Can ^{18}F-FDG PET/CT scan change treatment planning and be prognostic in recurrent colorectal carcinoma? A prospective and follow-up study

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Abstract

Objective: To prospectively study whether in patients with resected primary colorectal cancer fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) examination could diagnose the stage, specify treatment procedure and be prognostic. **Subjects and methods**: This prospective study included 75 patients with resected primary colorectal adenocarcinoma referred for ^{18}F-FDG PET/CT to the National PET Center, at the Clinical Center of Serbia, Belgrade, from January 2010 to May 2013. Findings of ^{18}F-FDG PET/CT were compared to findings of subsequent histopathological examinations or with results of clinical and imaging follow-up. Patients were followed after PET/CT examination for a mean follow-up time of 16.7±5.9 months. **Results**: In the detection of recurrent disease ^{18}F-FDG PET/CT showed overall sensitivity, specificity, PPV, NPV and accuracy of 96.6%, 82.4%, 94.9%, 87.5% and 93.3%, respectively. In the detection of stages I and II sensitivity, specificity and accuracy of ^{18}F-FDG PET/CT were: 88%, 96.6% and 94.7%, respectively, and in the detection of stages III and IV sensitivity, specificity and accuracy were 94.9%, 87.5% and 93.3%, respectively. These findings prevented or changed intended surgical treatment in 12/32 cases. Univariate and multivariate Cox proportional regression analyses revealed that metastatic recurrence (stages III and IV) was the only and independent prognostic factor of disease progression during follow-up (P=0.012 and P=0.023, respectively). Although, survival seemed better in patients with local recurrence compared to metastatic recurrent disease, this difference did not reach significance (Log-rank test; P=0.324). In addition, progression-free survival time was significantly longer in patients in whom ^{18}F-FDG PET/CT scan led to treatment changes (Log-rank test; P=0.037). **Conclusion**: ^{18}F-FDG PET/CT was sensitive and accurate for the detection and staging of local and metastatic recurrent colorectal carcinoma, with higher specificity in the detection of local recurrences. The ^{18}F-FDG PET/CT scan induced treatment changes in 30/75 patients, including 12/32 patients in which surgical treatment was previously planned, and progression free survival time was significantly longer in these patients.

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Introduction

Colorectal carcinoma represents the third most common malignant tumor in both men and women in developed world and the third leading cause of cancer-related death [1]. Despite the advances in surgical treatment and introduction of combined therapeutical modalities, 5 years survival rarely exceeds 60%, varying from 90% in localized disease to 11% in patients with spread to distant organs [2].

Current guidelines after apparently curative resection recommend surveillance with imaging tests and regular serum measurements of carcinoembryogenic antigen (CEA) [3]. Despite widespread use of CEA as a marker of early relapse, studies have shown contradictory data, with a large number of false-positive results [4]. Moreover, in practice, increased values of CEA signify recurrent disease and necessitate imaging diagnostic procedures, which may not be necessary [5]. Fluorine-18-fluoro-deoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) is valuable in the detection of recurrent disease in patients after curative resection of colorectal carcinoma [6] and superior to other imaging modalities, such as contrast-enhanced multidetector computed tomography (MDCT) and magnetic resonance imaging (MRI) in differentiating benign post-treatment changes from local recurrence and in detecting of unsuspected metastases [7, 8]. However, some researchers reported lower sensitivity and specificity of ^{18}F-FDG PET/CT compared to MDCT and MRI, in the detection and staging of lymph nodes and liver metastases [9, 10]. Other researchers suggest that pa-

tients with suspected recurrence of colorectal carcinoma, increased CEA levels and negative or equivocal contrast-enhanced MDCT findings should undergo ^{18}F-FDG PET/CT examination [3, 11]. It seems that we still need to study the best use of this imaging modality in various settings [12].

