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Colonoscopy following the positron emission tomography/computed tomography scan in patients with incidental colorectal uptake: what is the most effective management?

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SUMMARY

OBJECTIVE: Colorectal cancer is one of the most common malignancies. Survival rates are directly related to the stage of cancer at the time of diagnosis, emphasizing the value of early diagnosis. Positron emission tomography with 18F-fluorodeoxyglucose is the gold standard imaging technique in staging, monitoring after treatment, and follow-up. We aimed to assess the importance of incidental ^{18}F-fluorodeoxyglucose uptake by colon and rectum in positron emission tomography–computed tomography imaging to determine a significant cutoff value for further investigation using colonoscopy and histopathological assessment.

METHODS: We performed a retrospective analysis of patients with both ^{18}F-fluorodeoxyglucose-positron emission tomography/computed tomography scan and colonoscopy during 1 year and included the cases who had undergone a colonoscopy within 3 months following the positron emission tomography/computed tomography scan due to an incidental positive finding. Patients with a diagnosed colorectal malignancy or with a history of previous colorectal operations were excluded.

RESULTS: A total of 81 patients were included in this study. Among 81 colonoscopic evaluations, histopathology revealed malignancy in 8 patients, and the prevalence of incidental colorectal cancer ^{18}F-fluorodeoxyglucose uptake was found to be 9.87%. SUVmax was found to be significantly related to malignancy and other colonoscopic findings ($p<0.001$). SUVmax cutoff value to suggest colorectal cancer was found to be median [7.9 (4.1–12.7)] ($p<0.001$).

CONCLUSION: Regarding the studies determining a significant cutoff value, incidental colonic ^{18}F-fluorodeoxyglucose uptake on positron emission tomography/computed tomography should lead the clinician to further investigation with colonoscopic biopsy, although the cutoff values for SUVmax are not certain and different in almost every published study, and negative positron emission tomography.computed tomography findings should not completely rule out malignancy, especially in high-risk patients.

KEYWORDS: Colonoscopy. Colorectal cancer. Positron emission tomography. Screening.

INTRODUCTION

Colorectal cancer (malignancies of the colon and rectum, CRC) is the third most common malignancy in the world[1,2]. Adenomatous colorectal polyps are also considered malignant precursors of CRC[3]. Survival rates are directly related to the cancer stage at the time of diagnosis[4].

Colonoscopy is the gold standard screening method in CRC with high sensitivity and specificity, because it provides not only early detection of precursor lesions but also the ability to remove them[1]. For CRC, the main precursor lesion is adenomas[5]. Colorectal screening with colonoscopy reduces both CRC incidence and mortality. The decrease in these rates depends on the removal of the precursor lesion. In a recent systematic review and meta-analysis, Jodal et al. showed reduced CRC mortality in a 15-year follow-up with colonoscopy[6].

Positron emission tomography (PET-CT) with ^{18}F-fluorodeoxyglucose (FDG) is generally the gold standard imaging technique in staging, monitoring after treatment, and follow-up in cancer patients[7]. A whole body scan with PET-CT is performed for a cancer suspicion or the staging of a diagnosed cancer, and sometimes it may show an incidental FDG uptake in any part of the body. PET-CT is considered a useful technique in CRC and has been shown to have extra value in the detection of disease recurrence[8]. Following the first report by Yasuda et al. in 1998 showing an increased ^{18}F-FDG uptake in a colonic adenoma[9], several studies have evaluated its ability

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to detect CRC. Although a premalignant colorectal lesion can be incidentally detected by standard PET-CT performed for other indications, the technique is not recommended for routine CRC screening or initial diagnosis in patients with high suspicion of CRC[10]. PET-CT is not appropriate for the evaluation of the colonic wall for staging because of its limited resolution in bowel wall layers, and it may also be false positive in cases of colitis, diverticulitis, and even because of physiological colon metabolism and anal canal uptake[11]. Studies have shown that up to 45% of the patients with FDG uptake did not have any lesions in colonoscopic control[12].

Therefore, a possible optimal cutoff SUVmax value may be helpful. This study aimed to assess the importance of incidental FDG uptake by the colon and rectum in PET-CT imaging in patients with a non-CRC diagnosis and to determine a significant cutoff value for further investigation using colonoscopy and histopathological assessment as the gold standard.

