Journal of Pharmacy and Pharmacology 5 (2017) 940-952
doi: 10.17265/2328-2150/2017.12.016

IS There A Role of ^{18}F-FDG PET/CT for Initial Staging of Rectal Cancer?

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Abstract: Background: The management of the rectal cancer requires accurate initial staging. Besides routinely performed conventional imaging, during the last decade ^{18}F-FDG PET/CT became a popular whole-body metabolic imaging for preoperative TNM classification. The purpose of the study was to evaluate the role of ^{18}F-FDG PET/CT in the rectal cancer staging. Patients and methods: 45 patients with rectal cancer who preoperatively underwent ^{18}F-FDG PET/CT imaging in the period from 2011 to 2014 were analyzed. All patients were referred to the surgery afterwards. Histopathologic findings were used as a standard of reference. Descriptive techniques were used for frequency analyses and sensitivity calculations. The χ^2 test was used for significance calculation of the contingency tables while Monte Carlo simulation and Fisher's exact test were used for the table fields where number of cases was smaller than demanded. Results: The average SUV_{max} value of the primary tumor for all T stages was 26.02 gm/mL. The average SUV_{max} values of the lymph nodes in N1 stage and N2 stage were 6.04 gm/mL and 6.33 gm/mL, respectively. PET/CT detected benign lesions in 17 (28.3%) patients with average SUV_{max} of 15.4 mg/mL. The vaginal wall infiltration was detected in 2 (4.4%) patients. Penetration of mesorectal fascia was detected in 21 (46.7%) of patients. Four patients (8.9%) had liver metastases identified by ^{18}F-FDG PET/CT. The overall sensitivity, specificity and accuracy of ^{18}F-FDG PET/CT in T staging was 90.7%, 91.9%, and 90.5%, respectively. The overall sensitivity, specificity and accuracy of ^{18}F-FDG PET/CT in detection of metastatic lymph node was 85.8%, 89.8%, and 89%, respectively. PET/CT shows low sensitivity (77.3%) and specificity (25%) in analyzing mesorectal fascia involvement. The overall sensitivity of ^{18}F-FDG PET/CT in M staging was 100%. Conclusions: ^{18}F-FDG PET/CT is highly sensitive for initial T staging of rectal cancer especially in advanced disease. This imaging modality is highly accurate in detection of metastatic lymph nodes and liver metastases, but it has no role in defining of mesorectal fascia involvement. Therefore, ^{18}F-FDG PET/CT should be incorporated routinely in preoperative staging together with conventional imaging.

Key word: Rectal cancer, initial staging, positron emission tomography/computed tomography.

1. Introduction

In the United States, CRC (colorectal cancer) is one of the most common malignancies in humans. It is at third place behind lung and prostate cancer in men and behind breast cancer and lung cancer in women, accounting for 8% of all new cancer cases for both genders [1]. The American Cancer Society estimates 95,520 new cases of colon cancer and 39,910 new cases of rectal cancer in the United States for 2017 [2].

Surgical resection is a routine treatment option for rectal cancer. However, in patients with advanced tumor stages preoperative neoadjuvant radiochemotherapy has become a standard procedure. Adequate treatment protocol and prognosis are dependent on the size and extent of the primary tumor, involvement of the mesorectal fascia and nodal and distal metastases. For these reasons, accurate initial staging is essential for selection of the treatment algorithm in each patient [3]. It is recommended that staging should be performed according to the AJCC

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(American Joint Cancer Committee)/UICC (Union for International Cancer Control) TNM classification, 8th edition. This classification uses the TNMs (tumor, node, metastases) classification, which assesses local infiltration, lymph node involvement and distant metastases [4].

In rectal cancer, the conventional imaging including endorectal ultrasound, contrast enhanced CT and MRI shows high accuracy for local T staging, but low sensitivity for N staging. However, MR is currently the most advanced staging modality in patients with rectal tumors allowing the exact evaluation of the topographic relationship of tumor margins to the mesorectal fascia [5, 6]. Since accumulation of 2-[fluorine-18] FDG (fluoro-2-deoxy-D-glucose) is increased in malignant tumors, ^{18}F-FDG PET/CT became a popular non-invasive imaging modality for diagnostics of rectal cancer. Its ability for early detection of malignancy makes possible detection of metastatic normal-sized lymph nodes. However, new edition of ESMO clinical practice guidelines on rectal cancer does not recommend PET/CT as a routine procedure for initial staging; PET/CT imaging can be used only in addition to conventional methods (liver MRI and contrast enhanced CT of the thorax, abdomen and pelvis) to assess features at presentation associated with a high risk of metastases (e.g. extensive extramural vascular invasion on MRI or high levels of carcinoembryonic - CEA markers) [7].

Although metabolic imaging improves the accuracy of initial staging by clarifying equivocal findings on conventional imaging (CT and MRI), the role of PET/CT imaging remains controversial.

The aim of the study was to assess the diagnostic value of ^{18}F-FDG PET/CT imaging in the initial staging of rectal cancer.