The improvement of survival in patients with colorectal carcinoma could be achieved by identifying disease recurrence and progression, as well as by specifying their treatment planning. The use of various biomarkers for this purpose, although confirmed by a number of studies has not yet been fully accepted in clinical practice [13]. The prognostic role of imaging tools, including ^{18}F-FDG PET/CT in the evaluation of therapy response in colorectal carcinoma has been studied by many researchers, aiming for treatment individualization in order to achieve an optimal therapeutic result [14]. The biological effect of therapy, shown on PET/CT images, was considered to be a stronger prognostic factor compared to anatomical changes [15]. However, data about the role of ^{18}F-FDG PET/CT in disease prognosis and response to treatment in patients after curative resection of colorectal carcinoma are insufficient, with results suggesting a limited rate of the hybrid imaging. Thus, further investigations in this field are indicated [16, 17].

The aim of this study was to determine prospectively in patients with resected colorectal carcinoma whether ^{18}F-FDG PET/CT scan could identify the stage and specify their treatment planning.

Subjects and methods

Study population

This prospective study included patients with colon and rectum adenocarcinoma, after curative resection, which were referred to the National PET Center, at the Clinical Center of Serbia, Belgrade, from January 2010 to May 2013 for ^{18}F-FDG PET/CT examination. The inclusion criteria were: histopathologically confirmed colorectal adenocarcinoma, curative resection of the primary tumor, at least 3 months before and availability for follow-up after ^{18}F-FDG PET/CT for at least 12 months. After exclusion of 15 patients with previous history of another type of malignancy, 10 patients with mucinous colorectal adenocarcinoma, and 16 patients with insufficient follow-up data, 75 patients were finally eligible for the study.

Procedures

The ^{18}F-FDG PET/CT examination was performed when patients had symptoms and signs suggesting recurrence: abnormal or equivocal contrast-enhanced MDCT and/or MRI imaging findings or elevated tumor marker levels. Prior to ^{18}F-FDG PET/CT all patients underwent contrast-enhanced MDCT, measurements of serum levels of CEA, with additional MRI being performed in fifteen patients. During 12 months of follow-up clinical data, results of imaging tests and laboratory data were collected and evaluated after 3, 6 and 12 months. Findings of ^{18}F-FDG PET/CT were compared with findings of histopathological examination or with results of clinical and imaging follow-up. Twenty-six patients underwent control PET/CT scan at our institution during follow-up: 7 patients at 6 months, 14 at 12 months and 5 patients after more than 12 months. Management plan before the ^{18}F-FDG PET/CT scan was considered and compared to the final decision for treatment after the PET/CT scan. The primary endpoint was progression-free survival, based on imaging findings, clinical examination and/or cancer related death. After PET/CT examination, patients were followed for 12 months (38 patients) or more (37 patients), with a mean follow-up time of 16.7±5.9 months. The study was approved by the Ethics Committee of the Faculty of Medicine of the University of Belgrade.

Data acquisition and interpretation

The patients underwent ^{18}F-FDG PET/CT examination on a 64-slice hybrid PET/CT scanner (Biograph, TruePoint64, Siemens Medical Solutions, Inc. USA) at National PET Center, Clinical Center of Serbia, Belgrade. After fasting for 6h patients received an intravenous injection of 5.5MBq/kg of ^{18}F-FDG. Blood glucose level over 11mmol/L was considered as exclusion criteria on PET/CT examination. Following injection of ^{18}F-FDG, patients rested in a quiet and darkened room for 60min, after which images of PET/CT were obtained. Low-dose non-enhanced CT scans (120kV with automatic, real-time dose-modulation amperage, slice thickness of 5mm, pitch of 1,5 and a rotation time of 0.5s) and 3-dimensional PET scans (6-7 fields of view, 3min/field) were acquired from the base of the skull to the mid thigh. Non-corrected and attenuation-corrected CT, PET and fused PET/CT images were displayed for analysis on a Syngo Multimodality workplace (Siemens AG).

