World J Nucl Med 2020;19:36-40.
2. Akkuş G, Güney IB, Ok F, Evran M, Izol V, Erdoğan Ş, Bayazıt Y, Sert M, Tetiker T. Diagnostic efficacy of 18F-FDG PET/CT in patients with adrenal incidentaloma. Endocr Connect 2019;8:838-845.
3. Servente L, Gigirey V, García Fontes M, Alonso O. Incidental focal colonic uptake in studies (18)F-FDG PET/CT. Rev Esp Med Nucl Imagen Mol 2018;37:15-19.
4. Miljić D, Manojlović-Gačić E, Skender-Gazibara M, Milojević T, Bogosavljević V, Kozarević N, Petrović N, Stojanović M, Pekić S, Doknić M, Petakov M, Popović V. All that glitters on PET is not cancer! 18F-deoxy-glucose avidity versus tumor biology: pituitary incidentaloma in a survivor of two previous unrelated malignancies. Endokrynol Pol 2017;68:352-359.
5. Mannas MP, Lee T, Pourghiasian M, Wilson DC, Black PC. Incidentalomas of the prostate detected by 18-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography. Can Urol Assoc J 2020;14:180-184.
6. Adams SJ, Rakheja R, Bryce R, Babyn PS. Incidence and economic ımpact of ıncidental findings on 18 F-FDG PET/CT imaging.Can Assoc Radiol J 2018;69:63-70.
7. Ding A, Eisenberg JD, Pandharipande PV. The economic burden of incidentally detected findings. Radiol Clin North Am 2011;49:257-265.
8. Treglia G, Taralli S, Salsano M, Muoio B, Sadeghi R, Giovanella L. Prevalence and malignancy risk of focal colorectal incidental uptake detected by (18)F-FDG-PET or PET/CT:a meta-analysis. Radiol Oncol 2014;48:99-104.
9. Sone Y, Sobajima A, Kawachi T, Kohara S, Kato K, Naganawa S. Ability of 18-fludeoxyglucosepositron emission tomography/CT to detect incidental cancer. Br J Radiol 2014;87:20140030.
10. Choy AT, van Hasselt CA, Chisholm EM, Williams SR, King WW, Lİ AK. Multiple primary cancers in Hong Kong Chinese patients with squamous cell cancer of the head or neck. Cancer 1992;70:815-820.
11. Wu B, Cui Y, Tian J, Song X, Hu P, Wei S. Effect of second primary cancer on the prognosis of patients with non-small cell lung cancer. Thorac Dis 2019;11:573-582.
12. Pencharz D, Nathan M, Wagner TL. Evidence-based management of incidental focal uptake of fluorodeoxyglucose on PET-CT. Br J Radiol 2018;91:20170774.
13. Farquharson AL, Chopra A, Ford A, Matthews S, Amin SN, Noronha RD. Incidental focal colonic lesions found on (18)fluorodeoxyglucose positron emission tomography/computed tomography scan: further support for a national guideline on definitive management. Colorectal Dis 2012;14:56-63.
14. Fuertes J, Montagut C, Bullich S, Coma MI, Mestre-Fusco A, Suárez-Piñera M, Trampal C, Bellmunt J. Incidental focal uptake in colorectal location on oncologic ^{18}FDG PET and PET/CT studies: histopathological findings and clinical significances. Rev Esp Med Nucl Imagen Mol 2015;34:95-101.

15. Putora PM, Müller J, Borovicka J, Plasswilm L, Schmidt F. Relevance of incidental colorectal FDG-PET-CT-enhanced lesions. Onkologie 2013;36:200-204.
16. Peng J, He Y, Xu J, Sheng J, Cai S, Zhang Z. Detection of incidental colorectal tumours with 18F-labelled 2-fluoro-2- deoxyglucose positron emission tomography/computed tomography scans: results of a prospective study. Colorectal Dis 2011;13:374-378.
17. Treglia G, Calcagni ML, Rufini V, Leccisotti L, Meduri GM, Spitilli MG,Dambra DP, De Gaetano AM, Giordano A. Clinical significance of incidental focal colorectal (18)F-fluorodeoxyglucose uptake: our experience and a review of the literature. Colorectal Dis 2012;14:174-180.