2. Material and Methods

2.1 Patients

Forty-five patients with colorectal cancer who underwent ^{18}F-FDG PET/CT imaging during the period from 2011 to 2014 were analyzed in this study. Inclusion criteria for this study were: patients under 70 years of age with histologically proven rectal malignancy after endoscopy in whom surgical treatment was indicated; no coexisting second primary malignancy; ECOG (Eastern Cooperative Group) patient performance status was 0, 1 or 2; and no presence of comorbidities (e.g. decompensated cardiovascular or respiratory diseases, unregulated diabetes, acute renal failure, or acute infective diseases). Patients who underwent chemotherapy, and/or radiotherapy 6 months before PET/CT exam or those who had surgery during the past 3 months prior to the ^{18}F-FDG PET/CT scanning were excluded from the study.

TNM staging of patients was done according to the ^{18}F-FDG PET/CT findings. The following parameters were analyzed in the study: tumor extension beyond rectal wall, mesorectal fascia involvement, localization and number of involved lymph nodes. After ^{18}F-FDG PET/CT imaging all patients underwent surgery. Patients underwent different surgical procedures including total mesorectal excision, amputation of the rectum, anterior rectal resection, and rectosigmoid resection. Lymphadenectomy was performed for each patient following the recommended 12-node standard. Liver metastases were resected.

After the PET/CT imaging, patients were operated in different surgical centers in the region. Histopathologic reports were obtained for all patients, but no immunohistochemical analysis was done for any of the patient. Histology was the reference standard for initial staging and different stages were determined (T, N and M). Stages were defined according to the ^{18}F-FDG PET/CT result and correlated with histological rectal cancer stages.

The Institutional Ethical Committee had approved this study and written consent was obtained from all patients.

2.2 ^{18}F-FDG PET/CT

Dual modality whole body imaging was performed using a PET/CT scanner (Biograph True64, Siemens Medical Solutions, USA Inc.). Patients were required to fast for at least 6 hours before scanning, and blood glucose levels were checked before the ^{18}F-FDG injection. The optimal glucose levels were < 10 nmol/L. An oral contrast agent was given to all patients. Intravenous contrast agents were not used. Patients rested during the 60 minutes of uptake period in a quiet room without any administration of muscle relaxant during the waiting period.

PET images were obtained approximately one hour after an intravenous injection of 3.7 MBq/kg of ^{18}F-FDG. The CT scans were acquired from the base of the scull to the upper thighs with automatic, real-time dose modulation amperage (CareDose4D—Siemens), using the following parameters: 40 mAs, 120 kV, 5 mm slice thickness, pitch of 1.5; and a rotation time of 0.5 s. Immediately after the CT scanning, PET data were acquired with the patient in the same position on the table covering the same field of view as CT for 3 min/bed position in 3-dimensional mode. The patient maintains normal tidal respiration throughout the study that lasts approximately about 30 to 40 minutes. PET images were reconstructed using noncontrast CT data for attenuation correction.

2.3 Image Analysis

^{18}F-FDG PET, CT and fused ^{18}F-FDG PET/CT images were reviewed on the dedicated workstation (syngo Multimodality Workplace—Siemens AG) that can display three orthogonal planes for CT, PET and PET/CT fused images (transaxial, coronal and sagittal) and maximum-intensity projection images. All ^{18}F-FDG PET/CT images were interpreted by two experienced nuclear medicine physicians and one radiologist by consensus. Anatomic confirmation was done with CT images. The maximum standardized uptake values (SUV_{max}) were calculated automatically by software for all pathological lesions. The positive FDG-PET finding was accepted as ^{18}F-FDG hypermetabolism (SUV_{max} value over 2.5) at the site of pathological changes on CT. A physiologically increased ^{18}F-FDG uptake was excluded.

2.4 Statistical Analysis

Descriptives were used for frequency analyses and for calculation of sensitivity. For significance calculation of the contingency tables χ^2 test was used. In addition, the Monte Carlo simulation and Fisher's exact test were used for the table fields where the number of cases was smaller than demanded.

3. Results

There were 45 patients with CRC, 21 (46.7%) women and 24 (53.3%) men; the mean age of the patients was 62.91 years (range: 41-78 years). According to the PET/CT scans, all patients were staged into T (T2, T3, and T4), N (N0, N1 and N2) and M stages (M0 and M1) (Table 1).

Table 1 Patients' staging according to the PET/CT.

Stage	Number of patents (%)
T staging	
T2	11 (24.4)
T3	31 (68.9)
T4	3 (6.7)
Total	45 (100.0)
N staging	
N0	16 (35.6)
N1	15 (33.3)
N2	13 (28.9)
Total	45 (100.0)
M staging	
M0	41 (91.1)
M1	4 (8.9)
Total	45 (100.0)

3.1 T staging

Eleven (24.4%) patients were staged as T2, 31 (68.9%) patients as T3, and 3 (6.7%) patients as T4. The average tumor diameter measured as the FDG activity diameter for all T stages was 6.023 cm. The average tumor diameters measured as the FDG activity diameter for T2, T3 and T4 stages were 4.46 cm, 6.37 cm, and 8.87 cm, respectively. The average SUV_{max}

value of the primary tumor for all T stages was 26.02 gm/mL. The average SUV_{max} values of the primary tumors for T2, T3 and T4 stages were 20.64 gm/mL, 27.64 gm/mL, and 29.31 gm/mL, respectively. According to ^{18}F-FDG PET/CT results, the penetration of mesorectal fascia was detected in 21 (46.7%) of patients (Figs. 1 and 2). Involvement of the mesorectal fascia was excluded in 7 (15.6%) patients,

