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Does PET-CT Contribute to Sitoreductive Surgery in Advanced Stage Colorectal Cancers?

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Abstract

Colorectal cancers are seen at a high rate in developed countries. The 5-year survival rate varies according to the stage of the disease at the time of diagnosis. Therefore, it is very important to detect the disease at an early stage, to stage it correctly and to determine the appropriate treatment options according to the stage. Surgical resection, neoadjuvant chemoradiotherapy and adjuvant chemotherapy are the treatment options according to the staging of the disease at the time of first diagnosis. Positron Emission Tomography-Computed Tomography (PET-CT) is used in the indications of diagnosis, staging, restaging, detection of recurrence and evaluation of treatment response in colorectal cancers. In this review, the limitations of current imaging methods and the place of PET-CT imaging in colorectal cancer staging and its potential future uses will be explained.

Keywords**:** *colorectal cancer, staging, positron emission tomography.*

Introduction

Colorectal cancers are the 3rd most common tumor for both genders. The incidence has increased with the widespread use of screening programs. Colorectal cancers are at the top of the list of cancer-related deaths. While the 5-year survival rate is 90% in patients diagnosed at an early stage, whereas it is 14% in metastatic disease (1). It tends to be at a higher stage and more symptomatic in younger patients. 95% of colorectal cancers are adenocarcinoma, which is known to have a very high FDG sensitivity. The general consensus is that FDG PET-CT does not provide an additional contribution to conventional imaging methods in non-metastatic early stage colorectal cancers. Nevertheless, the use of PET-CT imaging in the initial staging of colorectal cancers changes patient management at a rate of approximately 14-50% (2,3,4). The only curative treatment modality for colorectal cancers is surgical resection of potentially resectable lung or liver metastases and locoregional disease. In the early stages, curative surgery is the main treatment.

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The main purpose of imaging methods in colorectal cancers are to determine the prevalence of locoregional disease in the initial surgical planning, to evaluate the metastatic disease in terms of treatment with surgery or other methods, to evaluate the transition of the initially inoperable disease to potential surgical stages as a result of neoadjuvant treatments. Clinical guidelines still recommend conventional imaging (CT, MRI) in colon and rectal cancers. Thorax, abdomen, pelvis CT is recommended for colon tumors, pelvic MRI is recommended for rectum and distal colon tumors. PET-CT imaging seems to be the second-line technique in this scenario at initial staging. Guidelines specifically recommend PET-CT in potentially operable patients. PET-CT is recommended for initial staging if other methods are contraindicated, if other methods have uncertain results, in patients for whom intravenous contrast is contraindicated, if there is a potential liver-targeted treatment plan (such as radioembolization, chemoembolization, or ablation). In conventional methods, if there is potential operable metastasis, PET-CT imaging comes into play in terms of excluding metastases that may prevent surgery in other body regions.

FDG PET-CT in the evaluation of T Staging

Because of its low resolution in T staging, it is not suitable for determining the depth of invasion of the primary tumor. Due to intense physiological intestinal activity, it may not provide sufficient information in terms of invasion into neighboring structures. However, 94% accuracy in T staging has been reported PET is recommended if there is extensive extramural invasion on MRI (5). Even if the addition of PET-MR imaging to imaging has the disadvantage of prolonging the time, it is beneficial in T staging.

In another very recent prospective study, which included 101 patients with rectal cancer and compared FDG PET-MR and conventional imaging methods (pelvic MRI, thoracic and abdominal CT) in primary staging, PET-MR for extramural vascular invasion and distant metastases had higher accuracy than conventional methods. has been reported.

Eight patients who were initially M0 were evaluated as M1 after PET-MRI (6).

It was determined that PET-MR decreased the number of suspicious lesions reported in CT examination and it was concludd that liver, lung and especially non-regional lymph nodes were detected at a high rate.

