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Restaging of colorectal cancer and PET/CT

Alev Çınar[1], Esra Arzu Gençoğlu[2], Meliha Korkmaz[1]

ABSTRACT

Positron Emission Tomography/Computerized Tomography (PET/CT) is an important assessment method in restaging of oncology patients. Its ability to detect the metabolic/functional changes in patients with colorectal cancer during the early stages, in which morphological changes cannot be documented, is significantly superior to other imaging modalities.

Key Words: Colorectal cancer, restaging, PET-CT

INTRODUCTION

Colorectal cancer recurrence usually develops in the first 4 years following surgery and mostly presents with hepatic involvement (33%). While Positron Emission Tomography gathers information on the body's metabolic / functional activity, concurrent CT provides anatomical details of normal and pathological tissues in the body. The superiority of PET/CT to other radiologic methods is its ability to demonstrate metabolic/functional changes in tumor tissues at an early stage where morphological changes have not yet occurred. With this method, early detection of tumor tissue, early treatment planning, and thus prolongation of survival is possible.

Colorectal Cancer

In our country, the incidence of colorectal cancer is reported as 18.2/100 000 in men and as 12, 1/100 000 in women (1-5). Age is an important factor in the incidence of colorectal cancer. Sporadic colorectal cancer incidence significantly increases over the age of 45-50 (6). Thirty percent of colorectal cancer tumors are located in the rectum, 28% in the sigmoid, 9% in the descending colon, 11% in the transverse colon, 9% in the ascending colon, and 13% in the cecum (6). 3 to 6% of colorectal carcinomas are multicentric (7-9). Local invasion of the tumor into deeper tissues lead to peritoneal metastasis, whereas its spread through vascular structures and regional drainage lead to liver, lung and bone marrow metastasis. Rectal cancer can spread to adjacent structures such as adjacent adipose tissue, vagina, prostate, bladder, ureter and the bony pelvis (10-15).

Restaging of Colorectal Cancer

Recurrence in rectal cancer differs from those of other parts of the colon. Local recurrence in rectal cancer (7-33%) occurs at a higher rate as compared to colon cancer (1-19%). Sites of distant metastasis relies on the venous drainage of the primary site; venous drainage of the colon and upper part of rectum is into the liver through the portal vein therefore causing liver metastases, whereas the lower part of the rectum has a dual drainage, isolated pulmonary metastases without liver metastases can be observed. Orband and Gordon, in their recurrence analysis of 146 patients with colorectal cancer, reported 46% local, 52% local and distant recurrence rates. In studies, it has been shown that 20% patients with recurrence have isolated hepatic metastases, and if untreated 5-year survival rate of these patients is 28% (16-23).

Positron Emission Tomography (PET)

A PET/CT scan begins with detection of scanning area with an explorative CT, continues with helical CT scan, and is completed by PET scan. Positron emission tomography/CT does not contain fused images, the PET and CT images are always separated. Merging the two images together is the process of placing images over each other rather than creating a new image. In positron emission tomography imaging for oncological applications, the most preferred method is to follow glucose metabolism. For this purpose, an 18F radioisotope fluorodeoxyglucose (18F-FDG) is being used. Because it is not a specific agent for

[1]Clinic of Nuclear Medicine, Ankara Teaching Hospital, Ankara, Turkey

[2]Department of Nuclear Medicine, Başkent University Faculty of Medicine, Ankara, Turkey

Address for Correspondence

Dr. Alev Çınar

Clinic of Nuclear Medicine, Ankara Teaching Hospital, Ankara, Turkey
Phone.: +90 312 595 36 07
e-mail: alevcnr@gmail.com

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cancer, its uptake can also be detected at the sites of infection and inflammation but in malignant lesions the retention continues even in the late periods in contrast to benign pathologies (24-28).

PET in Colorectal Cancer

It has been reported that positron emission tomography/CT changed staging in 31% of patients who underwent conventional imaging. The altered staging has changed the planned treatment in 8% of cases. The sensitivity and specificity of PET / CT and CT in detecting tumors is reported as 98.1% and 66.7% ($p<0.0001$), 75% and 62.5% ($p=0.056$), respectively (29). Imaging with FDG in patients with colorectal cancer is accepted as an effective method that could lead to changes in patient treatment. Early detection of liver metastases allows the opportunity of neoadjuvant chemotherapy and resection in colorectal cancer patients, with a possible increase in survival. In a meta-analysis comparing the effectiveness of CT, MR and PET/CT for the detection of liver metastasis of colorectal cancer, the sensitivity of imaging methods were determined as 83.6%, 88.2% and 94.1%, respectively (30-32). The most important effect of positron emission tomography/CT imaging is the ability of detecting extra-hepatic metastases that prevent surgical treatment in colorectal cancer patients with liver metastases. In 11-32% of patients with liver metastases who were planned for surgery, PET detected extra-hepatic metastases. This situation leads to a change in treatment to a more systemic route by including chemotherapy (33-35). However, PET has limitations due to false-positive results in the context of size and inflammation. In addition, since cystic tumors or mucinous lymph node metastases do not show a significant FDG uptake, FDG PET images is not reliable in ruling out lymph node metastasis of colorectal cancer (Figure 1, 2).

