



Prognostic Value of FDG-PET/CT Parameters in Patients with Locally Advanced Rectal Cancer Treated with Neoadjuvant Approach

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OBJECTIVE

To determine the prognostic and/or predictive role of 18F-FDG PET/CT parameters, such as SUVmax, SUVmean, Metabolic Tumor Volume (MTV) and Total Lesion Glycolysis (TLG=MTVxSUVmean), for the patients with locally advanced rectal cancer (LARC) treated with neoadjuvant radiotherapy±chemotherapy.

METHODS

Between January 2005 and December 2016, a total of 106 patients with clinical T3-4 and/or N+ rectal cancer without distant metastasis were included in this study. Correlation between metabolic and volumetric parameters and tumor characteristics was evaluated. Prognostic factors for overall survival (OS), local recurrence-free survival (LRFS), and distant metastasis-free survival (DMFS) were analyzed.

RESULTS

The median follow-up duration for all patients was 39.0 months (range, 6–103 months). Pathologic complete response (pCR) was defined as the absence of viable cancer cells in the resected specimen (ypT0N0). pCR was achieved in 17% of all cases (18/106). There was a weak correlation between SUVmax of primary tumor and MTV ($[r]=0.238$; $p<0.001$). However, SUVmax of primary tumor and TLG were significantly correlated ($r=0.538$; $p<0.001$). Neither SUVmax nor SUVmean was affected by patient and tumor characteristics. Posttreatment extensive stage of disease ($p=0.013$), absence of concomitant CT ($p=0.012$), MTV ≥ 14.65 cm³ ($p=0.008$), and TLG ≥ 117.00 ($p=0.023$) were unfavorable prognostic factors for OS on multivariate analysis.

CONCLUSION

Although FDG-PET is not a standard imaging modality for the treatment of rectal cancers, a negative effect of high MTV and TLG on OS was shown in our study. We should consider more intense treatment approaches for tumors with high MTV and TLG values.

Keywords: FDG-PET/CT; locally advanced rectal cancer; prognostic factors; radiochemotherapy.

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Introduction

For locally advanced rectal cancer (LARC) patients, neoadjuvant radiochemotherapy (nRCT) followed by total mesorectal excision (TME) is the standard treatment.[1,2] Studies have shown that nRCT provides better local control with lower toxicity rates than adjuvant treatment approaches.[3,4] On the other hand, the patients show heterogeneous responses to treatment concerning pathological response and survival. Approximately 10–30% of the patients show pathologic complete response, 40–45% show variant tumor regression, and the remaining 20–30% have no response to nRCT.[5–7] In addition, the 10-year cumulative incidence of local relapse was 7.1% in the preoperative arm of the German CAO/ARO/AIO-04 randomized phase 3 trial.[4] Therefore, additional efforts are required to predict the prognostic factors for these high-risk patients.

Several imaging modalities are currently used for staging the disease and monitoring the response to nRCT in patients with LARC. Concomitant use of conventional computed tomography (CT), magnetic resonance imaging (MRI) has been shown to be effective for local staging of rectal cancer by accurately determining the T4 stage with circumferential resection margin involvement.[8] These morphological evaluations have no relation with either prognosis or treatment response. Positron emission tomography (PET) using 18 fluorodeoxyglucose (18F-FDG) has been reported to be valuable functional imaging modality that has demonstrated distinguished capabilities in fields of primary cancer detection, planning and monitoring treatment, prognosis prediction, early detection of recurrent disease, and the diagnosis of regional lymph node and distant metastasis in various cancers.[9–11] Several parameters of 18F-FDG PET/CT, such as the SUVmax, SUVmean, SUVpeak, tumor functional longitudinal length, metabolic tumor volume (MTV), and total lesion glycolysis (TLG) have been suggested to be useful prognostic indicators in cancer patients.[12,13] Among these parameters, volumetric parameters, such as MTV and TLG, are expected to help in measuring volumetric tumor burden, and they could have roles as prognostic factors in malignant disease.[14]

Is the present study aims to determine the prognostic and predictive role of 18F-FDG PET/CT parameters, such as SUVmax, SUVmean, MTV and TLG, for the patients with LARC treated with nRCT.