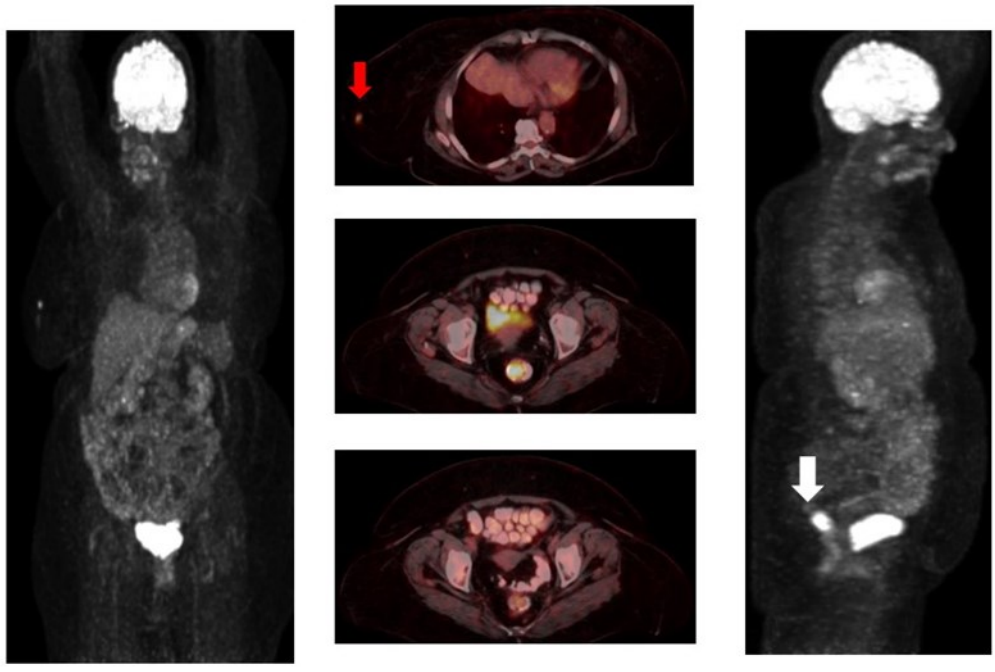

Figure 1: FDG PET-CT MIP (Maximum intensity projection) images and axial fusion images demonstrate rectal hypermetabolic (SUVmax: 41) primary malignancy with an axial diameter of 27x22 mm and 3 cm sagittally (White arrow) and left pararectal metastatic milimetric lymph node (SUVmax: 2.14). Additionally, 1 cm hypermetabolic (SUVmax: 10.8) nodular lesion was detected in right breast suspected for second primary in a 67 years old women (Red arrow).

FDG PET-CT in the evaluation of Lymph Node Staging:

Lymph node staging is important in the treatment plan and prognosis. It affects the decision to give additional treatment in the early period or to expand the dissection area. CT and MRI are the most commonly used conventional methods in lymph node staging in rectal cancer. However, both tests have low sensitivity, especially in small metastases (7-10). Metastatic lymph nodes less than 1 cm in size can be found not uncommonly in patients with rectal cancer. Generally, lymph nodes with a short diameter greater than 1 cm are defined as pathological in conventional imaging methods. The size limit may vary according to tumor type and anatomical localization. Evaluations based on size criteria are often insufficient. The accuracy of PET/CT in nodal staging was reported as 79% in a study of 37 patients (11). In a large series including 473 patients with colorectal carcinoma, sensitivity was reported as 66%, specificity 60%, and accuracy 63% in lymph node staging (12). In general, the sensitivity is relatively low and the specificity is high in regional LN. Application of lower SUVmax cut-off values according to lymph node size increases the diagnostic performance of FDG PET-CT in patients with rectal cancer. In one study, sensitivity and specificity were determined as 35.8% and specificity as 97.2% when 2.5 fixed SUVmax cut-off values were used, while sensitivity and specificity were reported as

76.1% and 74.3%, respectively, when size-optimized SUVmax cut-off values were used (13). Although false negative results in small lesions and false positive results in inflammation, PET-CT provides more information in LN staging.