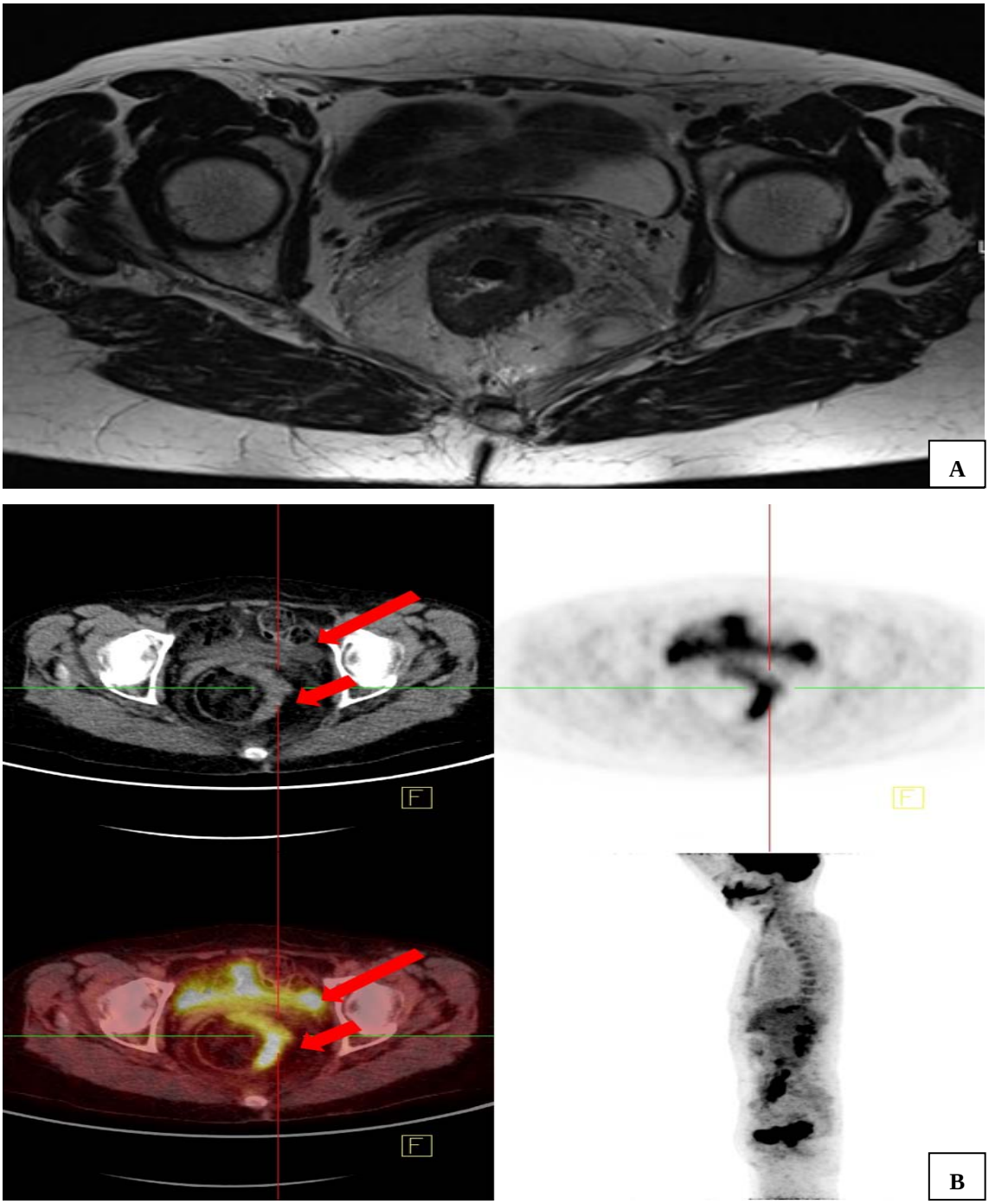

Fig. 1 65-year old woman, histologically confirmed Adenocarcinoma invasivum intestini crassi, G2, pT3N1b.
A. MR T2W, axial plane, shows infiltration of the rectum with an extramural involvement of the perirectal fat and mesorectal fascia. B. ^{18}F-FDG PET/CT scan, axial plane shows hypermetabolic soft-tissue mass in the left posterior wall of the rectum, SUV_{max} 9.15 with involvement of the adjacent perirectal fat (short arrow), corresponding to the primary tumor. Additionally, there is an FDG avid lymph node in the pararectal region, SUV_{max} 5.0, corresponding to the nodal involvement (long arrow).