Materials and Methods

Eligibility Criteria

Between January 2005 and December 2016, a total of 106 patients with clinical T3–4 and/or N+ rectal cancer without distant metastasis were included in this retrospective evaluation. The following inclusion criteria were considered: (1) patients scheduled to receive CRT followed by TME surgery; (2) without metabolic diseases, such as diabetes mellitus or hyperthyroidism; (3) staged with 18F-FDG PET/CT before the nRCT and (4) informed consent was signed and obtained before the treatment. The neoadjuvant treatment consisted of intensity-modulated radiation therapy (IMRT) or 3-dimensional conformal RT (3DCRT) to a total dose of 50 Gy in 25 fractions or 50.4 Gy in 28 fractions delivered concurrently with 5-Fluorouracil (5-FU) based chemotherapy (5-FU plus leucovorin or oral capecitabine). Surgery was scheduled at a minimum of six weeks after the completion of nCRT. TME was mandatory, whereas the form of surgery—anterior resection or abdominal-perineal resection—and whether a temporary colostomy should be performed was decided by the surgeon. Postoperative maintenance 5FU-based chemotherapy was given according to the postoperative pathologic evaluations of patients. The study was approved by the institutional review board of Ege University Medical School & Hospital.

Patients were pathologically staged according to the 2017 American Joint Committee on Cancer (AJCC), 8th edition.[15] Pathological tumor response was evaluated according to the 2010 AJCC tumor regression grade (TRG) system, which recorded the degree and the volume of the residual primary tumor cells. Details of AJCC TRG system are defined as follows: Grade 0, defined as no viable cancer cells; Grade 1, characterized by single or small groups of tumor cells; Grade 2, involves residual cancer outgrown by fibrosis, but fibrosis still predominates; and Grade 3, defined as the minimal or no tumor cells killed (Table 1). The nCRT-sensitive patients were defined as those with TRG Grades 0–1, while the resistant patients were defined as those with TRG Grades 2–3.

Follow-up

The patients were followed every three months for two years, then every six months up to five years and annually thereafter. Failure was defined as biopsy-proven recurrence or documented progression of disease in serial-imaging studies. Failure patterns were determined by follow-up imaging studies and were divided

Table 1 Tumor regression grading system of the American Joint Committee on Cancer (15)

Grade	Treatment response	Histologic features	Classification
3	Poor	Minimal or no tumor cells killed, extensive residual tumor	Non-responder
2	Minimal	Residual tumor overgrown by fibrosis	Non-responder
1	Moderate	Single or small groups of cancer cells	Responder
0	Complete	No viable cancer cells	Responder

into two groups: local and distant failure (including para-aortic and supraclavicular lymph nodes and also a distant organ).

18F-FDG PET/CT Technique

The patients were imaged using a dedicated 18F-FDG PET/CT system, as previously described.[16] The patients fasted for at least six hours before intravenous administration of 370 to 555 MBq (10–15 mCi) FDG. Preinjection blood glucose levels were measured to make sure that they were below 150 mg/dL. During the distribution phase, the patients laid supine in a quiet room. Combined image acquisition began 60 min after FDG injection. The patients were scanned on a flat-panel, carbon-fiber composite table insert. First, an unenhanced CT scan (5-mm slice thickness) from the base of the skull to the inferior border of the pelvis was acquired using a standardized protocol (140 kV and 80 mA). The subsequent PET scan was acquired in three-dimensional (3D) mode from the base of the skull to the inferior border of the pelvis (6 to 7-bed positions, 3 min per position) without repositioning the patient on the table. CT and PET images were acquired with the

patient breathing shallowly. Attenuation was corrected using the CT images. Areas of FDG uptake were categorized as malignant based on location, intensity, shape, size, and visual correlation with CT images to differentiate physiologic uptake from pathologic uptake. A lymph node was considered PET-positive if its FDG uptake was higher than blood pool activity or surrounding background tissues, depending on the size of the node.

