

Evaluation of patients via colonoscopy who underwent positron emission tomography/computerized tomography due to colon involvement

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SUMMARY

OBJECTIVE: Fluorodeoxyglucose is not a tumor-specific agent and it can also be involved in benign conditions, which may cause diagnostic confusion. This research aims to elucidate the colonoscopic findings of patients who underwent colonoscopy due to colon involvement in positron emission tomography/computerized tomography.

METHODS: A total of 71 patients who underwent colonoscopy due to colonic involvement in positron emission tomography/computerized tomography at SBU Keçiören Training and Research Hospital Gastroenterology Clinic Endoscopy Unit have been analyzed retrospectively. Demographic characteristics of the patients, areas of involvement in positron emission tomography/computerized tomography, and severity have been obtained from the hospital database.

RESULTS: The gastrointestinal involvement area of 22.5% (n=16) of the patients was ascending colon, 15.5% (n=11) was sigmoid, 15.5% (n=11) was rectum, 12.7% (n=9) was stomach, 11.3% (n=8) was transverse colon, 8.5% (n=6) was anal canal, 5.6% (n=4) was esophagus, and 5.6% (n=4) was descending colon. The endoscopic findings of 19.7% (n=14) patients were normal, whereas 29.6% (n=21) had polyps, 9.9% (n=7) had cancer, 2.8% (n=2) had an ulcer, 15.5% (n=11) had gastritis, 14.1% (n=10) had hemorrhoids, and 7% (n=5) had colitis.

CONCLUSION: Fluorodeoxyglucose-positron emission tomography can detect unexpected distant metastases with high sensitivity because it allows whole-body imaging. Curative resection significantly contributes to the choice of treatment modality in the pre-operative period of colorectal cancer patients with planned surgery.

KEYWORDS: PET-CT. Colorectal cancer. Colonoscopy. Metastasis.

INTRODUCTION

Colorectal cancers (CRCs) are the third most common cancer among newly diagnosed cancer patients¹. Liver metastases are detected in approximately half of the CRC patients within the first 5 years after diagnosis. Rectal cancers constitute approximately one-third of all CRCs, with metastatic disease observed in approximately one-quarter of cases at diagnosis².

Accurate and complete staging is essential for effective treatment. Contrast-enhanced computerized tomography (CT) is frequently used in staging CRCs but it has limitations³. These limitations pave the way for fluorodeoxyglucose (FDG) positron emission tomography (PET/CT), a functional imaging method that can provide helpful pre-operative staging and follow-up information. A multimodality approach is recommended for evaluating treatment response because no guideline recommends the ideal method to evaluate the treatment response⁴.

Imaging methods are crucial in evaluating the localization, borders, and spread of CRC, but no imaging format can meet all diagnostic expectations⁵. Anatomical techniques such as

ultrasonography, CT, and MRI are used to detect metastases. Still, PET/CT has been widely used in recent years due to its non-invasive nature and ability to diagnose stage and follow-up treatment response⁶. Also, FDG-PET allows whole-body imaging in a single session and can detect relapse and metastatic disease with high accuracy. However, FDG is not a tumor-specific agent and may cause diagnostic confusion⁷. This research aims to elucidate the colonoscopic findings of patients who underwent colonoscopy due to colon involvement in PET-CT.

METHODS

We analyzed 71 patients who underwent colonoscopy from colonic involvement in PET/CT at SBU Keçiören Training and Research Hospital Gastroenterology Clinic Endoscopy Unit between January 2016 and December 2018. Ethical standards were followed according to Declaration of Helsinki 1975, as revised in 2008. Ethics committee approval has been granted from our institution with protocol number 2012-KAEK-15/23179, and informed consent was obtained.

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Demographic characteristics of the patients (age, gender, and comorbidity), areas of involvement in PET-CT, and severity were recorded.