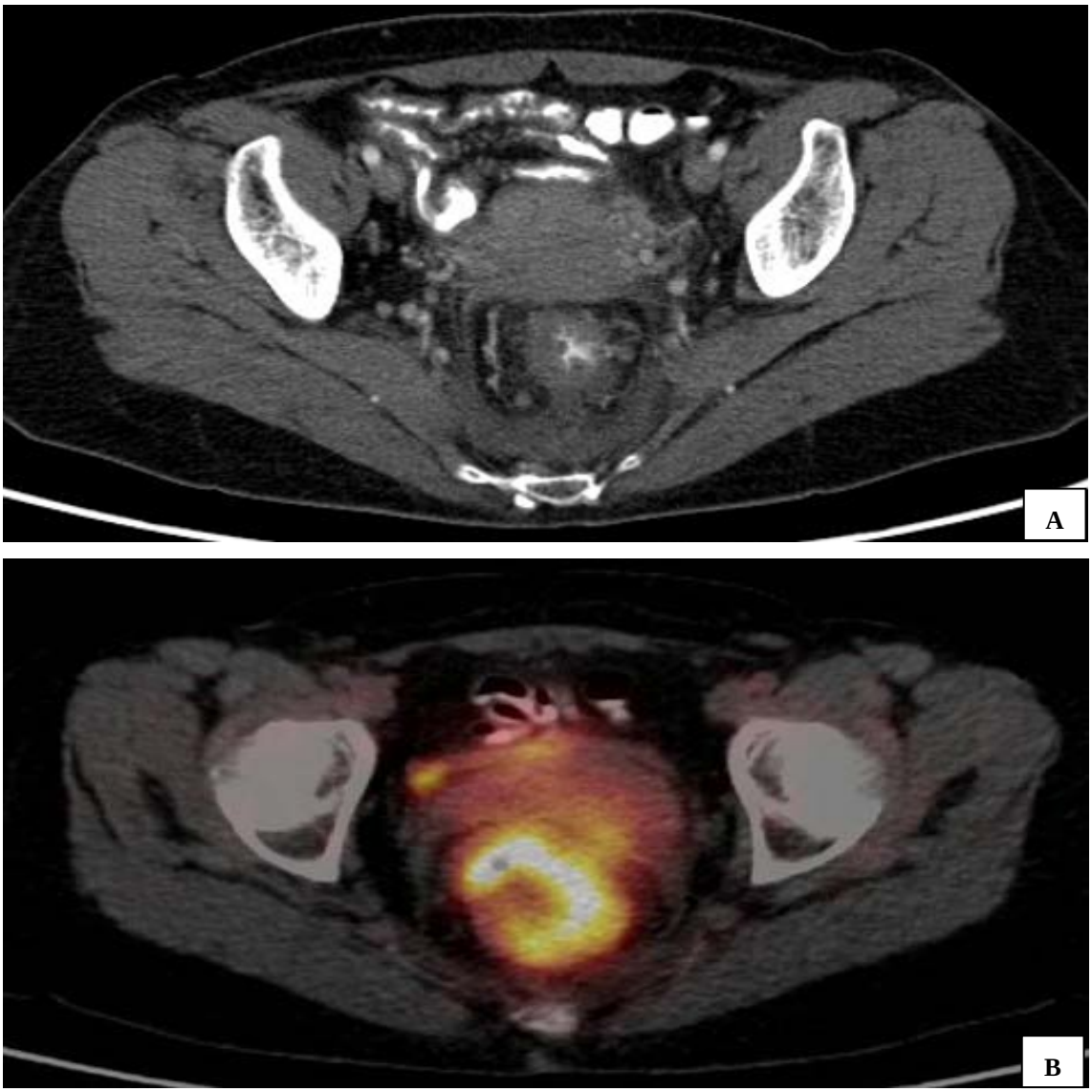

Fig. 2 52-year old woman, histologically confirmed Adenocarcinoma partim mucinosum recti, HG2, pT4N0.
A. CT scan, axial plane, shows the infiltration of the rectum with transmural extension toward perirectal fat, as well as involvement of mesorectal fascia.
B. ^{18}F-FDG PET/CT scan, axial plane, shows FDG avid soft-tissue infiltration of the rectum, without clear delineation from uterus, SUV_{max} 32.71, corresponding to the primary tumor.

while mesorectal fascia infiltration was not able to define in 15 (33.3%) of patients. The vaginal wall infiltration was detected in 2 (4.4%) patients. ^{18}F-FDG PET/CT scan detected benign lesions (most likely polyps) in 17 (28.3%) patients. Criteria in discrimination between malignant and benign lesions included size and shape of the lesion. The average SUV_{max} values of these benign lesions were very high—up to 15.4 gm/mL. The overall sensitivity, specificity and accuracy of ^{18}F-FDG PET/CT in T staging was 90.7%, 91.9%, and 90.5%, respectively (Table 2).

3.2 N Staging

Sixteen (35.6%) patients were staged as N0, 15 (33.3%) patients as N1, 13 (28.9%) patients as N2, while N stage was not determined in 1 (2.2%) patient. FDG avid lymph nodes were localized in presacral, perirectal and inguinal regions. The average diameter of the lymph nodes measured as the FDG activity

diameter for all N stages was 6.177 cm. The average diameters of the lymph nodes measured as the FDG activity diameter for N1 stage and N2 stage were 2.29 cm and 2.23 cm, respectively. The average SUV_{max} values of the lymph nodes in N1 stage and N2 stage were 6.04 gm/mL and 6.33 gm/mL, respectively. The overall sensitivity, specificity and accuracy of ^{18}F-FDG PET/CT in detection of metastatic lymph node was 85.8%, 89.8%, and 89%, respectively (Table 3).