Image Analysis

The tumor size is the maximum diameter measured on 18F-FDG PET/CT images. For each 18F-FDG PET/CT study, the SUVmax, SUVmean, MTV and TLG values of the primary tumor were measured. The SUV value higher than 2.5 was considered positive. A volumetric region of interest (ROI) around the outline of the primary tumor was placed on the axial 18F-FDG PET/CT images using the semi-automatic software. The ROI borders were manually adjusted by visual inspection of the primary tumor for avoiding an overlap on adjacent FDG-avid structures, and the 18F-FDG uptake of the urinary tract and bladder are excluded. MTV was defined as the regions equal to or

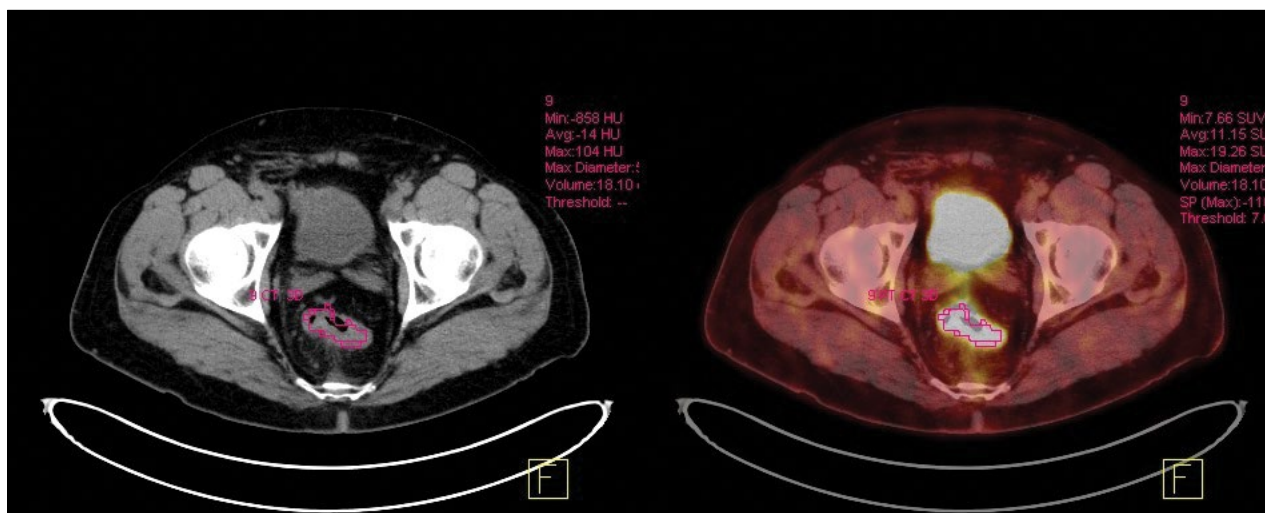


Fig. 1. Measurement of metabolic tumor volume (MTV) using a standardized uptake (SUV)-based automated contouring program.

higher than 42% of the SUVmax (Fig. 1). To prevent the inclusion of adjacent normal structures, such as the bladder, lymph nodes, and the bowel, the tumor region was expanded from a single-seed voxel within the tumor via the region-growing morphologic operation. The PET parameters, including SUVmean, MTV, and the SUVmax, were automatically acquired with automatically generated ROI of the primary tumor. The TLG was calculated by multiplying SUVmean and MTV.

Statistical Analysis

All statistical analyses relied on standard software (SPSS v22; SPSS Inc. [IBM], Chicago, IL, USA). The time to event was calculated as the time interval from the date of diagnosis to the date of first finding on clinical or imaging examination that suggested disease recurrence. All time-related events (failure or death) were calculated from the first day of biopsy-proven diagnosis to the last follow-up or death. Disease-free survival (DFS) and overall survival (OS) rates were calculated using the Kaplan–Meier method. Correlations between parameters were calculated using the Pearson test. Variables shown to be significant or of borderline significance ($p < 0.1$) were also selected for multivariate analysis. Multivariate analysis was performed using the Cox proportional hazards model, using covariates with a p-value less than 0.20 based on univariate analysis. The same results were observed after forward and backward inclusion in multivariate analysis. Receiver operating characteristic curves (ROC) were generated for the SUVmax, SUVmean, MTV and TLG values to determine the cut-off values for predicting recurrence and survival that yielded optimal sensitivity and specificity. Clinicopathological factors and follow-up data from our patient cohort were analyzed for correlations with SUVmax, SUVmean, MTV and TLG. All p-values ≤ 0.05 were considered statistically significant.

