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Incidental focal 18F-FDG uptake in colorectal locations on PET/CT for oncologic reasons: pathologic correlation with endoscopic finding

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ABSTRACT

Aims: Incidental focal 18-fluorodeoxyglucose (18F-FDG) uptake in the colorectal region on positron emission tomography/computed tomography (PET/CT) may indicate premalignant lesions, such as adenomas or malignancies. Early detection and diagnosis are crucial for cancer prevention. This study aimed to assess the characteristics of incidental focal colonic FDG uptake associated with benign, premalignant, and malignant lesions, and to determine when colonoscopy is necessary.

Methods: A retrospective review of PET/CT reports was conducted on 5.380 patients with confirmed or suspected malignancies who underwent whole-body 18F-FDG PET/CT between January 2019 and April 2024. Patients exhibiting focal colonic 18F-FDG uptake and subsequently referred for colonoscopy were included in this study.

Results: Among 110 patients who underwent colonoscopy, 63 (57.3%) had adenomas and 14 (12.7%) had malignant tumors. The receiver operating characteristic (ROC) curve based on the maximum standardized uptake value (SUVmax) showed an AUC of 0.958. A cutoff value of 13.80 was optimal for distinguishing malignant lesions from nonmalignant lesions, with a sensitivity of 92%, specificity of 89%, positive predictive value of 56%, and negative predictive value of 98%. The SUVmax significantly differentiated malignancy from other colonoscopic findings ($p<0.001$). No significant differences were observed between adenomas and benign or physiological findings ($p>0.05$).

Conclusion: The colonoscopy results indicated that malignant lesions had significantly elevated SUVmax values compared to other lesion types or physiological uptake. However, the SUVmax was not sufficient to distinguish benign lesions from adenomas. Therefore, all incidental colonic findings should be thoroughly assessed, and lesions with SUVmax ≥13.80 should be promptly evaluated.

Keywords: PET/CT, focal uptake, SUVmax, colonoscopy, malignancy

INTRODUCTION

With its expanding role in diagnosing, staging, and evaluating treatment responses for a range of cancers, 18F-fluorodeoxyglucose (18-FDG) positron emission tomography/computed tomography (FDG PET/CT) has established itself as an invaluable tool.[1,2] The main radiotracer used in PET scans, 18F-fluorodeoxyglucose, is absorbed by different body tissues via glucose metabolism.

FDG PET/CT relies on the principle that cancer cells metabolize glucose more quickly than healthy cells, which serves as the foundation for its effectiveness in detecting malignant tissues.[3,4] However, malignancy is only one of the possible reasons for FDG uptake. Increased FDG uptake, which signals hypermetabolic activity, may also occur in nonmalignant conditions such as inflammation, infections, hyperplasia, and gastrointestinal polyps.[5] PET/CT scans conducted for different medical reasons may sometimes identify unexpected regions of elevated radiopharmaceutical uptake in the large intestine. Colorectal FDG uptake may occur in focal, segmental, and diffuse patterns. Focal uptake seen in the colorectal region is more often an indicator of actual lesions than physiological uptake, which usually appears as long-segment diffuse activity.[6] The early detection of 18F-FDG-avid lesions, whether neoplastic, preneoplastic, or related to inflammatory bowel disease, can significantly influence patient management and outcomes. Specifically, colonic adenomas have the potential to transition from benign to carcinoma, gradually advancing in asymptomatic patients.[7] The integrated PET/CT approach may enable the precise localization and characterization of abdominal FDG uptake, particularly in the intestine.