18. Gutman F, Alberini JL, Wartski M, Vilain D, Le Stanc E, Sarandi F. Incidental colonic focal lesions detected by FDG PET-CT. AJR Am J Roentgenol 2005;185:495-500.
19. Kang JY, Kim H , Chang Y, Yun Y, Ryu S, Shin H, Kim HL. Gut microbiota and physiologic bowel (18)F-FDG uptake. EJNMMI Res 2017;7:72.
20. Delbeke D. Oncological applications of FDG PET imaging: brain tumors, colorectal cancer, lymphoma and melanoma. J Nucl Med 1999;40:591-603.
21. Engel H, Steinert H, Buck A, Berthold T, Böni HRA, von Schulthess GK. Whole-body PET: physiological and artifactual fluorodeoxyglucose accumulations. J Nucl Med 1996;37:441-446.
22. Strauss LG. Fluorine-18 deoxyglucose and falsepositive results: a major problem in the diagnosticsof oncological patients. Eur J Nucl Med 1996;23:1409-1415.
23. Liu T, Behr S, Khan S, Osterhoff R, Aparici CM. Focal colonic FDG activity with PET/CT: guidelines for recommendation of colonoscopy. World J Nucl Med 2015;14:25-30.
24. Cho SH, Kim SW, Kim WC, Park JM, Yoo IeR, Kim SH, Oh ST. Incidental focal colorectal 18F-fluorodeoxyglucose uptake on positron emission tomography/computed tomography. World J Gastroenterol 2013;19:3453-3458.
25. Hoeij FB, Keijsers RG, Loffeld BC, Dun G, Stadhouders PH, Weusten BL. Incidental colonic focal FDG uptake on PET/CT: can the maximum standardized uptake value (SUVmax) guide us in the timing of colonoscopy? Eur J Nucl Med Mol Imaging 2015;42:66-71.
26. Weston BR, Iyer RB, Qiao W, Lee JH, Bresalier RS, Ross WA. Ability of integrated positron emission and computed tomography to detect significant colonic pathology: the experience of a tertiary cancer center. Cancer 2010;116:1454-1461.
27. Oh JR, Min JJ, Song HC, Chong A, Kim GE, Choi CSeo JH, Bom HS. A stepwise approach using metabolic volume and SUVmax to differentiate malignancy and dysplasia from benign colonic uptakes on 18F-FDG PET/CT. Clin Nucl Med 2012;37:134-140.
28. Luboldt W, Volker T, Wiedemann B, Zöphel K, Wehrmann U, Koch A, Toussaint T, Abolmaali N, Middendorp M, Aust D, Kotzerke J, Grünwald F, Vogl TJ, Luboldt HJ. Detection of relevant colonic neoplasms with PET/CT: promising accuracy with minimal CT dose and a standardised PET cut-off. Eur Radiol 2010;20:2274-2285.
29. Kei PL, Vikram R, Yeung HW, Stroehlein JR, Macapinlac HA. Incidental finding of focal FDG uptake in the bowel during PET Ğ CT: CT features and correlation with histopathologic results. AJR Am J Roentgenol 2010;194:401-406.
30. Israel O, Yefremov N, Bar-Shalom R, Kagana O, Frenkel A, Keidar Z, Fischer D. PET/CT detection of unexpected gastrointestinal foci of 18F-FDG uptake: incidence, localization patterns, and clinical significance. J Nucl Med 2005;46:758-762.
31. Rigault E, Lenoir L, Bouguen G, M, Lièvre A , Garin E, Siproudhis L, Bretagne JF. Incidental colorectal focal 18 F-FDG uptake: a novel indication for colonoscopy. Endosc Int Open 2017;5:924-930.
32. Kamel EM, Thumshirn M, Truninger K, Schiesser M, Fried M, Padberg B. Significance of incidental 18F-FDG accumulations in the gastrointestinal tract in PET/CT: correlation with endoscopic and histopathologic results. J Nucl Med 2004;45:1804-1810.