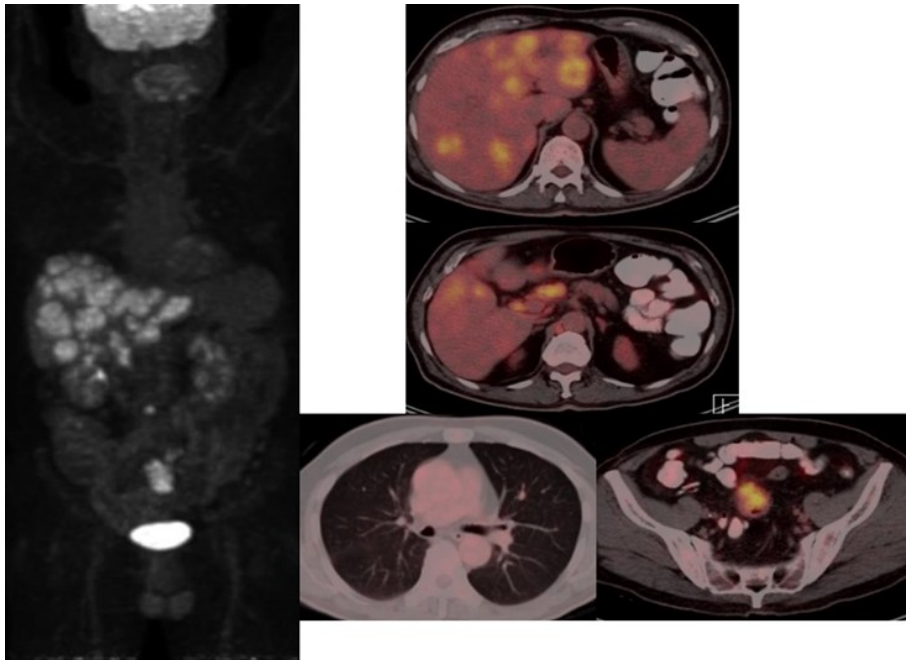

Figure 2: FDG PET-CT MIP (Maximum intensity projection) images and axial fusion images demonstrate rectosigmoid colon hypermetabolic (SUVmax: 14.97) primary malignancy with an axial diameter of 4x3.5 cm and 5 cm sagittally, hepatic multiple metastatic nodules (SUVmax: 13.68), intraabdominal metastatic lymphadenopaties (SUVmax: 13.47) and mezenteric implants. Additionally, inflamatuar fibronodüler lesion in left lung and left surrenal adenoma were detected.

Premalignant Lesions

FDG PET-CT can also detect precancerous lesions such as adenomatous polyps. The sensitivity of PET-CT imaging in detecting these lesions is about a quarter of that of colonoscopy. Because the examination is expensive, FDG PET-CT examination is not recommended for screening in this indication. In PET-CT imaging performed for another purpose, focal hypermetabolic foci in the colon can be detected incidentally at a rate of approximately 1.3%. Because of the high probability of malignant/premalignant lesion such as villous adenoma, carcinoma or hyperplastic polyp, close follow-up of these lesions is recommended. Since the focal FDG activity in PET-CT may be physiological or inflammatory, endoscopic examination is not required if no lesion is detected in the CT correlation regardless of the SUV value in the area where the focal activity is seen.

FDG PET-CT in the evaluation of Distant Metastases

PET-CT imaging excels in the detection of distant metastases. FDG PET-CT is far superior to other imaging modalities in detecting different M1 catogories in colorectal cancers (Figures 1 and 2). It is used to detect intrahepatic and extrahepatic metastases in preoperative locally advanced disease. It has 91% and 95% sensitivity and specificity in detecting metastases before neoadjuvant therapy. Therefore, PET-CT imaging is