In patients with pathologically confirmed lung cancer, PET-CT was performed for staging purposes, and patients with an SUV_{max} value of 2.5 and above in the gastrointestinal tract (GIS) were evaluated. TNM staging system is used in the cases of gastrointestinal system involvement. Stage 0: Cancer is at the earliest possible stage. At this stage, the disease is also called in situ or intramucosal carcinoma (*T_{is}*). Cancer cells are found only in the mucous layer, which is the innermost wall layer of the colon or rectum. Stage 1: Cancer cells have reached the submucosa from the mucosa to a lower layer (T1) or the underlying muscle layer (T2). No regional lymph nodes or distant metastases (N0 and M0). Stage 2A: Cancer has reached the outermost layer of the colon or rectum wall but has not exceeded it (T3) and has not spread to surrounding organs. There are no regional lymph nodes or distant metastases (N0 and M0). Stage 2B: Cancer has invaded all colon or rectum wall layers, but has not spread to surrounding organs or tissues (T4a). There is no distant metastasis in regional lymph nodes or distant metastases yet (N0 and M0). Stage 2C: Cancer has spread beyond the colon or rectum wall and has adhered to or grown into the surrounding organs or tissues (T4b). There are no distant metastases in the regional lymph nodes or distant metastases yet (N0 and M0). Stage 3A: Cancer cells have reached the submucosa (T1) or the underlying muscle layer (T2) from the mucosa. The regional lymph nodes (1–3) are involved (N1a/N1b), or there is tumor not in the lymph nodes but in the adipose tissue close to the lymph nodes (N1c). There is no distant metastasis (M0). Stage 3B: Cancer has reached the outermost layer of the colon or rectum wall (T3) or has involved all layers of the colon or rectum wall (T4a) but has not spread to the surrounding tissues and organs. The regional lymph nodes (1–3) are involved. Stage 4: Regardless of T and N stages, cancer can reach one distant organ (e.g., liver or lung) or has metastasized to distant lymph nodes (M1a).

Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS) software. Descriptive statistics, t-tests, Mann-Whitney U tests, and correlation analyses were performed with a 95% confidence interval and p-value of <0.05 as statistically significant. In comparing variables according to gender groups, the Student's t-test was used for normally distributed variables, and the Mann-Whitney U test was used for non-normally distributed variables.

RESULTS

This study observed 71 patients who had colonoscopies due to colonic involvement. Most patients (78.9%) were males and the average age was 68.52 years. There were no significant age differences between male and female patients. No statistically significant difference has been observed between the mean ages by gender.

Male patients had a mean thorax SUV_{max} of 10.15±6.38 (IQR 0–24.52), while female patients had a mean of 9.16±8.46 (IQR 0–27.2). There were no significant differences in SUV_{max} values between genders. Details are shown in Table 1.

Of the 71 patients who underwent PET/CT, 66.2% (n=47) had lung cancer, 16.9% (n=12) had nodules, 8.5% (n=6) had infiltration, and 4.2% (n=3) had other cancer types. Male patients were more likely to have lung cancer than female patients [71.4% (n=40)].

PET stages varied among the patients, with 26.8% (n=19) having stage 0 and 28.2% (n=20) having stage 4. The gastrointestinal involvement area of 22.5% (n=16) of the patients was ascending colon, 15.5% (n=11) was sigmoid, 15.5% (n=11) was rectum, 12.7% (n=9) was stomach, 11.3% (n=8) was transverse colon, 8.5% (n=6) was anal canal, 5.6% (n=4) was esophagus, and 5.6% (n=4) was descending colon (Table 2).

Notably, 22.5% (n=16) of patients had involvement in the ascending colon, 15.5% (n=11) in the sigmoid, and 15.5% (n=11) in the rectum. Most of them had focal involvement (81.7%) and diffuse involvement was observed in 18.3%.

Table 1. Analyses of gastrointestinal tract SUV_{max} averages by gender.

Continuous variables and gender		n	Mean	SD	Minimum	Maximum	Median	p-value	t	u
Age (years)	Male	56	67.93	8.805	53	85	68.5	0.326	-0.99	
	Female	15	70.73	12.775	43	92	72			
Primary thorax mass SUV _{max} value	Male	56	10.155	6.38	0	24.52	10	0.569	0.572	
	Female	15	9.16	8.46	0	27.2	5.32			
GIS SUV _{max} value	Male	56	10.025	6	2.78	35	8.04	0.811		403
	Female	15	10.25	5.96	3	24	8.65			

In comparing variables according to gender groups, the Student's t-test was used for normally distributed variables, and the Mann-Whitney U test was used for non-normally distributed variables. GIS: gastrointestinal tract, SD: standard deviation.