Fluorine-18-FDG PET/CT findings were defined as positive if any abnormal ^{18}F-FDG uptake was observed after exclusion of benign and physiological lesions, with or without clearly visible corresponding CT malformation. If the focus of abnormal ^{18}F-FDG uptake was observed at the area close to the primary tumor, the finding was considered as local recurrence (stage I and II). If distant sites of increased ^{18}F-FDG uptake were seen, metastatic recurrent colorectal cancer was reported (stages III and IV). Semi-quantitative analysis of ^{18}F-FDG uptake was based on maximum standardized uptake value (SUVmax), which was corrected for individual body weight and dose injected, and calculated as follows: tissue activity (counts/pixel) multiplied by calibration factor divided by injected ^{18}F-FDG dose (MBq/kg of body weight). Findings were interpreted separately by two nuclear medicine physicians. Consensus was reached in cases of discrepancy.

Final diagnosis of recurrent disease was made either by histopathological examination of the specimens after biopsy or by surgery, or based on clinical, laboratory and imaging evaluation during the first six months after the PET/CT scan. In 32/75 patients ^{18}F-FDG PET/CT findings were confirmed by histopathology examination after surgery or biopsy. The PET/CT study was defined as true-positive when ^{18}F-FDG avid lesions were histopathologically confirmed to be malignant or responded to therapy. The ^{18}F-FDG PET/CT study without abnormal ^{18}F-FDG uptake was considered as physiological or benign, and, if remained so during the follow-up period, was considered true-nega-

tive. A false-positive PET/CT study showed at least one lesion characterized as malignant, but without evidence of disease on the follow-up study. Finally, false-negative studies had evidence of recurrence on further examination during the first six months after PET/CT, despite a negative PET/CT scan at first.

Progression of the disease was considered in cases when: new lesions were detected during follow-up or when the existing lesions increased in size and/or in metabolic activity in any imaging modality of if the disease was fatal. The date of progression was noted and thus, the progression-free survival time was calculated from the day of the first PET/CT examination.

Statistical analysis

The diagnostic value of ^{18}F-FDG PET/CT was assessed by its specificity, sensitivity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy. Chi-square test was used to assess the difference in treatment changes after PET/CT scan between different patient groups. Cox proportional hazards regression model was used to determine whether age (≤60 vs >60), gender (male vs female), localization of primary tumor (colon vs rectum), chemo-radiotherapy before and/or after resection of the primary tumor (yes vs no), CEA levels (normal vs increased), MDCT and MRI imaging results (positive vs negative) and ^{18}F-FGD PET/CT results (negative vs stage I and II recurrence vs stage III and IV) were associated with the higher risk of progression of the disease during follow-up. These analyses consisted of determination of hazard ratios (HR) for all factors with 95% confidence interval (CI). Survival analyses were performed using Kaplan-Meier method, and the groups were compared using the Log-rank test. A P value of less than 0.05 was considered significant.

Results

The demographic and clinical characteristics of patients included in this study are given in Table 1. In our study population, ^{18}F-FDG PET/CT suggested recurrent disease in 59/75 of cases, while in 16/75 of patients no foci of abnormal 18F-FDG uptake suggesting malignant disease were observed. In 10/75 of patients local recurrence was suggested (stages I and II), while distant spread of the disease (stages III and IV) was seen in another 49/75 of patients. PET/CT examination suggested liver metastases in 26/59, lung metastases in 22/59, and other sites of involvement (bone, peritoneum) in 5/59 of patients.

The PET/CT scan changed the stage of the disease suggested by previous imaging modalities in 32 patients, out of which 20 patients were up-staged and 12 were down-staged.

The diagnostic efficiency of ^{18}F-FDG PET/CT

The ^{18}F-FDG PET/CT scan was true positive in 56/75 of patients, and false positive in 3/75. In 14/75 of patients, PET/CT study was negative and no signs of the disease were observed during the first 6 months of follow-up (true negative). Overall, ^{18}F-FDG PET/CT showed sensitivity of 96.6% and specificity of 82.4% in the detection of recurrent disease. PPV and NPV of the PET/CT were 94.9% and 87.5%, respectively. The diagnostic accuracy of ^{18}F-FDG PET/CT in the detection of recurrent disease was 93.3%.