Results

Patient Characteristics

Patient and tumor characteristics are presented in Table 2. All patients had adenocarcinoma histology and more than 80% had T3 and/or N1 disease. All patients were treated with concurrent chemotherapy, except 18 (17%) patients. 5-FU+leucovorin or oral capecitabine was the chemotherapeutic agents used concomitantly. Among the patients receiving concurrent chemotherapy, 68 patients (64%) received oral capecitabine, and

Table 2 Patient and tumor characteristics

Characteristic	Number (%)
Age (year)	
Median, range	61 (29-86)
Sex	
Female	49 (46%)
Male	57 (54%)
Location	
Proximal+rectosigmoid	18 (17%)
Middle rectum	34 (32%)
Distal rectum	54 (51%)
Histopathology	
Adenocarcinoma	102 (96%)
Signet ring cell carcinoma	2 (2%)
Mucinous adenocarcinoma	2 (2%)
Lymphovascular Invasion	
(+)	20 (18%)
(-)	86 (82%)
Perineural invasion	
(+)	20 (18%)
(-)	86 (82%)
cT Stage AJCC 2010	
T2	6 (6%)
T3	90 (85%)
T4	10 (9%)
cN Stage AJCC 2010	
N0	24 (22%)
N1	77 (73%)
N2	5 (5%)
Concomitant chemotherapy	
Yes	88 (83%)
No	18 (17%)
Chemotherapy type	
Capecitabine	68 (64%)
5-Fluorouracil+leucovorin	20 (19%)
None	18 (17%)
Radiotherapy technique	
IMRT	94 (89%)
3DCRT	12 (11%)
Pathological response to nCRT	
TRG 0/1	45 (42.5%)
TRG 2/3	61 (57.5%)
Complete response	18 (17%)
FDG-PET/CT results, mean \pm SD	
SUVmax	16.9 \pm 9.6
SUVmean	9.6 \pm 6.3
MTV (cm ³)	24.7 \pm 26.4
TLG	268.7 \pm 474.5

IMRT: Intensity modulated radiation therapy; 3DCRT: 3 dimensional radiation therapy; TRG: Tumor regression grade; TLG: Total lesion glycolysis; FDG-PET/CT: Fluorodeoxy glucose positron emission computed tomography; MTV: Metabolic tumor volume

20 (19%) received 5-FU+leucovorin. External beam RT was administered with 1.8-2 Gy daily fractions to a total dose of 50-50.4 Gy. IMRT technique was used in 94 patients (89%), while the rest were treated with 3DCRT technique.

Treatment Outcomes

The median follow-up for all patients and surviving patients was 39.0 months (range, 6-103 months) and 40 months (range, 22-103 months), respectively. Of the 106 patients in our study cohort, 21 (20%) patients developed local, locoregional, distant failure, or a combination of local/locoregional and distant failures. Of these, 16 (15%) developed distant metastases, and five (5%) patients had local/locoregional failure.

At the time of the last follow-up, 94 patients (89%) were alive (11 [10%] patients with disease), and 12 patients (11%) were dead.

Pathologic complete response (pCR) was defined as the absence of viable cancer cells in the resected specimen (ypT0N0). pCR was achieved in 17% of all cases (18/106). According to TRG system, grade 0-1 and grade 2-3 responders were 45 patients (42.5%) and 61 patients (57.5%), respectively.