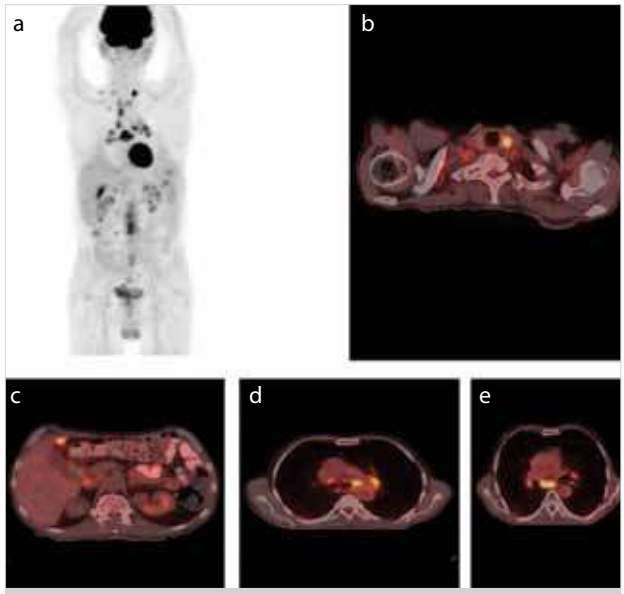

Figure 1. PET/CT for re-staging; 6 years old male, colon cancer a)Total body PET view b) Slightly increased FDG uptake in the neck adjacent to the left thyroid lobe c) Subcapsular metastatic foci in Segment 2 and 10x9 mm lymph nodule in the right para-caval region d) Left paraoesophageal and aortopulmonary lymph nodes e) 14x9 mm lymph node right lateral to the ascending aorta

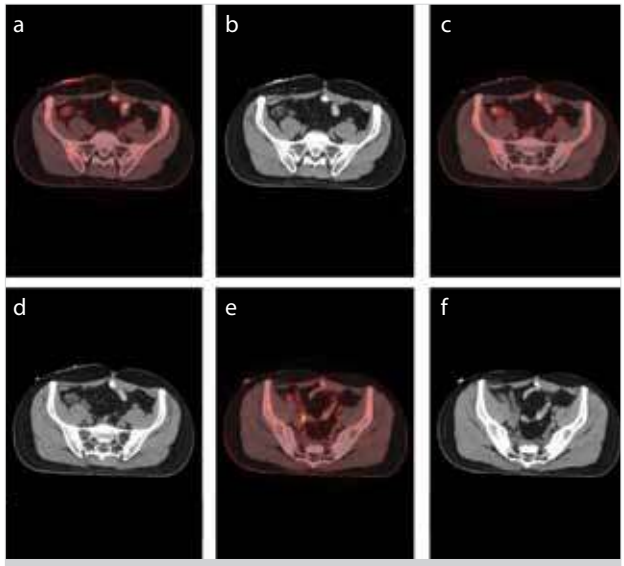

Figure 2. Re-staging PET/CT; 98 years-old male, rectal carcinoma. a,b,c,d) Peritoneal implants posterior to the anterior abdominal wall at the pelvic level e,f) Rectosigmoid mass, presacral 12 mm lesion at the operation field

The lung is another target organ other than the liver for spread of colorectal cancer. Pulmonary involvement of lymph nodes and pleural involvement are findings of metastatic disease. Approximately 10% of colorectal cancer patients develop pulmonary metastases. In 2-4% of patients it is seen as isolated pulmonary metastases and surgery can applied in about half of them. After successful surgery, the 5-year survival rate ranges from 28% to 40% (36-39). The sensitivity and specificity of positron emission tomography/CT in the detection of malignant solitary pulmonary lymph nodules have been reported as 96% and 83%, respectively. Positron Emission Tomography/CT's CT component is the most sensitive method for the detection of pulmonary metastases, whereas FDG PET images provide additional specificity in lymph nodes larger than 8 mm (36). A negative finding in Positron Emission Tomography/CT scan does not rule out the presence of pulmonary metastases due to the limited spatial resolution, still it confirms suspicious findings observed on CT.