the imaging modality that has the most potential to contribute to sitoreductive surgery in patients with advanced colorectal cancer. There is liver metastasis in 25% of patients with rectal cancer at the time of diagnosis. In approximately 50-60% of patients, liver metastases develop within 5 years (14). Most commonly lymph node, lung, bone metastases and synchronous colon tumors are detected outside the liver. The detection rate of extrahepatic metastases in PET-CT ranges from 0-68%. PET-CT imaging changes disease management with a 21% detection rate of extrahepatic metastases not detected in contrast-enhanced CT. Peritoneal metastases are evaluated in the M1c category according to AJCC. Peritoneal involvement is an indicator of poor prognosis in these patients, the disease-free period and survival is short. Peritoneal and mesenteric metastases can be easily detected in FDG PET-CT imaging, except for lesions with a very small volume (<1 cm). In a study conducted in patients with abdominal malignancy, the accuracy, sensitivity and specificity of PET-CT in peritoneal metastases were reported as 87.7%, 72.7% and 93%, respectively (15). In the staging of colorectal cancers, 3.1% false positive and 1.3% false negative rates are reported in PET-CT examination. Considering the resolution limits of PET-CT, there may be false negative results in lung and liver lesions smaller than 5-6 mm. Variable FDG physiologic uptake in the colon is the most common cause of false positives. Due to the high number of lymphocytes in the cecum and right colon, there may be a relatively high physiological uptake compared to other segments of the colon. In addition to physiological involvement, various inflammatory causes also constitute false positive causes. Causes such as ileostomy-colostomy areas, inflammatory changes in the post-operative wound healing process, inflammatory bowel diseases, diverticulitis may cause false positive results. Diabetic patient, small tumor size and microscopic disease states can cause false negative results in all cancer types in FDG PET-CT imaging. In addition, lesion size, mucinous and signet ring cell histologies are the most important causes of false negative results.

FDG PET-CT in the evaluation of Therapy Response

The major role of PET-CT Imaging is to evaluate the treatment response after neoadjuvant therapy, and it can identify unresponsive and responding patients in the early period, to evaluate the transition of the initially inoperable disease to potential surgical stages as a result of neoadjuvant treatments and to detect recurrence in the anastomotic area or presacral area in patients with rectal cancer (Figures 3 and 4). Sensitivity and specificity is 94% in discriminating fibrotic and neoplastic tissue. metabolic changes occur before morphological changes.

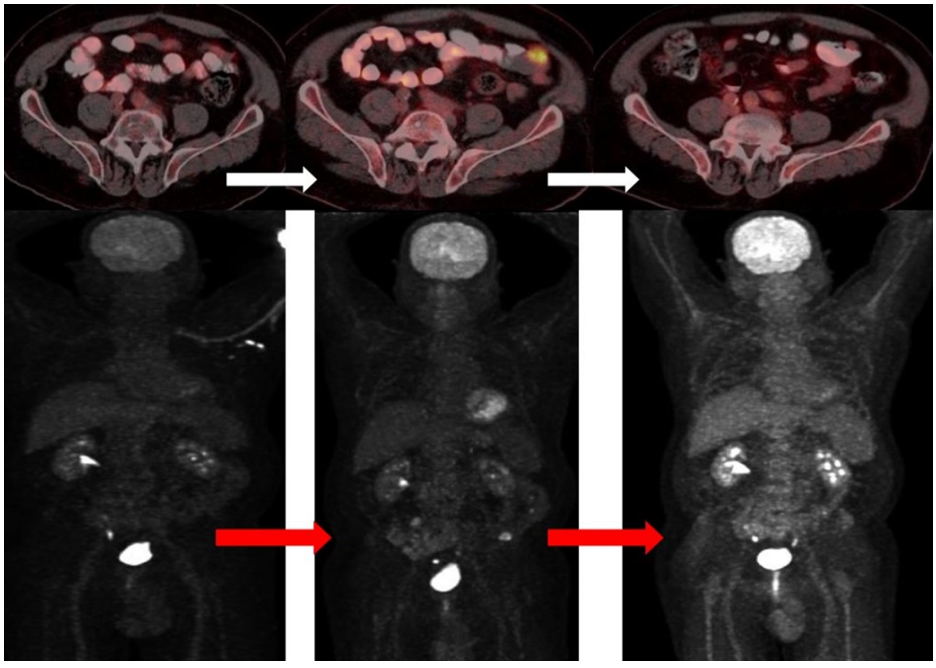

Figure 3: Follow-up of recurrence and treatment responses in a 62 years old man patient followed up for rectal cancer.