***Table 1**. Demographic and clinical characteristics of patients included in the study, N=75*

		Number
Gender	Male	45
	Female	30
Age	Mean 60.1±10.6	
	≤60	34
	>60	41
Localization of primary tumor	Rectum	39
	Colon	36
Time elapsed from surgery	Median 24 mts	
	≤12	13
	12-24	27
	>24	35
Chemo-radiotherapy before ^{18}F-FDG PET/CT	Preoperative	5
	Postoperative	52
	Pre + postoperative	5
	None	13
CEA	Normal	31
	Increased	44
MDCT and MRI results	Positive	51
	Negative	24
^{18}F-FDG PET/CT	Negative	16
	Stage I/II	10
	Stage III/IV	49
Progression during follow-up	Yes	39
	No	36

CEA: Carcinoembryogenic antigen; MDCT: Multi-detector computed tomography; MRI: Magnetic resonance imaging; ^{18}F-FDG PET/CT: Fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography

In the detection of local recurrence (stages I and II) sensitivity, specificity, PPV, NPV and accuracy ^{18}F-FDG PET/CT were 88%, 96.6%, 88%, 96.6% and 94.7%, respectively. Moreover, in the detection of distant metastatic disease (stages III and IV) the sensitivity, specificity, PPV, NPV and accuracy of ^{18}F-FDG PET/CT were 94.9%, 87.5%, 96.6%, 82.4% and 93.3%, respectively.

^{18}F-FDG PET/CT findings and treatment changes

We analyzed the impact of ^{18}F-FDG PET/CT on further treatment of patients included in the study. We compared the treatment plan before ^{18}F-FDG PET/CT, suggested by clinical examination and previous imaging findings, with the treatment decisions made after ^{18}F-FDG PET/CT scan (Table 2).

Overall, ^{18}F-FDG PET/CT results led to treatment changes in 30/75 patients. Out of 32 patients planned to have curative surgical treatment before PET/CT, in 11 patients futile surgical treatment was averted due to PET/CT scan findings of disseminated disease, and in 1 patient surgical approach was modified, resulting in exclusion of unnecessary surgery or change in surgical approach in 12/32 patients (Table 2).

We analyzed the association of specific pathological find-

Table 2. *The change of treatment plan after ^{18}F-FDG PET/CT scan*

Treatment plan before ^{18}F-FDG PET/CT	N	Treatment after ^{18}F-FDG PET/CT	N
Surgery	23	Surgery *	10
		Chemo/radiation	5
		Palliative	0
		None**	8
Surgery+chemo/ radiation	9	Surgery+chemo/ radiation	9
Chemo-radiation	19	Surgery	2
		Chemo/radiation ***	14
		Surgery+chemo/ radiation	1
		Palliative	2
		None	0
None	24	Surgery	3
		Chemo/radiation	8
		Surgery+chemo/ radiation	1
		Palliative	2
		None	10

^{18}F-FDG PET/CT: Fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography;
** In one patient surgical approach was modified after ^{18}F-FDG PET/CT scan. ** In two patients ^{18}F-FDG PET/CT also suggested surgery, which was cancelled due to the clinical status of patients. *** In one patient, the current chemotherapeutic protocol after ^{18}F-FDG PET/CT scan was modified*

Table 3. *Clinical and demographic patients' data as possible prognostic factors of disease progression*

		Progression	Without progression
Gender			
	Male	22	23
	Female	17	13
Age			
	≤60	18	16
	>60	21	20
Localization of primary tumor			
	Rectum	21	18
	Colon	18	18
Chemo-radiotherapy before PET/CT			
	Yes	33	29
	No	6	7
CEA			
	Increased	27	17
	Normal	12	19
MDCT and MRI			
	Positive	25	26
	Negative	14	10
^{18}F-FDG PET/CT			
	Negative	4	12
	Stage I and II	5	5
	Stage III and IV	30	19