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A detailed meta-analysis, that examined 89.061 patients who underwent PET/CT for various reasons found that approximately 3.6% of the patients had incidental focal colonic uptake. Approximately one-third of the patients (n=1.044) underwent either colonoscopy or histopathological examination. The average risk of detecting premalignant and malignant lesions during colonoscopy was 68% (95% CI: 60-75%). Nevertheless, when evaluating the maximum standardized uptake value (SUVmax), there was a significant overlap in the mean values across benign, premalignant, and malignant lesions.[8]

Given the frequent discrepancy between focal colonic FDG uptake and the corresponding histopathological findings in previous studies, determining the need for additional diagnostic evaluations is challenging. Colonoscopy is an invasive medical procedure that carries potential risks such as bowel perforation, bleeding, and complications related to anesthesia.[9] A predictor of malignancy risk would be useful for assessing the urgency of performing colonoscopy. The SUVmax, which reflects the level of FDG uptake intensity, can be crucial for differentiating between nonmalignant and malignant lesions. Therefore, this study sought to evaluate PET-positive focal colonic uptake in a substantial patient population and to examine the relationship between the SUVmax and the results of the corresponding colonoscopy.

METHODS

Ethics

The Institutional of the Dr. Abdurrahman Yurtaslan Oncology Training and Research Hospital Non-interventional Clinical Researches Ethics Committee approved this study (Date: 28.12.2023, Decision No: 2023-12/118). For this retrospective study, informed consent was deemed unnecessary, and no personal data were exposed. All research followed the principles outlined in the Declaration of Helsinki.

Study Design and Patient Data

The electronic records of 5.380 patients aged ≥18 years who visited the Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital between January 2019 and April 2024 were retrospectively reviewed. The reason for PET/CT application in these patients was either to stage existing malignant diseases or to investigate primary cancers when metastatic sites were found in imaging studies. Patients diagnosed with colorectal cancer or with a known history of inflammatory bowel disease were excluded from this study. All PET/CT records reported by nuclear medicine specialists with more than a decade of experience were reviewed for incidental focal uptake in the colorectal region. Focal radiotracer accumulation between the anus and cecum was characterized as colonic 18-FDG uptake. Patients who underwent colonoscopy within the 90-day period following their PET/CT scans were documented. An independent researcher recorded data from the hospital system, including various factors such as age, sex, reason for undergoing a PET scan, type andz diagnosis of primary cancer, location of colonic findings, SUVmax of FDG, lesion size, and histological findings.

PET/CT Acquisition

Patients were advised to abstain from consuming any oral fluid containing glucose for six hours prior to FDG injection. Diabetic patients were instructed to discontinue oral hypoglycemic medications containing metformin for 48 hours before the scan in accordance with European Association of Nuclear Medicine (EANM) guidelines. Before the injection, the blood glucose levels were checked, and if values exceeding 200 mg/dl were detected, their appointments were rescheduled. The patient was administered an intravenous injection of 18F-FDG at a dose of 3.2-5.3 MBq/kg based on weight. PET/CT imaging was performed one hour after the injection of 18F-FDG, using a Siemens Biograph TruePoint 6 PET/CT system (Siemens Healthcare, USA) with three-dimensional capabilities. During the same session, simultaneous images were taken with a 3 mm sliced multidetector CT scanner and PET scanner. Attenuation correction and anatomical correlation were performed by using low-dose CT scans that did not require intravenous iodinated contrast.

Image Data Analysis and Endoscopic Correlation

The nuclear medicine specialists assessed both the PET and CT components utilized in this study. The axial, sagittal and coronal views of the PET and fused images were examined by readers. Intense focal bowel uptake was defined as any metabolic activity in the bowel that surpassed that observed in the normal hepatic tissue. The CT component of this study was used to evaluate any soft tissue abnormalities associated with regions that exhibited focal colorectal uptake. The SUVmax within a defined region of interest was measured using the attenuation-corrected PET component. In our study, histopathological diagnoses were categorized into three groups: malignant lesions, comprising primary carcinoma and metastatic gastrointestinal tract disease; premalignant lesions, encompassing adenomas with varying levels of dysplasia; and benign lesions, involving radiation proctitis and hyperplastic polyps. Physiological uptake was determined when focal bowel activity increased without any detectable mucosal or structural abnormalities during the colonoscopy. Uptake detected on PET/CT was confirmed as true-positive if it corresponded to an abnormality identified during colonoscopy. The true-positive results included benign, premalignant, and malignant lesions. In contrast, a false-positive result was identified as FDG uptake that did not correlate with an abnormality detected during colonoscopy, which was interpreted as a benign or physiological uptake. The size of the lesions detected during colonoscopy was also recorded.