3.3 M Staging

PET/CT imaging revealed liver metastases in 4 (8.9%) patients, with diameter sized in a range from 1.2 cm to 2.7 cm while SUV_{max} values ranged from 3.99 gm/mL to 6.24 gm/mL. The overall sensitivity of ^{18}F-FDG PET/CT in M staging was 100%. The example of liver metastases in patients with CRC is shown in Fig. 3.

Table 2 Characteristics of the primary tumors measured according to PET/CT.

Diameters of the primary tumor measured by PET/CT			
Stage	T2	T3	T3
Mean	4.464	6.368	8.867
95% Confidence interval for lower bound	3.628	5.514	4.270
95% Confidence interval for upper bound	5.299	7.222	13.463
Mean	4.500	6.500	7.900
Variance	1.547	4.281	3.423
Standard deviation	1.2436	2.0692	1.8502
Minimum	3.0	4.1	7.7
Maximum	6.0	13.0	11.0
Range	3.0	8.9	3.3
Interquartile range	3.0	2.2	-
SUV_{max} values of the primary tumor measured by PET/CT for T2, T3 and T4 stage			
Stage	T2	T3	T3
Mean	20.6445	27.6129	29.3100
95% Confidence interval for lower bound	17.9288	24.1820	12.5732
95% Confidence interval for upper bound	23.3603	31.0438	46.0468
Mean	21.2200	25.8800	32.7100
Variance	16.341	87.488	45.394
Standard deviation	4.04244	9.35351	6.73748
Minimum	15.87	15.36	21.55
Maximum	25.91	47.33	33.67
Range	10.04	31.97	12.12
Interquartile Range	8.33	15.27	-

Table 3 Characteristics of the involved lymph nodes measured by PET/CT.

Diameters of the involved lymph nodes measured by PET/CT		
Stage	N1	N2
Mean	2.2857	2.2308
95% Confidence interval for lower bound	1.8750	1.9646
95% Confidence interval for upper bound	2.6964	2.4969
Mean	2.2000	2.3000
Variance	.506	.194
Standard Deviation	.71129	.44043
Minimum	1.40	1.40
Maximum	4.00	2.80
Range	2.60	1.40
Interquartile Range	87	55

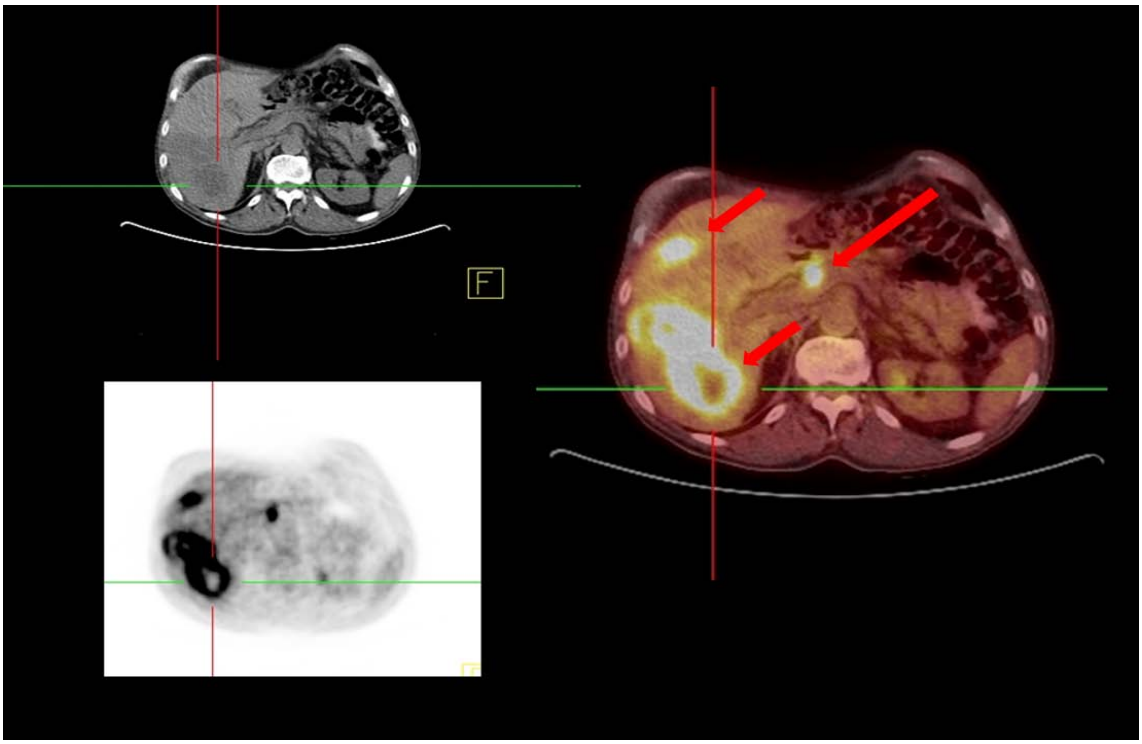

Fig. 3 41-year old woman, histollogicaly confirmed as Adenocarcinoma infiltrativum recti, HG2, pT3 N1a.
Two FDG avid soft tissue masses located in the liver (S7/8 and S7), SUV_{max} 20.3, consistent with liver metastases (short arrows). FDG avid lymph node in the liver hilum, SUV_{max} 4.55 consistent with metastatic nodal involvement (long arrow).