¹⁸F FDG PET/CT Findings

The mean±SD SUVmax, SUVmean, MTV and TLG values were 16.9±9.6 (range, 3.6-60.2), 9.6±6.3 (range, 2.4-49.2), 24.7±26.4 cm³ (range, 2.8-160.5 cm³) and 268.7±474.5 (range, 21.8-3.092.0) for the entire group, respectively. There was a weak correlation between the SUVmax of the primary rectal tumor and MTV (Pearson correlation coefficient [r]=0.238; p<0.001), whereas the correlation between SUVmax of the primary rectal tumor and TLG were moderate (r=0.538; p<0.001). A weak correlation between tumor size and SUVmax (r=0.248; p<0.001), and a moderate correlation between tumor size and MTV (r=0.489; p<0.001), and TLG (r=0.512; p<0.001) were observed.

The cut-off values for SUVmax, SUVmean, MTV, and TLG determined from the ROC curves were 13.5 g/ml [area under the curve (AUC)=0.357, 95% confidence interval(CI)=0.185-0.529], 8.44 g/ml (AUC=0.366, 95% CI=0.186- 0.545), 14.65 cm³ (AUC=0.549, 95% CI=0.348-0.750), and 117.00 (AUC=0.445, 95% CI=0.255-0.636), respectively. Patients were divided into groups based on their values for each factor being below (low group) and at or above (high group) the cut-off value. The low and high SUVmax, SUVmean, MTV, and TLG groups included 44 (41%) and 62 (59%) patients, 50 (47%) and 56 (53%)

patients, 51 (48%) and 55 (52%) patients, and 48 (45%) and 58 (55%) patients, respectively.

We could not find any significant correlation between FDG-PET/CT parameters and treatment response to nCRT according to TRG system.

Correlations between FDG-PET/CT Parameters and Patient/Tumor Characteristics

Neither SUVmax nor SUVmean was affected by patient and tumor characteristics. On the other hand, MTV and TLG were significantly higher in patients with larger tumors (>3 cm) (p=0.031, and p=0.002 respectively), advanced cT stage (p=0.004, and p=0.043 respectively), and other than distal locations (p=0.049, and p=0.037 respectively) (Table 3).

Survival Analysis and Prognostic Factors

The 3- and 5-year overall survival (OS) rates were 92% and 80%, respectively (Fig. 2a). On univariate analysis, perineural invasion (PNI), concomitant CT usage, posttreatment T (ypT) stage, ypN stage, and any response to treatment according to TRG system were prognostic factors for OS.

The 3- and 5-year local recurrence-free survival (LRFS) rates were 95% and 92%, respectively (Fig. 2b). On univariate analysis, the complete nodal response was the only prognostic factor for LRFS.

The 3- and 5-year distant metastasis-free survival (DMFS) rates were 87% and 38%, respectively (Fig. 2c). On univariate analysis, lymphovascular invasion (LVI), posttreatment stage, ypN stage and treatment response according to the TRG system were prognostic factors for DMFS.

On multivariate analysis, we could not find any statistically significant prognostic factor both for LRFS and DMFS. On the other hand, posttreatment extensive stage of disease (p=0.013), absence of concomitant CT (p=0.012), MTV ≥14.65 cm³ (p=0.008), and TLG ≥117.00 (p=0.023) were unfavorable prognostic factors for OS (Table 4).

Discussion

Stage of disease, tumor size, and concomitant CT application are the strongest prognostic factors in patients with locally advanced rectal cancer.[4,17] However, FDG-PET/CT parameters were also considered as prognostic factors in some series for better assessing the tumor characteristics in patients treated both with the neoadjuvant and adjuvant settings. Thus, FDG-PET/CT is a valuable tool that incorporates metabolic tumor

Table 3 Correlations between metabolic parameters of FDG-PET/CT and patient/tumor characteristics