CEA: Carcinoembryogenic antigen; MDCT: Multi-detector computed tomography; MRI: Magnetic resonance imaging; ^{18}F-FDG PET/CT: Fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography; CRT: Chemo-radiotherapy; The first column presents data on patients who developed disease progression during follow-up (n=39), and the second column contains data of patients who did not developed disease progression (n=36)

ings on ^{18}F-FDG PET/CT (local recurrence or stages III and IV) with the treatment decision after the PET/CT scan. The results showed that local recurrence diagnosed by PET/CT was significantly associated with more treatment alterations as compared to metastatic recurrent cancer (Chi-square test; P=0.008).

^{18}F-FDG PET/CT findings and disease progression

Disease progression during follow-up was observed in 39/75 patients. Progression in terms of local recurrence during follow-up was observed in only three patients, so these patients were upstaged from no disease to stages I and II. In 36 patients progression of the disease was presented with distant metastatic disease (stages III and IV). Among patients with no disease at the time of ^{18}F-FDG PET/CT, 1 patient developed stage III disease, while 2 patients developed stage IV during follow-up. One patient changed the stage from I or II to III, five patients progressed from I or II to stage IV. Twenty-seven patients progressed within stage IV during follow-up, eight of them progressing from only hepatic to extra-hepatic disease.

Possible clinical and demographic prognostic factors, including ^{18}F-FDG PET/CT findings compared between patients with and without disease progression are summarized in Table 3.

Univariate Cox proportional hazardous analysis showed that there was no higher risk of disease progression in patients diagnosed with local recurrence (stage I or II) on ^{18}F-FDG PET/CT (P=0.143, HR 2.94, CI(95%) 0.69-12.38) compared to those with normal scans. However, findings of stages III or IV on the ^{18}F-FDG PET/CT scan were significantly more associated with disease progression compared to patients with normal PET/CT scan (P=0.012, HR 4.64, CI(95%) 1.41-15.27).

In multivariate analysis, stages III and IV of recurrent disease seen on ^{18}F-FDG PET/CT remained the only and independent prognostic factor of disease progression during follow-up (P=0.023, HR 4.28, CI(95%) 1.23-14.92). These results are shown in Table 4.

Median progression-free survival (PFS) times in patients with normal and abnormal ^{18}F-FDG PET/CT scan were 15 (range 8-36) and 12.5 (range 3-30) months, respectively. The Log-rank test showed a significant difference in survival times between patients with PET/CT positive and PET/CT negative studies (P=0.007). However, there was no significant difference in survival times between patients with local recurrence and stages III and IV diagnosed on PET/CT (Log-rank test; P=0.324) (Figure 1).

In further analysis we evaluated the effect of treatment changes induced by ^{18}F-FDG PET/CT on progression-free

***Table 4**. Variables and their significance in prognosis of disease progression during follow-up (Cox proportional hazardous model)*

	Univariate			Multivariate		
Variable	HR	95% CI	P	HR	95% CI	P
Age	0.99	0.97-1.03	0.929	1.37	0.68-2.77	0.378
Gender	0.74	0.39-1.41	0.451	0.76	0.37-1.56	0.451
Localization	1.04	0.55-1.99	0.897	0.90	0.46-1.75	0.754
CEA	1.98	0.98-4.01	0.056	1.71	0.79-3.68	0.171
Chemo-radiotherapy	0.77	0.39-1.51	0.455	1.17	0.44-3.06	0.755
MDCT and MRI	1.03	0.43-2.47	0.951	0.52	0.25-1.06	0.072
^{18}F-FDG PET/CT						
Local recurrence						
Stage III and IV	2.94	0.69-12.38	0.143	1.92	0.42-8.77	0.400
	4.64	1.41-15.27	0.012*	4.28	1.23-14.92	0.023*