Statistical Analysis

Data are presented as numerical values (percentages), mean ±standard deviation, and median (minimum-maximum). Differences in colonoscopic findings based on the SUVmax were evaluated using ANOVA and the Bonferroni posthoc test. To determine the ideal threshold for differentiating between malignant and nonmalignant lesions, a receiver operating characteristic (ROC) curve was employed. The SPSS software, version 27, was used for all statistical analyses. Statistical significance was set at $p<0.05$.

RESULTS

Between January 2019 and March 2024, 5.380 patients underwent PET/CT at the Abdurrahman Yurtaslan Oncology

Training and Research Hospital. Unexpected focal FDG uptake in the colon was observed in 211 (3.9%) patients. Of whom 163 (77%) underwent colonoscopy within 90 days of scanning. In total, 53 of 163 patients were excluded from our study because of a previously known colorectal malignancy or inflammatory bowel disease (Figure 1). Among the remaining 110 patients with focal FDG uptake, 88 (80%) had corresponding lesions identified during colonoscopy.

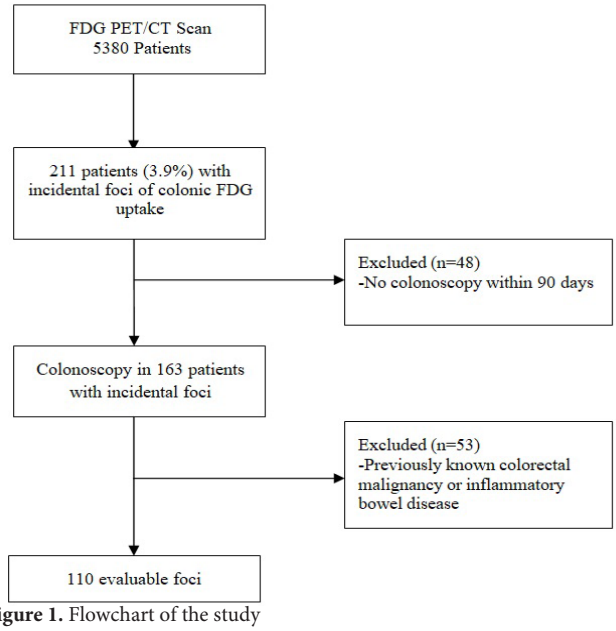

Figure 1. Flowchart of the study

Table 1 presents the baseline characteristics of the 110 patients with colonic FDG uptake along with the results of their corresponding colonoscopies and histopathological findings. Colorectal uptake was predominantly observed in the rectum (36.4%) and the sigmoid colon (35.5%). Histopathological examination of 18F-FDG uptake sites revealed that 22 patients (20%) had no corresponding lesions, 11 (10%) had benign lesions, 50 (45.5%) had adenomas with low-grade dysplasia (LGD), 13 (11.8%) had adenomas with high-grade dysplasia (HGD), and 14 (12.7%) had malignant lesions (Figure 2, 3). Therefore, 77 cases (70%) of incidental hypermetabolic foci were found to be premalignant (polyps with dysplasia) or malignant. In 9 of the 14 patients with malignancy, malignant lesions were determined either by measuring the long axis during colonoscopy or with histopathological assessment following surgery in patients with obstructive masses. The lesion sizes for the remaining five malignant cases could not be determined because of either obstruction caused by the mass during colonoscopy or inoperability of the patient. The average longest dimension of malignant lesions was measured as 43.13±12.98 mm.