Variables	n	%	SUVmax (Mean±SD)	p	SUVmean (Mean±SD)	p	MTV (Mean±SD)	p	TLG (Mean±SD)	p
Age (years)										
≤65	71	67	17.4±10.1	0.493	9.9±6.9	0.460	24.8±25.4	0.974	274.5±467.5	0.858
>65	35	33	16.0±8.7		9.0±4.9		24.5±28.5		256.9±495.0	
Sex										
Female	49	46	17.8±9.6	0.416	10.4±7.1	0.227	23.3±27.0	0.617	237.5±344.0	0.533
Male	57	54	16.2±9.7		8.9±5.4		25.9±26.0		295.5±564.9	
Tumor size (cm)										
≤3	32	30	16.7±10.1	0.231	9.8±6.9	0.315	12.7±10.3	0.031	120.8±480.4	0.002
>3	74	70	18.1±9.7		10.9±7.8		26.8±25.8		284.8±497.5	
Tumor location										
Distal	54	51	15.6±8.2	0.152	8.8±4.5	0.145	19.7±21.8	0.049	189.1±384.5	0.037
Other	52	49	18.3±10.9		10.5±7.6		29.8±29.7		351.3±544.2	
cT Stage										
T2/3	96	91	17.2±9.9	0.514	9.8±6.4	0.577	22.5±22.5	0.004	244.5±448.0	0.043
T4	10	9	15.0±7.6		8.6±4.6		47.2±46.5		519.1±671.0	
cN Stage										
N0	24	23	14.6±6.9	0.181	8.3±4.0	0.244	30.4±34.6	0.229	290.3±462.0	0.801
N1/2	72	77	17.6±10.2		10.0±6.7		23.0±23.4		262.4±480.7	
Treatment response										
TRG 0/1	45	43	16.7±8.8	0.802	9.4±5.2	0.801	20.6±17.7	0.178	221.7±312.3	0.384
TRG 2/3	61	57	17.1±10.3		9.8±7.0		27.6±31.1		303.3±565.3	

FDG-PET/CT: Fluorodeoxy glucose positron emission computed tomography; 3DCRT: 3 dimensional radiation therapy; TRG: Tumor regression grade; TLG: Total lesion glycolysis