3.4 Surgical Treatment

After ^{18}F-FDG PET/CT all patients underwent different types of primary surgery: 13 (28.9%) patients underwent resection of recto-sigmoid colon; 13 (28.9%) patients underwent low anterior rectal resection; 8 (17.8%) patients underwent proctectomy, and 11 (24.4%) patients underwent resection of sigmoid colon. The findings of histopathology analysis indicated the presence of adenocarcinoma in 21 (91.1%) patients and mucinous adenocarcinoma in 4 (8.9%) patients. Based on the positive FDG PET/CT findings, 4 (8.9%) patients with detected liver metastases were operated and metastatic disease was confirmed histologically in all of them.

Patients who were assigned for surgical treatments in our institution were preoperatively examined by MRI. In patients with T3 stage (with mesorectal fascia penetration and nodal involvement) radiochemotherapy was performed instead of surgery.

Histopathological reports were used to determine TNM staging 7th edition in all patients. Comparison between the results obtained by ^{18}F-FDG PET/CT imaging and histological findings shows no statistical significance in T staging (p = 0.000). However, there was statistically significant difference between these two methods in mesorectal fascia involvement analysis.

In the settings of N staging, we detected a significant correlation between ^{18}F-FDG PET/CT imaging and histological results (p = 0.000). By analyzing lymph node size measured by two methods, our results showed negative correlation of high significance (p = 0.01). Lymph node diameters measured on ^{18}F-FDG PET/CT images were larger than nodal diameters obtained by the histopathology.

3.5 Diagnostic Value of ^{18}F-FDG PET/CT Imaging

Diagnostic values of ^{18}F-FDG PET/CT imaging for T and N staging were done by comparing ^{18}F-FDG PET/CT results to histological findings. Overall, the ^{18}F-FDG PET/CT imaging in T staging shows 90.7% of sensitivity, 91.9% of specificity, 83.6% of PPV,

Table 4 Diagnostic value of PET/CT in T and N staging.

Stage	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
T staging					
T2	87.7	85.7	54.5	96.8	85.7
T3	84.4	90	96.4	64.3	85.7
T4	100.0	100.0	100.0	100.0	100.0
N staging					
N0	73.7	90.9	87.5	80.0	82.9
N1	91.7	86.2	73.3	96.1	87.8
N2	80.0	93.5	80.0	93.5	90.2

87.03% of NPV and 90.5% of accuracy. The ^{18}F-FDG PET/CT imaging in N staging shows 85.8% of sensitivity, 89.8% of specificity, 80.3% of PVP, 89.9% of NPV, and 89% of accuracy. The sensitivity, specificity, PVP, NVP, and accuracy of ^{18}F-FDG PET/CT imaging in detection of mesorectal fascia involvement were 77.3%, 25%, 85%, 16%, and 69.2%, respectively. Diagnostic values for different T and N stages are presented in Table 4.

3.6 Change in Treatment Management

Our results showed that treatment modality would have been changed in 80% of patients if each of our patients had undergone ^{18}F-FDG PET/CT imaging preoperatively; with upstaging in 2 (4.4%) patients (from T2 stage into T3 stage) and downstaging in 43 (95.6%) patients. In relation to the change in T staging, patients with advanced tumor stage would have been treated by neoadjuvant chemoradiation therapy instead of curative surgery.

4. Discussion

Accurate staging is crucial for individual treatment algorithm in patients with rectal cancer. The optimal treatment selection improves patients' overall survival and quality of life. Among various diagnostic-imaging modalities, conventional imagings including EUS (endoscopic ultrasound) and CT are routinely used as a first-line diagnostic option because of their wide availability and low cost. The EUS is the oldest and most common imaging technique for local staging of rectal cancer [8-11]. It is mostly used for the assessment of early stages of rectal cancer (T1 and T2), while its role is limited in evaluation of advanced disease, in highly stenosing tumors and in patients with mesorectal fascia involvement [12]. In such cases, MR or CT should be used instead [13, 14]. Skandarajah et al. [15] detected EUS overall accuracy in rectal cancer staging of 81.8%. Recent study by Garcia-Aguilar [12] reported that overall accuracy in T and N rectal cancer staging was 69% and 64%, respectively. Similarly to MR, EUS cannot accurately delineate peritumoral inflammation from transmural tumor extension, which results in inaccurate results and overstaging T2 lesions [12, 16]. Recent studies including three-dimensional EUS are superior to CT and two-dimensional EUS in accurate delineation of tumor margins. These results indicate T stage accuracy of 91% and N stage accuracy of 90% in correctly interpreted images [17].

The CT imaging has low accuracy in T staging of 52%-74%, but it increases in more locally advanced tumors reaching the accuracy of 79%-94% [18-21]. The main disadvantage of CT is low spatial and contrast resolution, however its role is mostly in the detection of distant metastases. CT technology has significantly advanced with the development of multidetector row CT (MDTC), which allows high-resolution imaging and reduces acquisition time [22]. Despite improved resolution, however, CT has limitations in the N staging of CRC patients [23]. Ahmetogly et al. [24] reported 86% overall accuracy of MDTC for T staging in rectal cancers. Some authors obtained detectability rate of 78.8% for MDTC in relation to histopathological tumor stage of the resected colorectal cancer [25]. Main disadvantages responsible for low specificity and sensitivity of MDTC for T

staging are lack of clear delineation between tumor and intact visceral tissue and inadequate bowel distension [26].