METHODS

Following the approval of the local ethics committee, we performed a retrospective analysis of patients with both ^{18}F-FDG-PET/CT scan and colonoscopy during 1-year period (May 2021 to June 2022). The patients who had undergone colonoscopy within 3 months following the PET/CT scan due to an incidental positive finding were included in the study. Patients with a diagnosed colorectal malignancy or with a history of colorectal operation were excluded. In our study group, the PET/CT scans had been performed for staging or the evaluation of response to treatment or screening.

Protocols and criteria for 18F-fluorodeoxyglucose-positron emission tomography/computed tomography imaging

The 18F-FDG-PET/CT scanning was performed as a standard procedure, similar to the recent studies[13,14]. PET-CT scanning was performed using Philips Ingenuity TFÒ (Koninklijke Philips N.V., The Netherlands). The patients were included due to a follow-up because of a primary malignancy rather than a CRC or a suspicion of malignancy following laboratory tests or other imaging techniques. All the reports were reviewed by the same nuclear medicine specialist. Positive FDG findings were classified into patient demographics, the reason for undergoing the PET/CT scan, the localization of the suspected finding, and later to be matched with colonoscopic findings. A false positive PET/CT finding was defined if there were no colonoscopic findings on the colonic segment with abnormal FDG uptake, while a true positive PET/CT finding referred to a relevant colonoscopic finding.

Colonoscopic procedures

Colonoscopic procedures were carried out after adequate bowel preparation, with the addition of dietary recommendations, and performed by experienced endoscopists. A total colonoscopic procedure was defined as evaluating all colon parts adequately. Abnormal mucosal findings were excised or biopsied and sent for histopathological examination. Each specimen was studied by experienced pathologists. We included the procedures with a total colonoscopy with sufficient bowel cleaning and performed them within 3 months following the PET/CT scan with incidental positive findings. Colonoscopic findings were classified as normal, polyp, inflammation (diverticulitis), and malignancy. Patients with a history of colorectal operation were excluded.

The study was conducted according to the Declaration of Helsinki.

Statistical analysis

Data were shown in means of numbers (percentage), mean±standard deviation, and median (minimum-maximum). Statistical analysis was performed with the Kruskal-Wallis test. Conover's test of multiple comparisons was used to define the difference between the two groups. A ROC (receiver operating characteristic) curve was used to define a cutoff point for Suvmax value in patients with and without malignancy. A p-value less than 0.05 was accepted as statistically significant. The IBM SPSS Statistics 26.0 software was used for statistical analysis (SPSS, Inc., version 26.0, Chicago, IL, United States).

RESULTS

Our retrospective study included a total of 81 patients (43 men and 38 women) with a mean age of 60,741 (±14,207) years.

In 1-year period, a total of 7,097 PET/CT scans and 17,144 colonoscopic procedures had been performed in our tertiary center. The most common indication for performing the PET/CT scan was the follow-up or staging of a primary malignancy rather than CRC (65.43%). The most common malignancy diagnosed was lung cancer, followed by breast cancer and prostate cancer. Although it is not recommended in international guidelines, other indications for PET/CT include the need for further investigation when a suspicious finding was positive in other imaging techniques or high values of tumor markers. The left colon was found to be the most common colonic segment with pathological FDG uptake (40.74%). The most common colonoscopic finding was a normal colonoscopic evaluation. The PET/CT scan indications, localization of FDG uptake, and colonoscopic findings are

shown in Table 1. Significant colonic lesions were observed only in 27 patients. Among 81 colonoscopic evaluations, histopathology revealed malignancy in 8 patients, and the prevalence of incidental CRC FDG uptake was found to be 9.87%. In those patients, tumor localizations were found to be 4 in the rectum and 4 in the left colon (Table 2).

While evaluating the values of SUVmax, statistical analysis demonstrated the results with a sensitivity of 100% and a specificity of 90.3% as shown on the ROC curve (Figures 1A, B). Per-lesion analysis of SUVmax values in colonoscopic findings is shown in Table 2. Suvmax was found to be significantly related to malignancy and other colonoscopic findings ($p<0.001$). SUVmax cutoff value to suggest CRC was found to be median [7.9 (4.1–12.7)] ($p<0.001$).