To assess the efficacy of SUVmax in differentiating between malignant and nonmalignant lesions, an ROC curve was constructed. The optimal cutoff SUVmax was 13.80, with a sensitivity of 92%, specificity of 89%, positive predictive value of 56%, and negative predictive value of 98%. The area under the curve was 0.958 (standard deviation ±0.018). Focal uptake with SUVmax ≥13.80 was strongly correlated with a high risk of malignancy (Figure 4).

Table 1. Characteristics of patients and their incidental lesions at baseline (n=110)

		n (%)
Age(years)	Min-max	35-85
	Mean±SD	66.56±8.58
Sex	Male	61 (55.5)
	Female	49 (44.5)
Location	Rectum	40 (36.4)
	Sigmoid colon	39 (35.5)
	Descending colon	7 (6.4)
	Splenic flexure	3 (2.7)
	Transvers colon	4 (3.6)
	Hepatic flexure	5 (4.5)
	Ascending colon	9 (8.2)
	Cecum	3 (2.7)
SUVmax	Min-max	3.02-27.96
	Mean±SD	11.30±5.70
Histopathology	Physiologic	22 (20)
	Benign*	11 (10)
	Malignant	14 (12.7)
	Adenoma with LGD	50 (45.5)
	Adenoma with HGD	13 (11.8)
Size (mm, mean±SD)	Malignant†	43.13±12.98
	Adenoma with LGD	12.08±9.56
	Adenoma with HGD	27.92±11.37
Primary malignancy	Lung cancer	25 (22.7)
	Skin cancer	9 (8.2)
	Pituitary gland tumor	1 (0.9)
	Larynx carcinoma	5 (4.5)
	Lymphoma	2 (1.8)
	Carcinoma of unknown primary	28 (25.5)
	Breast carcinoma	17 (15.5)
	Gastric carcinoma	7 (6.4)
	Multiple myeloma	4 (3.6)
	Ovarian carcinoma	5 (4.5)
	Pancreas carcinoma	4 (3.6)
	Renal cell carcinoma	1 (0.9)
	Cervix carcinoma	1 (0.9)
	Thyroid carcinoma	1 (0.9)

Min: Minimum, Max: Maximum, SD: Standard deviation, SUVmax: Maximum standardized uptake value, LGD: Low-grade dysplasia, HGD: High-grade dysplasia, *Benign: Hyperplastic polyp (n=6), radiation proctitis (n=2), solitary rectal ulcer syndrome (n=2), diverticulosis (n=1), †n=9

Table 2 shows the SUVmax values for lesions observed during colonoscopy. The SUVmax was significantly associated with distinguishing malignancy from other colonoscopic findings ($p<0.001$). Statistical significance was not observed between adenomas, regardless of the degree of dysplasia, or benign and physiological findings ($p>0.05$). The average SUVmax threshold indicative of colorectal cancer was determined to be 16.99±2.76 ($p<0.001$).

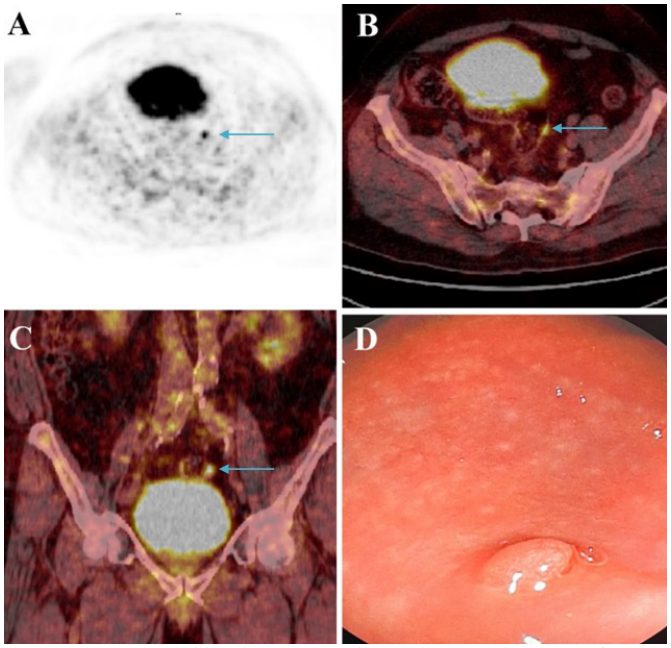

Figure 2. A 70-year-old male patient undergoing 18F-FDG PET/CT for lung cancer staging. (A-C) (blue arrows). Abnormal 18F-FDG PET/CT uptake in the sigmoid colon (SUVmax: 7.39). (D) Colonoscopy revealed a sessile polyp, and pathology confirmed the diagnosis of an adenomatous polyp with low-grade dysplasia