Bone metastases in colorectal cancer have been rarely reported. In a study of 5000 patients, bone metastasis with visceral metastases is reported as 6.6%, and isolated bone metastasis as 1.1% (38). Studies reported that PET/CT is both sensitive and specific in the diagnosis of malignant bone metastases. In another study bone metastasis was detected in 59 out of 712 patients with PET/CT examination, with a positive predictive value of 98% (37-39). Distinction of scar tissue from surgery, radiation or recurrence scar is important in patients with previous colon cancer, this is a particular problem for distal colon and rectal cancer where pre-sacral and pelvic scarring changes are common. The PET/CT performed at the postoperative 6th month is superior to CT or MRI alone in the differentiation of malignant and benign pre-sacral changes. Currently PET CT scan is accepted as the imaging method of choice, with its ability to detect disease at once, to show its localization and to guide diagnosis and treatment in such patients.

DISCUSSION

In our country when the results of a survey conducted by the Ministry of Health are evaluated; colorectal cancer ranks third after lung and breast cancer. The incidence is reported as 7.7%; the distribution as 59% male, 41% female and the male/female ratio as 1.44. For this type of cancer diagnosis age was 62 years (1).

A study conducted by Willkomm et al. (40) reported relapse within 3 years after resection of the primary tumor. Early diagnosis and treatment of recurrent disease increases quality of life, diagnosis of potentially resectable metastases or recurrence improves prognosis (41). Surgical resection can be performed in 12-60% of patients with proven tumor recurrence. The expected life span is at least 80-month in approximately half of these patients. Asymptomatic tumor recurrence is important even though surgical resection cannot be performed. Systemic treatment regimens are more effective than symptomatic treatment. Scott et al. (42) conducted a study in 10 patients with elevated serum tumor marker (CEA) levels, and identified recurrence with PET in 8 of them. Haseman et al. (43) used radioimmunoscintigraphy as an alternative approach under same clinical circumstances in 140 patients, and reported sensitivity as 79%, and specificity as 84%. Morales - Gutierrez et al. (44) have shown that CA 19, 9elevations during patient follow-up is an independent risk factor for relapse and that patients with these high values have poor prognosis. Willkomm et al . (40) compared FDG-PET and CEA 123 scans for detection of recurrence, and they reported sensitivity and specificity of CEA -scan as 89% and 100% , and of FDG PET as 100% and 95% , respectively. So far, imaging modalities have been compared in terms of accuracy in identification of colorectal recurrence and metastasis. The sensitivity and specificity of fluorodeoxyglucose PET in the detection of colorectal cancer recurrence and metastasis is higher as compared to CT and MR. With fluorodeoxyglucose PET distinction between tumor and scar tissue could be made. The false-positive findings on FDG PET can be explained by inability of complete analysis of especially the dorsal pelvic region in the studied patient groups due to; FDG's being a nonspecific agent, accumulation in foci of inflammation, renal elimination and formation of artifact around the kidney and bladder after image reconstruction (45-49). Because fluorodeoxyglucose is expensive the CEA -scan was tested as an alternative; sensitivity, specificity and accuracy rates of CEA- scan were reported as 89%, 100% and 96%, while the same values for FDG PET were stated as 100%, 95% and 96%, respectively (45, 46).

In studies regarding tumor location, the sensitivity of FDG-PET in determining liver metastases was reported as 91% with a specificity of 100%, whereas the sensitivity of CT was 74% and specificity was 85% (47). Locoregional pelvic recurrence and liver metastasis are reported as the most frequently relapsing sites. Despite all advanced scanning methods and advanced treatment modalities, approximately 40% of patients with a diagnosis of primary colorectal cancer will develop liver metastases. 25 to 50% of patients who died of cancer have liver metastases. The positive effects of systemic chemotherapy on survival have not been shown. Besides systemic chemotherapy, selective chemoembolization, radiofrequency ablation, cryoablation, alcohol ablation, radiolabelled Yttrium 90 microspheres are also used in regional therapy. PET results for the evaluation of the results of therapeutic response after application of radiolabelled Yttrium 90 microspheres for liver metastases have been reported to have a better correlation than CT, MRI, or tumor marker changes. The importance of PET/CT scan in patient selection and evaluation of treatment response to this promising first line treatment for unresectable liver metastasis is highlighted in many publications.

Anastomotic recurrence can be detected in 2-4%, with a 10 times higher likelihood in rectal cancer (5). Due to physiological and post-surgical factors FDG uptake is increased, the specificity is low for anastomotic recurrence. Presacral abscess and inflammatory scar tissue are potential sources of false-positive results with PET/CT.

CONCLUSION

The shift in PET technology towards PET/CT providing anatomical and metabolic images, and its importance in determining clinical approach to colorectal cancer is emphasized. PET/CT is often used for detection of recurrence and/or metastasis incase of elevated tumor markers with unexplained etiology, patient selection for surgery, the decision to start treatment and choice of treatment, and evaluation of post-treatment response. Although the wide utilization of PET/CT scan increases the cost, it provides significant advantages in the treatment of colorectal cancer, as in many other cancer types if used with the correct indications.

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