In rectal cancers, MRI presents accurate and valid diagnostic tool for T staging. During the time, MR slowly surpassed CT imaging for evaluation of locoregional disease. At the beginning, the T staging accuracy of MR was similar to that of CT (59%-88%). However, by introduction of the endorectal coils that allow imaging of the rectal wall, MR accuracy for T staging resulted in significantly higher values of 71%-91% [27-32]. Since differentiation between normal and involved lymph nodes remains problematic, the role of MRI in N staging of rectal cancer is less effective. In recent publication, MR showed 81% overall agreement with histopathological findings for T and N stage prediction in rectal cancer, with improved N staging if MR with phased-array coil was used [33].

During the recent years FDG PET/CT has been widely introduced into the staging of colorectal cancer. Despite the fact that majority of intraluminal primary colorectal cancers are visible on PET/CT (95%-199% of cases), false negative PET/CT results are obtained in mucinous tumors and small tumors in tubulovillous adenomas [34, 35].

Gearhart et al. [36] performed FDG PET/CT in addition to spiral CT and transrectal ultrasound, or MR in patients with low rectal cancer. According to FDG PET/CT, discordant findings were detected in 38% of patients, while therapeutic management was changed in 27% of patients. Davey et al. [37] studied patients with primary rectal cancer and they performed FDG PET/CT after conventional imaging (CT, MRI, and endoanal ultrasound). They reported alteration in tumor and nodal stage of 31% and 46%, respectively, while change in patients' management occurred in 14% of patients. Similar results were obtained by others who performed PET alone or PET/CT imaging on much smaller number of patients [22, 38-40].

Results from our study indicate that in comparison with histopathology, the ^{18}F-FDG PET/CT was an accurate diagnostic method for T staging of rectal cancer, with no statistically significant difference between these two methods. We detected overall sensitivity of ^{18}F-FDG PET/CT in T staging of 90.7%. Our results are concordant with other literature data. Shuiciro et al. [25] and Mainenti et al. [41] report that PET/CT has high detectability rate increasing 90% for T colorectal cancer staging (95% and 94.3%, respectively). In addition, ^{18}F-FDG PET/CT shows higher sensitivity for T staging if compared to MDTC (95% versus 78.8%) [25]. Our results detected no significant difference in T staging after comparison between ^{18}F-FDG PET/CT results and histopathological results. Our data indicated that ^{18}F-FDG PET/CT imaging was highly accurate for T3 and T4 rectal staging.

Because PET/CT modality has not been often used for the initial rectal staging, the literature data on the alteration of preoperative management are limited. The benefits of the PET/CT imaging are particularly in avoiding futile surgical procedures and altering adjuvant therapy. While Gearhart et al. [36] report 27% of alteration in treatment planning, Davey et al. [37] suggest only 12% change in treatment management according to PET/CT results. In addition, similar data were obtained by other authors [34, 38]. Kantorova et al. [34] reported that according to PET results, 16 patients had treatment alteration. Heriot et al. [38] identified 17% of patients who had alteration in preoperative treatment modality; six patients avoided surgery while 2 patients had change of the radiotherapy field. According to our results, 80% of our patients would have had a different treatment management if each of them had undergone PET/CT imaging preoperatively; 4.4% of patients would have been upstaged from T2 stage into T3 stage and 95.6% of patients would have been downstaged. In relation to the change in T staging, patients in advanced tumor stage would have received neoadjuvant chemoradiation therapy instead of curative surgery.

In the present study there was a limitation of

^{18}F-FDG PET/CT in the detection of mucinous rectal carcinomas. Mucinous tumors usually occur in advanced stage of disease; they are more frequent than nonmucinous tumors and have worse prognosis and outcome [42]. In our study 4 (8.9%) patients had mucinous adenocarcinomas and ^{18}F-FDG PET/CT was less efficient. Similarly, Merkel et al. [43] evaluated ^{18}F-FDG PET/CT imaging in the detection of mucinous tumors. They identified mucinous neoplasms in only 59% of patients. In addition, they reported about positive correlation between tumor FDG uptake and cellularity and a negative correlation with the mucinous content.

In our study benign lesions (most likely polyps) were diagnosed in 28.3% of patients according to ^{18}F-FDG PET/CT results. Since average SUV_{max} of the lesions was 15.4 gm/mL, PET/CT is not useful for differentiation benign lesions from malignant tumors.

The most important factor for rectal cancer staging is the assessment of mesorectal fascia. The accuracy of CT for detection of involved mesorectal fascia depends on the localization of the primary tumor. CT has 74% overall sensitivity and 94% overall specificity in prediction of mesorectal fascia involvement. However, tumors in the lower third of the rectum show decreased values of sensitivity and specificity (66% and 82%, respectively). In contrast, sensitivity and specificity for the evaluation of mesorectal involvement using CT is much better for tumors located in the upper two-thirds of the rectum (76% and 96%, respectively) [42]. Currently, MR is the best technique for delineation of mesorectal fascia [5]. In a Mercury study, MR showed high accuracy in detection of extramural involvement in rectal cancer (95.6%) if compared to histopathology [13]. Similar results were obtained by Merkel et al. [43]. In the literature, there are no data on the utility of FDG PET/CT imaging in the evaluation of mesorectal fascia involvement. We reported 77.3% sensitivity and specificity of 25% for ^{18}F-FDG PET/CT examination in detection of mesorectal fascia penetration. PET/CT imaging was not reliable for the assessment of mesorectal fascia involvement because of the statistically significant difference detected between PET/CT results and histopathological results.