FDG: Fluorodeoxyglucose, PET/CT: Positron emission tomography/computed tomography, SUVmax: Maximum standardized uptake value

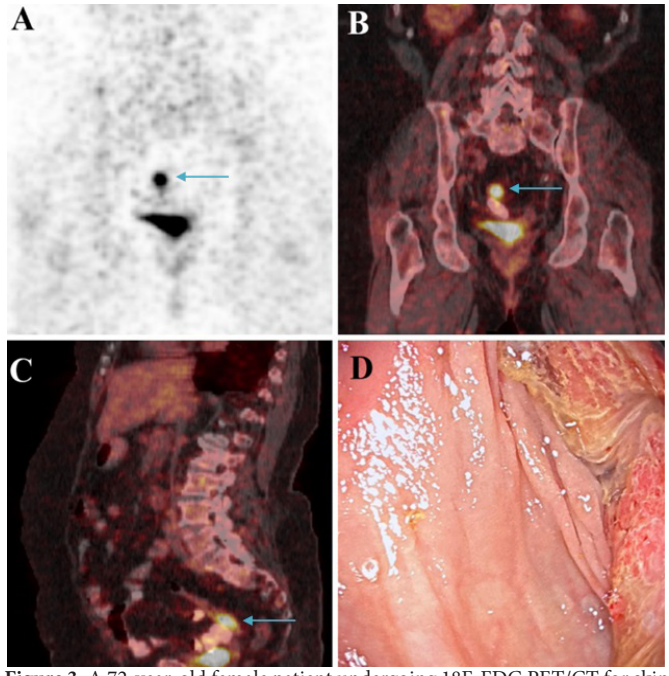

Figure 3. A 72-year-old female patient undergoing 18F-FDG PET/CT for skin cancer staging (A-C) (blue arrows). Abnormal 18F-FDG PET/CT uptake in the sigmoid colon (SUVmax: 18.01). (D) Colonoscopy revealed a mass in the sigmoid colon, and the pathological diagnosis confirmed adenocarcinoma

FDG: Fluorodeoxyglucose, PET/CT: Positron emission tomography/computed tomography, SUVmax: Maximum standardized uptake value