Endoscopic findings showed normal results for 19.7% (n=14), polyps for 29.6% (n=21), and cancer for 9.9% (n=7). Adenomatous polyps were found in only 5.6% (n=4) of patients, whereas hyper polyps were detected in 4.2% (n=3).

Endoscopic findings varied by PET stages, with PET stage 0 showing a significant difference (p=0.017). GIS uptake rates were not statistically different (p=1.00). Details are shown in Table 3.

As a result of ROC analysis (Table 4), it has been observed that the GIS SUV_{max} value did not predict lung cancer (AUC: 0.632, 95%CI: 0.457–0.747, p=0.162). However, the lung

mass SUV_{max} variable was important in predicting lung cancer (AUC: 0.916, 95%CI: 0.844–0.988, p<0.001).

DISCUSSION

FDG PET/CT is a powerful imaging tool used for tumor imaging, staging, and follow-up, providing valuable data on both primary indications and incidental findings. Incidental FDG uptake was found in 3.6% of patients in PET/CT evaluations for non-GI system diseases⁸. However, false positive involvements were detected in 9.3–63% of patients, emphasizing the need to interpret PET/CT results⁹ carefully.

Rigault et al. detected at least one lesion on colonoscopy in 46% out of 70% of patients with incidental focal colorectal FDG uptake¹⁰. Putora et al. identified colonoscopic lesions in 44 out of 51 patients with colonic involvement¹¹.

Many tests (colonoscopy, whole abdomen CT, thorax CT, endoscopic ultrasonography, and bone scintigraphy) should be performed together to evaluate the whole body for metastasis with conventional methods¹². FDG-PET imaging evaluates the whole body for metastasis in a single session without additional radiation exposure. This is particularly useful for patients with advanced or recurrent diseases who require frequent monitoring. Studies have shown that FDG-PET detected all extrahepatic metastases with 100% sensitivity¹³.

Table 2. Localization of gastrointestinal system involvement.

		Frequency	%
GIS Involvement	Anal canal	6	8.5
	Esophagus	4	5.6
	Stomach	9	12.7
	Cecum	2	2.8
	Ascending colon	16	22.5
	Transverse colon	8	11.3
	Descending colon	4	5.6
	Sigmoid	11	15.5
	Rectum	11	15.5
	Total	71	100.0

Table 3. Combined positron emission tomography stage and combined endoscopic finding cross-table analysis.

PET stage and GIS involvement			GIS attendance location		Total
			Esophagus, stomach, and duodenum	Cecum, ascending colon, transverse colon, descending colon, sigmoid, rectum, anal canal	
PET stage	0	n	3	16	19
		%	15.8%	84.2%	100.0%
	1- 1A-1B-2-2A-2B	n	3	14	17
		%	17.6%	82.4%	100.0%
	3A-3B-4	n	7	28	35
		%	20.0%	80.0%	100.0%
Total	n	13	58	71	
	%	18.3%	81.7%	100.0%	

p=1.00 and Fisher's test=0.201.

Table 4. Positron emission tomography computerized tomography SUV_{max} ROC analysis.

	AUC	p-value	Sensitivity %	Specificity %	Cutoff value	95%CI	Positive predictive value %	Negative predictive value %
Lung main mass SUV _{max}	0.916	0.000	0.723	0.958	9.575	0.844–0.988	97.1	63.9
GIS SUV _{max}	0.602	0.162	0.66	0.667	0.765	0.457–0.747	79.5	50

According to the ROC analysis, it was observed that the GIS SUV_{max} value did not predict lung cancer (p-value=0.162). However, the SUV_{max} value of the primary lung mass was significant in predicting lung cancer. The p-value was 0.000.

PET/CT is a non-invasive technique used to determine diagnosis, staging, and response to treatment, demonstrates tumor aggressiveness, and determines radiotherapy areas. In addition, PET/CT examination can detect focal or nodular hypermetabolic lesions in the GIS with a high probability of pre-malignant/malignant lesions. Therefore, colonoscopic evaluation is recommended for these lesions¹⁴.