*HR: hazard ratio; CI: confidence interval; CEA: Carcinoembryogenic antigen; MDCT: Multi-detector computed tomography; MRI: Magnetic resonance imaging; ^{18}F-FDG PET/CT: Fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography; *P<0.05*

survival. After exclusion of patients who were not planned to receive treatment neither before nor after PET/CT (n=10), patients subjected to palliative treatment after PET/CT scan (n=4) and patients in whom PET/CT did not affect previous therapy plan, but who were not treated due to poor clinical status (n=2), 59 patients were included in this analysis. Patients were divided in two groups: patients in whom PET/CT did not change treatment plan (group 1; n=33), and patients in whom PET/CT led to initiation of therapy or changes in treatment plan (group 2; n=26). Median PFS times in groups 1 and 2 were 12 (range 3-30) and 15 months (range 5-36),

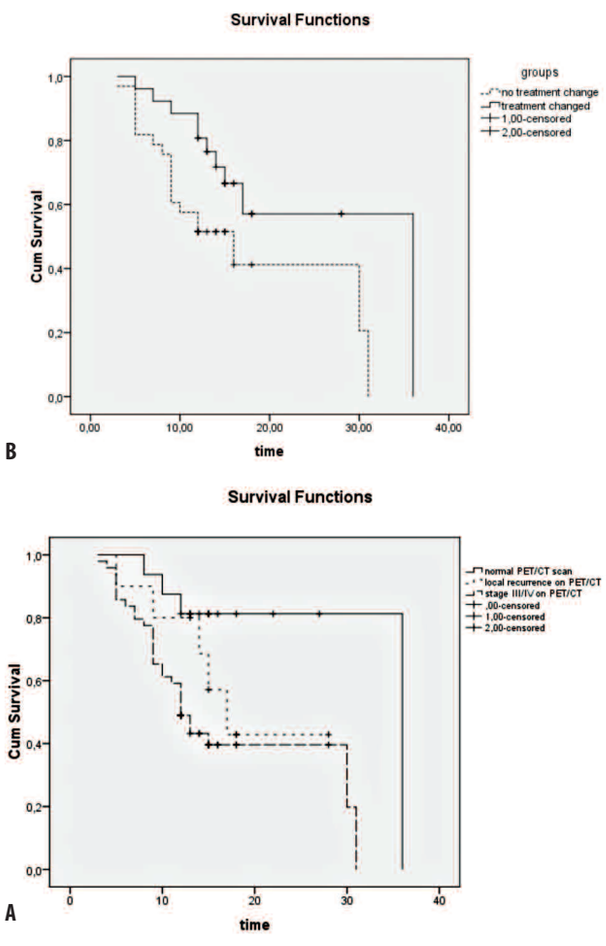

Figure 1. A. Kaplan-Meier analysis of progression-free survival in patients with normal ^{18}F-FDG PET/CT scan compared to those with local recurrence and stages III or IV diagnosed on PET/CT; B. Kaplan-Meier analysis of progression-free survival in patients in whom treatment plan was not changed after ^{18}F-FDG PET/CT vs. those in whom ^{18}F-FDG PET/CT led to treatment changes