Table 1. Positron emission tomography/computed tomography scan indications, localization of ^{18}F-fluorodeoxyglucose uptake, and colonoscopic findings.

Variables	Classification	Number (%)
PET/CT indication	Screening	28 (34.57%)
	Primary malignancy*	53 (65.43%)
Localization	Rectum	26 (32.10%)
	Left colon	33 (40.74%)
	Transverse colon	10 (12.35%)
	Right colon	12 (14.81%)
Colonoscopic finding	Normal	54 (66.67%)
	Polyp	16 (19.75%)
	Malignancy	8 (9.88%)
	Diverticulitis	3 (3.70%)

*Primary malignancy other than colorectal carcinom.

DISCUSSION

Individuals over 50 years of age are accepted to be at average risk for CRC even if they have no complaints, and therefore screening should be performed for possible early diagnosis[15]. PET/CT is more sensitive than laboratory tests, including tumor markers, which makes the technique more reliable for surveillance in CRC patients when compared to colonoscopy plus computerized tomography. However, there are still debates about the accuracy of PET/CT, and consensus recommendations in various guidelines are still in progress[16].

Table 2. Analysis of SUVmax using colonoscopic findings.

Variable*	Colonoscopic findings				p-value
	Normal	Polyp	Malignancy	Diverticulitis	
SUVmax	6 (1.9–13.4)	7.1 (4.1–14.4)	14.2 (5.1–35)	7.9 (4.1–12.7)	<0.001

*Variables are shown as median (min–max).

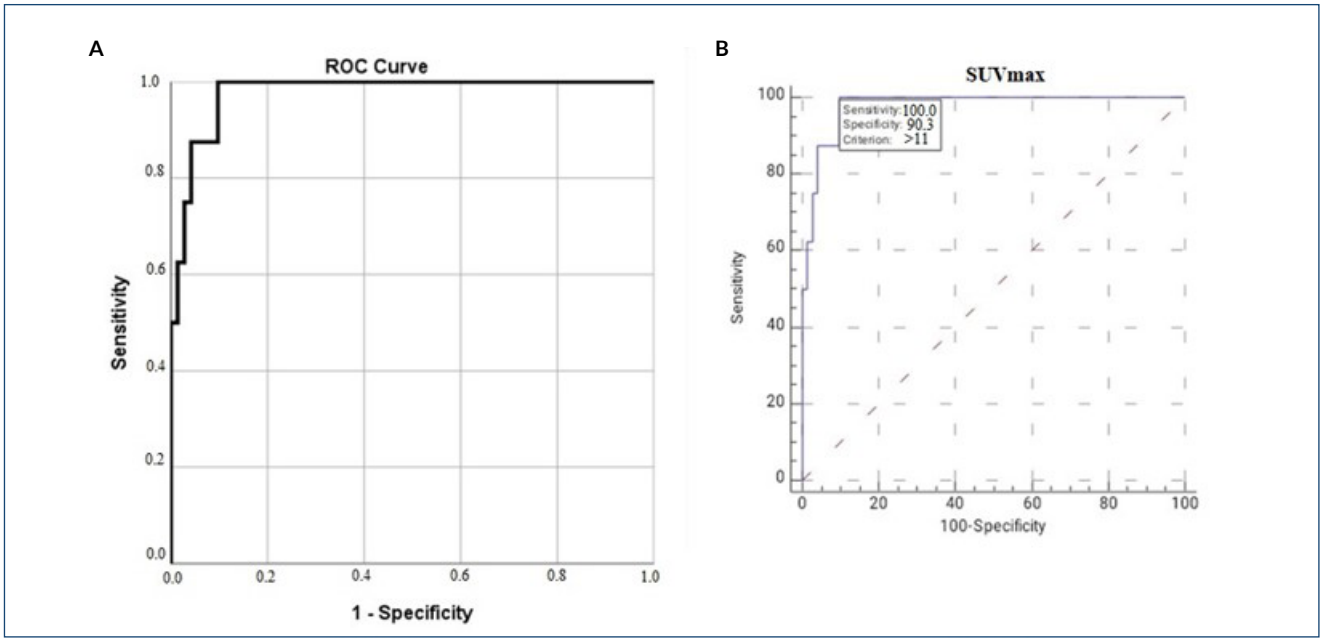

Figure 1. Statistical analysis results with a sensitivity and specificity on the receiver operating characteristic curve **(A)** and SUVmax **(B)**.