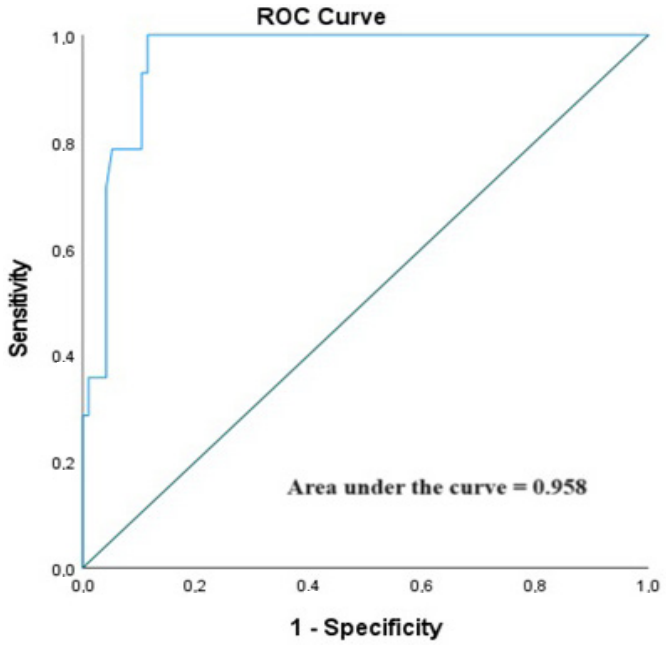

Figure 4. ROC curve analysis for differentiating malignant from nonmalignant incidental FDG-avid lesions in the colon on PET/CT, showing an area under the curve of 0.922. The optimal SUVmax threshold for distinguishing between malignant and nonmalignant incidental colonic lesions is 13.80, with a sensitivity of 92%, specificity of 88%, positive predictive value of 56%, and negative predictive value of 98%

ROC: Receiver operating characteristic, FDG: Fluorodeoxyglucose, PET/CT: Positron emission tomography/computed tomography, SUVmax: Maximum standardized uptake value

DISCUSSION

PET/CT is a noninvasive imaging technique used to diagnose and stage diseases, monitor treatment effectiveness, assess tumor aggressiveness, and delineate areas for radiotherapy.[10] Colonoscopy continues to be the leading screening method for colorectal cancer given its high sensitivity and specificity, enabling the early identification and removal of precursor lesions.[11] However, colonoscopy is a challenging procedure, given the associated risks and the demanding bowel preparation required. Therefore, determining which patients with focal colorectal 18F-FDG uptake on PET/CT scans should undergo further colonoscopic evaluation remains an ongoing debate.[12] Our study is one of the most extensive investigations of incidental focal colorectal uptake and its associated endoscopic findings.

In our investigation, the prevalence of incidental focal colorectal uptake was 3.9% (211/5.380), consistent with the 0.5%-3.6% range reported in other studies.[8,13] In a meta-analysis of 32 studies using colonoscopic or histopathological confirmation as the reference standard, focal FDG uptake was strongly associated with premalignant or malignant lesions (68%). Therefore, colonoscopy is recommended when a focal uptake is detected.[8] Similarly, in our study, 70% of 110 eligible lesions were malignant (12.7%, 14/110) or premalignant (57.3%, 63/110). The higher percentage of premalignant lesions

Table 2. Analysis of SUVmax based on colonoscopic findings

Variable	Colonoscopic findings			
	Benign + physiologic	Adenoma with LGD	Adenoma with HGD	Malignant
SUVmax	8.26±3.44	9.34±3.49	9.84±2.70	16.99±2.76[abc]

Data are presented as mean ± SD, SUVmax: Maximum standardized uptake value, SD: Standard deviation, LGD: Low-grade dysplasia, HGD: High-grade dysplasia, [a]Significantly different from benign + physiologic, [b]Significantly different from low-grade adenoma, [c] Significantly different from high-grade adenoma

compared to malignant lesions aligns with other studies, suggesting that colonoscopy should be performed for further assessment of focal hypermetabolism.[14,15]

Previous studies have reported that 14-38% of patients with focal colorectal FDG uptake who underwent colonoscopy showed no corresponding lesions during endoscopic examination.[16-18] In our study, while 80% of the 110 patients with focal FDG uptake had corresponding benign or malignant lesions detected during colonoscopy, 22 patients (20%) had no lesions despite thorough endoscopic examination, resulting in a false-positive rate of 20% for PET/CT lesions. Physiological uptake, transient inflammation, or FDG accumulation in gastrointestinal lymphoid tissue is a possible cause of false-positive lesions on PET/CT.[19] In cases of physiological uptake, FDG usually shows diffuse uptake in the gastrointestinal system; however, focal uptake can also occur. Physiological uptake in the colon may originate from factors such as smooth muscle contractions, activity in mucosa-associated lymphoid tissue, secretions, microbial metabolism, and FDG excretion.[20]