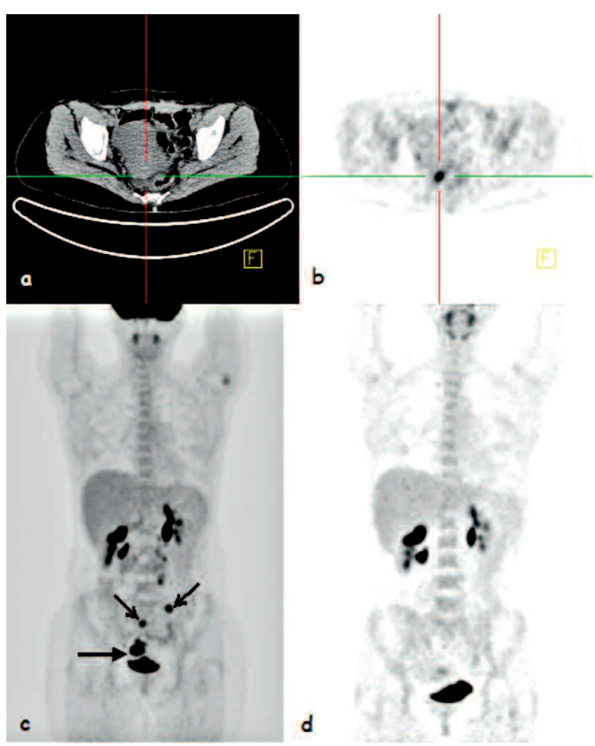

Figure 2. Serial ^{18}F-FDG PET/CT examination of a 36 years old female patient with resected adenocarcinoma of the ascending colon. First postoperative ^{18}F-FDG PET/CT scan revealed a focus of high ^{18}F-FDG uptake in the right pararectal area (cross-bars) (a, b); Contrast-enhaced MDCT was equivocal, and CEA 5.1ng/mL. Control PET/CT scan after one year, without any treatment, demonstrated progression of local recurrence (arrow) and spread of the disease to retroperitoneal lymph nodes (c). One year after treatment by FOLFIRI and bevacizumab, PET/CT showed metabolic regression of the disease and good response to treatment (d).

respectively, and this difference was statistically significant (Log-rank test; P=0.037) (Figure 1).

An example of one patient with serial ^{18}F-FDG PET/CT examination and disease progression during follow-up, is presented in Figure 2.

Discussion

The results observed in this study showed high sensitivity and accuracy of the ^{18}F-FDG PET/CT scan in the detection of recurrent disease in colorectal carcinoma patients, high specificity in the detection of local recurrence and played an important role in treatment planning, especially in local recurrence patients.

The sensitivity and accuracy of ^{18}F-FDG PET/CT in the detection of recurrent colorectal cancer was high, which complies with the findings of other researchers [18]. One meta-analysis underlined that although MDCT is the most widely used imaging modality in the evaluation of colorectal cancer patients with suspected recurrence, PET/CT shows the highest accuracy in the detection of recurrence, which is in accordance with our findings [19, 20]. However, there is evidence that combined ^{18}F-FDG PET/MR imaging can show even higher sensitivity in the detection of colorectal cancer liver metastases compared to PET/CT [21]. The overall specificity of ^{18}F-FDG PET/CT in our study was a little more than 80%. This complies with the results of meta-analysis from other researchers [22]. We reported high specificity in the detection of local recurrence, with only two false positive cases due to inflammatory changes and also high sensitivity and accuracy in the detection of metastatic recurrent colorectal cancer, which is in line with other studies [22].

Although treatment decision after ^{18}F-FDG PET/CT was not only based on scan results, this imaging modality had influenced treatment decisions by 40%. Our results showed that the decision to have treatment changes after the ^{18}F-FDG PET/CT scan was made in 8/10 patients with local recurrence. Recent meta-analysis showed that ^{18}F-FDG PET/CT affected the management in average of about one-quarter (ranging between 15%-42%) of patients with colorectal cancer and liver metastases in terms of exclusion from curative surgery and modification of surgical approach [10]. Our study showed even a larger proportion of patients with altered treatment regime, probably due to heterogeneity of our study population and a higher incidence of extra-hepatic disease. Other researchers showed that in patients with metastatic disease ^{18}F-FDG PET/CT was very valuable in restaging and optimizing treatment and in preventing futile surgical treatment in one third of the patients [23], which complies with our results.