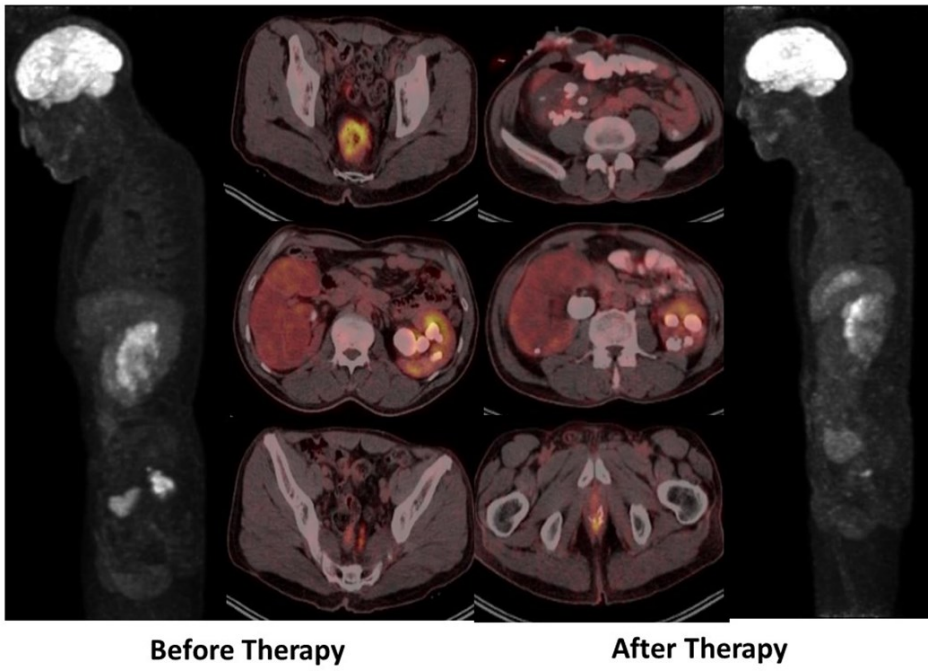

Figure 4: Before therapy and after chemoradiotherapy and surgery images are demonstrated in a 48 years old man patient with rectal cancer.

New Modalities

Diagnoses such as mucinous adenocarcinoma, signet ring cell carcinoma, small cell carcinoma, medullary carcinoma, papillary carcinoma and neuroendocrine carcinoma may also be less frequent. FDG affinity is low in low-grade neuroendocrine tumors. Ga-68 DOTAPEPTIDE PET-CT imaging is used in this diagnosis. Ga-68 DOTA FAPI (Fibroblast Activation Protein Inhibitor) PET is a new modality. FAPI is rarely expressed in normal tissue. Fibroblasts are expressed in epithelial tumors.There is no physiological uptake in gastric and intestinal mucosa. It is important in peritoneal metastases, especially in patients with gastrointestinal cancer. No patient preparation required for FAPI PET. Further studies with larger series are needed on this subject.

Why Should We Perform FDG PET-CT in Colorectal Cancer Patients?

PET-CT imaging has high accuracy rates as a whole-body imaging modality in nodal staging and metastasis screening, and relapse detection. It reduces the number of unnecessary examinations. Monitors treatment response and recurrences. Can evaluate morphology and metabolism simultaneously in LN staging. It can show regional LN as well as remote LN stations in a single examination.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: P.P.O., **Design:** P.P.O., G.Y., **Supervision:** P.P.O., G.Y., Z.P.K., **Data Collection and/or Processing:** P.P.O., G.Y., Z.P.K., **Analysis and/or Interpretation:** P.P.O., G.Y., Z.P.K., **Literature Review:** P.P.O., **Writer:** P.P.O.

Conflict of Interest: No conflict of interest was declared by the authors.

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