Adenomatous polyps in the colon are considered premalignant lesions, and their identification is crucial because early removal has been proven to greatly decrease the occurrence and fatality rates of colon cancer.[21] Traglia et al.[22] reported SUVmax values of 9.6±4.7 for malignant disease (n=12), 8.5±5.2 for adenomas (n=19), 6.5±3.6 for benign lesions (n=6), and 8.3±3.6 for normal colonoscopy groups (n=11). In a study by Gutman et al.,[23] SUVmax values were reported as 15±11.6 for malignant lesions (n=3), 12±3.7 for adenomatous polyps with HGD (n=4), 8.8±4.9 for adenomatous polyps with LGD (n=6), and 7.1±3.3 for lesions with negative colonoscopic findings (n=7). In a different study, Luboldt et al.[24] found that the SUVmax values for malignancy (n=23), adenomatous polyps with HGD (n=10), adenomatous polyps with LGD (n=25), and benign uptakes (n=48) were 11.9±6.8 and 11.6±4.1. In these studies, although SUVmax generally increased with progression from benign conditions to dysplasia, as well as from dysplasia to malignancy, the SUVmax values for various colonic lesions often overlapped significantly, making the differences between them statistically insignificant. According to our study, the mean SUVmax of colorectal malignancies was noticeably higher than that of all the other lesions. When comparing the benign-physiological and premalignant groups, statistical analysis revealed no significant difference in the SUVmax. Consistent with our findings, a study by Özarslan et al.[25] reported that among 84 patients with focal colonic uptake on PET/CT who underwent follow-up colonoscopy, the SUVmax was 15.0±10.6 for malignant disease, 10.2±4.3 for adenomas, 7.3±3.6 for inflammation, and 9.8±4.2 for normal endoscopy groups ($p<0.001$). Consequently, the overlap of SUVmax values among the different groups suggests that SUVmax is particularly crucial for diagnosing malignant diseases.

In a study conducted by Hosni et al.,[3] involving 32 individuals with focal uptake on PET/CT scans, an SUVmax value of 9.2 or higher demonstrated a high sensitivity (0.76) and specificity (0.885) for distinguishing malignant and premalignant lesions from benign uptakes. Lee et al.[13] reported that using an SUVmax threshold of 7.6 yielded a sensitivity of 0.686 and a specificity of 0.688 for distinguishing benign from cancer/precancerous lesions. In a study of 36 patients with focal uptake, Esmer et al.[26] identified an SUVmax cutoff point of 11.1 (sensitivity, 83.3%; specificity, 90%) using an ROC curve to distinguish benign from premalignant or malignant lesions. These studies showed no statistically significant differences in the average SUVmax values when comparing malignant and premalignant lesions. In our study, the absence of a significant difference in SUVmax between adenomas and benign-physiological uptake prevented the establishment of an effective SUVmax threshold for distinguishing cancer or precancerous lesions from benign lesions. Our findings suggest that focal colorectal uptakes with SUVmax ≥13.80 are significantly linked to an increased risk of malignancy and should be urgently assessed with colonoscopy, given their high sensitivity (92%) and specificity (89%). In a study by Van Hoeijet et al.[18] evaluating incidental focal colonic uptake detected by PET/CT in 7.318 patients, including 242 who underwent colonoscopy, it was emphasized that colonic focal uptakes with an SUVmax of ≥11.4 carry a high risk of malignancy, with 80% sensitivity and 82% specificity, and should be urgently evaluated with colonoscopy.

Limitations

A major strength of our study is that it has a larger sample size than most previous studies. However, its single-center design poses a limitation, potentially impacting the generalizability of the results. To minimize the heterogeneity among studies, a multicenter prospective study with uniform imaging protocols is required.

CONCLUSION

Our study revealed that colon malignancies had significantly higher SUVmax on FDG PET/CT than other lesion types, with a threshold of ≥13.80 effectively distinguishing malignant from benign lesions. However, as SUVmax cannot differentiate noncancerous uptake from adenomas, colonoscopy remains essential for evaluating incidental colonic hotspots, highlighting the need for advanced molecular probes in PET/CT imaging.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital Non-interventional Clinical Researches Ethics Committee (Date: 28.12.2023, Decision No: 2023-12/118).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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