The prognostic and predictive role of ^{18}F-FDG PET/CT in colorectal carcinoma was evaluated by a large number of studies, mostly preoperatively. One systematic review suggested that ^{18}F-FDG PET was a significant univariate predictor of overall survival, but not from the time of colorectal cancer recurrence [24]. Pretreatment ^{18}F-FDG uptake in metastatic colorectal cancer predicts the disease outcome, irrespective of the subsequent treatment modality, as patients with ^{18}F-FDG avid disease show reduced overall survival [25], which agrees with our study results. Although it was shown that metabolic response was associated with the overall survival, complete metabolic response was not predictive of disease-free survival [24]. In another study authors reported that quantitative PET parameters were independent predictors of pathologic response [26]. Similarly, low metabolic total volume and low total lesion glycolysis of the primary rectal tumor were found to be associated with better prognosis and longer recurrence-free survival [27]. In a recently published retrospective study, authors reported that ^{18}F-FDG glucose consumption at the anastomotic site 13±3 months after complete surgical resection of colorectal carcinoma, expressed as SUVmax, significantly contributed to the prediction of events such are newly diagnosed distant metastases and cancer-related death, suggesting that semi-quantitative ^{18}F-FDG PET may help identifying high risk patients [28]. However, we did not include semi-quantitative ^{18}F-FDG PET/CT parameters in our analyses. In addition, semi-quantitative analyses performed by other imaging tools, such as determination of the depth of tumor invasion and apparent diffusion coefficient (ADC) on MRI in rectal cancer are known to be strong predictors of treatment response and recurrence-free survival [29, 30]. Other authors, however, report that neither PET nor MDCT can be used as a valuable tool for the prediction of complete response following chemoradiotherapy in locally advanced rectal cancer [31].

In a multi-center prospective study the prognostic significance of additional lesions detected by ^{18}F-FDG PET in patients with recurrent colorectal cancer, compared to MDCT findings, was evaluated. Authors reported on shorter progression-free survival in patients with additional disease sites compared to patients with no additional lesions seen on PET scan [32]. Similarly, our study showed that patients diagnosed with stages III and IV of recurrent colorectal cancer on ^{18}F-FDG PET/CT had a poorer prognosis with inferior progression-free survival, compared to those with local recurrence detected on PET/CT, thus representing the high risk group for disease progression. In addition, better prognosis was observed in our patients with the change of treatment plan after PET/CT scan, suggesting the ability of this imaging modality to better specify further treatment procedure compared to standard imaging methods, which is in line with results of other researchers [32].

The limitations of our study were: a relatively limited and heterogeneous sample size, but large enough to suggest the important clinical role of ^{18}F-FDG PET/CT in prediction of colorectal cancer progression in patients after curative resection of the primary tumor. Recurrence of the disease was not in all patients confirmed by pathology findings, but the results were verified by a long follow-up. Despite these drawbacks, our results revealed the advantages of ^{18}F-FDG PET/CT for monitoring disease progression. However, a larger, multi-centre study is needed for further evaluation of the role of PET in these patients.

In conclusion, our results, although in a limited number of patients, showed that ^{18}F-FDG PET/CT was sensitive and accurate in the detection and staging of recurrent colorectal carcinoma after curative resection of the primary tumor, with high specificity of 96.6% in the detection of local recur-

rence. Patients diagnosed with stages III and IV of recurrent disease on ^{18}F-FDG PET/CT had worse prognosis and shorter survival times. ^{18}F-FDG PET/CT induced treatment changes in more than a third of our 75 patients, mostly in patients with local disease, preventing futile surgical treatment in about the same proportion of patients. Treatment changes based on the ^{18}F-FDG PET/CT scan improved prognosis and prolonged survival by 25%, indicating the benefit of ^{18}F-FDG PET/CT in optimizing therapeutic approach. This research and follow-up is continued aiming to investigate whether ^{18}F-FDG PET/CT scan in recurrent colorectal carcinoma patients can be of long-term prognostic significance.

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The authors declare that they have no conflicts of interest.

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