Colonoscopy is accepted as the gold standard diagnosing technique for CRC, which led the researchers to be able to control and decrease the rate of false positive results of PET/CT and to avoid the potential bias in studies addressing the efficacy of the technique in detecting CRC, similar to our study[13]. In previous studies, incidental focal colonic ^{18}F-FDG uptake and false positive results on PET/CT have been reported to be 1.3–2.7 and 16–33%, respectively[12]. These results may be indicative of the weak accuracy of PET/CT in specific colonic lesions when compared to endoscopic evaluation. In our study, we excluded patients with a diagnosed CRC, and we found 81 incidental colonic uptakes among 7,097 PET/CT studies in 1 year. In 81 PET/CT studies, significant colonic lesions had been detected in 27 patients (33.3%), and malignancy had been certified in 8 patients (29.6% in detected lesions and 9.87% overall), which shows better results when focusing on a specific patient group in the design of the study. In their study about the capacity of PET/CT in colonic pathologies, Weston et al. included the PET/CT scans with incidental colonic activity followed by colonoscopy; their rate was 0.6%, lower than previous studies and our results[13]. In their systematic review, Kousgaard et al. evaluated the correlation between FDG uptake and colonoscopic findings in four studies and found a rate of 82% when the lesion was located in the same colonic segment in both techniques[17]. In our study, the malignant lesion was found to be at the same segment in both PET/CT and colonoscopy, suggesting the high specificity of PET/CT in CRC. The most frequent use of PET/CT in our group was for staging or surveillance of patients with primary cancer rather than CRC (65.43%), similar to previous studies.

The mean SUVmax values between various types of lesions revealed some significant differences between benign and malignant lesions, similar to our study[18], while others found no significant differences[19]. In our data, the lowest SUVmax value to detect malignancy was 4.1 (mean cutoff value: 7.9). Na et al. found the same value as 2.5[13], while Luboldt et al. determined it as ≥5 in their retrospective study concerning the accuracy of PET/CT in CRC[20]. Our study design and aim do not suggest that CRC can always be diagnosed in PET/CT, but our mean SUVmax value for incidental malignancy may contribute to the existing literature, although it is different from previous studies.

Study limitations

The study is a retrospective analysis of a single-center experience. Our detected cutoff value may be strongly associated with the scanner type. The study is not designed to assess the accuracy of PET/CT in CRC as a screening method because of the selection bias in the study group, as our main aim was to guide incidental colonic findings when detected. However, the statistical analysis can be more accurate with a control group. Additionally, colonoscopies were planned to detect suspected lesions reported to be in specific segments. Prospective studies with large study and control groups may be more effective in determining a cutoff value for incidental FDG uptakes to lead patients to colonoscopy for a more cost-effective screening.

CONCLUSION

Although PET/CT has no significant role in detecting primary cancers, incidental colonic uptake is commonly encountered and leads clinicians to further investigations. We, therefore, assessed the significance of incidental focal FDG colonic activity in the PET/CT scans in diagnosing CRC by comparing it with colonoscopy and histopathology. In conclusion, incidental colonic FDG uptake on PET/CT should lead the clinician to further investigation with colonoscopic biopsy, although cutoff values for SUVmax are not certain and differentiate in almost every published study, and negative PET/CT findings should not completely rule out malignancy, especially in high-risk patients. Similar to our study, a cutoff value for an institute or a department may be accepted as the most cost-effective management to lead the clinician to further investigation with colonoscopy.

AUTHORS' CONTRIBUTIONS

YD: Conceptualization, Data curation, Writing – original draft, Writing –review & editing. **HK:** Writing – original draft, Writing – review & editing. **MKD:** Conceptualization, Data curation, Formal Analysis, Writing – original draft, Writing – review & editing. **SA:** Data curation, Formal Analysis. **SS:** Data curation, Formal Analysis.

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