In a study conducted by Hu et al. consisting of 149 patients diagnosed with cancers without a definite primary focus, FDG uptake consistent with malignancy was found in 50 patients (33.6%) with PET/CT, and in 37 patients (24.8%) with PET/CT and histopathological examination. As a result of the study, the sensitivity and specificity were determined as 86% and 87.7% with PET/CT¹⁵. In a study by Fencel et al. on 190 patients, the rate of detecting a primary focus was 47%, the sensitivity was 94%, and the specificity was 86%¹⁶. Pelosi et al. reported that PET/CT could reveal the primary focus in 35.2% of patients in their study who were proven to have metastatic carcinoma with 39 lymph nodes and 29 visceral biopsies. This study determined the positive predictive value (PPV) as 82%¹⁷. In this study, we found that GIS uptake rates were not statistically different according to PET stages ($p=1.00$, Fisher's test=0.201).

Kwee and Kwee have conducted a meta-analysis of 11 studies on 433 patients and found the range of primary tumor detection to be 22–73% by PET/CT. According to this meta-analysis, the lungs were the organs in which primary tumors were detected the most at 33%, followed by oropharyngeal cancers at 16%, and pancreatic cancers at 5%¹⁸.

Colonic FDG uptake in PET-CT was frequently associated with neoplastic pathology in different publications. In a different study, 10,978 patients were evaluated, and colonic FDG uptake was detected in 148 patients. Colorectal tumors were found in 23.5% of the cases, polyps in 20.5%, and normal findings in 56%. It has also been reported that the false positive rate of focal FDG uptake, especially in the right colon, is high¹⁹.

In a study comparing colonoscopy and PET/CT findings simultaneously of 123 polyps with focal involvement, 9 were adenocarcinoma and 6 were high-grade dysplasia. Regarding this, one could state that in polyps larger than 10 mm, FDG uptake was found to be less homogeneous in adenomas (>10 mm) than in adenocarcinomas (>10 mm)²⁰.

In FDG PET/CT studies, primary CRCs were detected as small as 14 mm with high FDG uptake²¹. The diameter of the undetected polyps was 13 mm and had the character of adenoma. It was found that the positivity of PET increased (90%) with the enlargement of the adenoma size (>13 mm)²². In another study, the sensitivity of FDG-PET was also determined by the enlargement of the adenoma (1–5 mm 21%, 6–10 mm 47%, and

>11 mm 72%) and the degree of dysplasia (low-grade dysplasia 33%, high-grade dysplasia 76%, and carcinoma 89%) increased²³.

In a different study, when compared with colonoscopy, the sensitivity of PET/CT was 74%, specificity was 84%, and PPV was 78%. Again, a good correlation was found between FDG uptake and the localization of endoscopy-positive lesions, supporting the usefulness of FDG PET/CT in the non-invasive follow-up of patients with CRC and the detection of other colonic lesions. In addition, the FDG uptake was proportional to the degree of dysplasia in the adenoma²⁴. However, it should not be forgotten that FDG accumulates in areas of inflammation or infection in whole-body scans of cancer patients. This causes a decrease in specificity in body scanning, as the infection may mimic metastasis²⁵. In this study, the rates of endoscopic findings were statistically different according to PET stages, and the difference was due to the PET stage 0 group ($p=0.017$).

CONCLUSION

FDG-PET can detect unexpected distant metastases with high sensitivity because it allows whole-body imaging. PET, which has become increasingly used with the advantage of being non-invasive in cancer staging and surveillance, can detect mostly adenomatous polyps incidentally. Curative resection significantly contributes to the choice of treatment modality in the pre-operative period in patients with CRCs with the planned surgery.

INFORMED CONSENT

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with Declaration of Helsinki 1975, as revised in 2008. Informed consent was obtained from all participants.

INSTITUTIONAL REVIEW BOARD APPROVAL

This study has been approved by the ethics committee with protocol number 2012-KAEK-15/23179.

AUTHORS' CONTRIBUTIONS

MÖE: Conceptualization, Methodology, Investigation, Resources, Writing – original draft, Writing – review & editing. **EKA:** Data curation, Formal Analysis, Funding acquisition, Project administration, Software, Validation, Visualization, Writing – review & editing.

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