Another important predicting factor for prognosis in patients with rectal cancer is N staging. Metastatic lymph nodes in the area surrounding mesorectal fascia are predictive for increased risk of local recurrence. For these reasons, the assessment of nodal involvement in preoperative rectal staging is challenging. Wide range of accuracy rates has been reported for N staging obtained by different imaging tools; 61-80% for endorectal ultrasound, 56-79% for CT, and 57-85% for MRI [5]. The introduction of MDCT allowing thin-collimation scanning and multiplanar reconstructions increases the role of CT in the evaluation of preoperative staging of rectal cancer [44, 45]. Filippone et al. [44] found that accuracy of N staging was significantly increased from 59% with axial images alone to 80% when using combined multiplanar reformation images of MDTC and axial images. Comparing the same two techniques in detection of lymph node metastases, Kulinna et al. [45] obtained similar results. They detected significant difference comparing combination of axial MDTC images and multiplanar reformation images versus axial images alone of $p = 0.01$ (accuracy of 80% versus 59%). Ahmetogly et al. [24] reported 84% overall accuracy of MDTC in N staging.

Although ^{18}F-FDG PET/CT has not been well established in T staging of colorectal cancer, it has increasing role in the assessment of N stage and M stage. In the study by Shuichiro et al. [25] FDG PET/CT showed lower sensitivity in detection of lymph node metastasis than MDCT (34.3% versus 68.6%, respectively). In contrast, PET/CT had specificity higher than that of MDCT (100% versus 72.5%). Limited spatial resolution of FDG PET/CT and its inability to detect tumor deposits in small lymph nodes results in low overall sensitivity for N staging (29-43%) although specificity is high (87%) [23, 35]. In another study, Tsunoda et al. [46] evaluated

diagnostic value of FDG PET/CT in preoperative assessment of lymph node metastases in colorectal cancer. They evaluated PET/CT images according to the three criteria: nodal diameter, abnormal uptake and maximum standardized uptake value (SUV_{max}). They reported that SUV_{max} is a better criterion than abnormal FDG uptake or nodal size in detection of metastatic lymph nodes. FDG PET/CT is therefore highly accurate in detection of distant nodal metastases in colorectal cancer. Mainenti et al. [41] reported 79.4% accuracy of ^{18}F-FDG PET/CT for N staging in CRC patients. In our study, the overall sensitivity, specificity and accuracy of ^{18}F-FDG PET/CT in detection of metastatic lymph node was 85.8%, 89.8%, and 89%, respectively. There was no significant correlation in N staging between ^{18}F-FDG PET/CT imaging and histological results (p = 0.000). Lymph node diameters measured on FDG PET/CT were larger when compared to diameters found by histopathologic analysis. It could be related to the preparation of histopathology samples. In particular, during the sample preparation process perilymphatic tissue is extracted but it contains malignant cells that concentrate FDG at PET/CT imaging. The results of our study indicated that FDG PET/CT was highly accurate in prediction of N rectal staging.

^{18}F-FDG PET/CT is highly accurate for the detection of hepatic and lung metastases, which significantly affects patients' treatment algorithm [47, 48]. Niekel et al. [48] recently made a meta-analysis in CRC patients and reported sensitivity of CT, MR and FDG PET in identification of liver metastases of 83.6%, 88.2%, and 94.1%, respectively. Due to limited spatial resolution, FDG PET is not able to detect liver metastases less than 1cm in size [49, 50]. In our study, liver metastases presented in 4 patients were detected by FDG PET/CT showing its overall sensitivity of 100% for M staging. According to our results, FDG PET/CT seems to be an excellent modality in identification of hepatic metastases in rectal cancer patients.

In the present study there were some limitations. Difficulties in ^{18}F-FDG PET/CT interpretation were influenced by low FDG avidity in mucinous tumors and by technical characteristics of PET/CT machine. Due to limited spatial resolution of low-dose CT, small metastatic lymph nodes were missed at PET/CT imaging, resulting with the false negative findings. The use of FDG PET/CT with contrast enhanced CT may overcome this limitation.

5. Conclusions

^{18}F-FDG PET/CT is highly sensitive for initial T staging of rectal cancer especially in advanced disease. This imaging modality is highly accurate in detection of metastatic lymph nodes and liver metastases, but it has no role in defining of mesorectal fascia involvement. Therefore, ^{18}F-FDG PET/CT should be incorporated routinely in preoperative staging together with conventional imaging.

More studies performed on large number of patients are needed in the future. Development of hybrid modalities, such as PET/MRI, decreases radiation and improves spatial resolution and image quality. In addition, the use of new non-FDG tracers for intracellular molecular imaging other than glycolysis will definitely improve assessment of cancer patients.

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