Table 4 Multivariate analysis of prognostic factors for overall survival

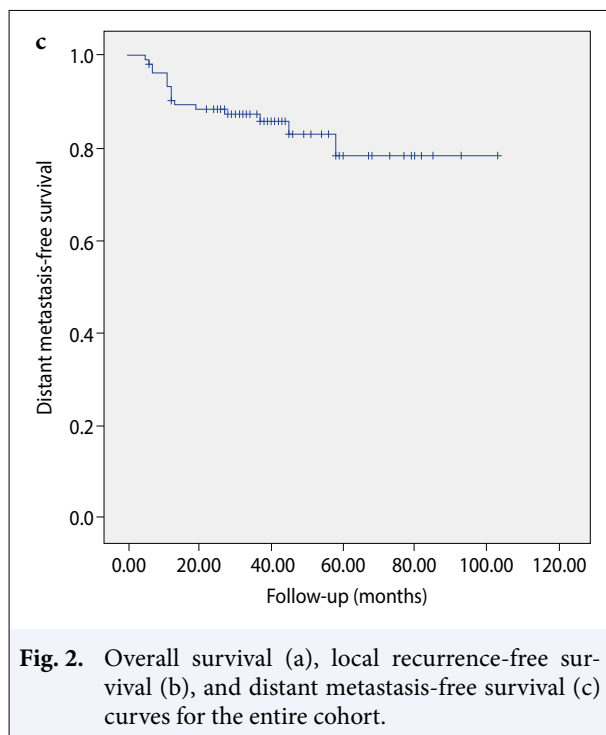
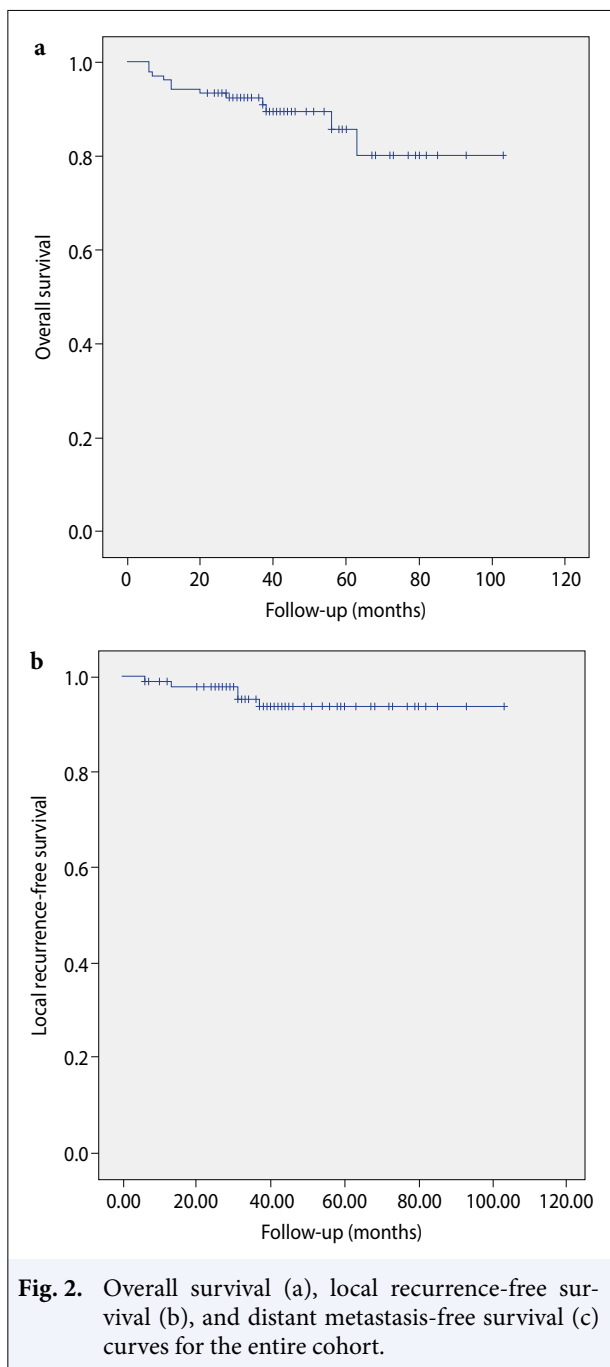
Variables	Risk factors	HR (95% CI)	p
Posttreatment stage of disease	Extensive vs early disease	1.99 (1.18-3.20)	0.013
Concomitant CT	Absent vs present	2.12 (1.15-3.45)	0.012
MTV	≥14.65 vs <14.65	2.10 (1.24-3.54)	0.008
TLG	≥117 vs <117	1.84 (1.20-2.89)	0.023

HR: Hazard ratio; CT: Chemotherapy; MTV: Metabolic tumor volume; TLG: Total lesion glycolysis

function with anatomical localization, and also can be accepted as an important imaging modality showing both distant metastasis and regional extension of disease, providing an opportunity for accurate treatment of these patients. The present study investigated the prognostic significance of FDG-PET/CT parameters (SUVmax, SUVmean, MTV, and TLG) in locally advanced non-metastatic rectal cancer patients treated with nCRT.

Several studies investigated the predictive role of FDG-PET/CT for metabolic tumor response in LARC after nCRT.[18-24] Sun et al.[22] concluded that volumetric FDG-PET/CT parameters could be accepted as important tools for evaluating the tumor response to nCRT in LARC patients. They compared

pre- and post- treatment FDG-PET/CT images, and they showed that the percentage change in MTV and TLG between pre- and posttreatment FDG-PET/CT scans could be used for giving more reliable prediction of the pathological response.[22] On the other hand, Hatt et al.[23] reported that early prediction of tumor response to nCRT in LARC with FDG-PET/CT could be misleading because of the limited reproducibility of FDG-PET scans.[23] We could not have a chance to compare pre- and post- treatment FDG-PET/CT due to the retrospective nature of our trial. We compared the pretreatment FDG-PET/CT findings with tumor response to nCRT, but we could not find any relation between them.



by the primary tumor correlates with a higher long-term OS.[25]

Bang et al.[16] evaluated metabolic and textural parameters from pretreatment FDG-PET/CT scans for the prediction of treatment response and 3-year DFS in patients with LARC. They performed a retrospective analysis of FDG-PET/CT scans of 74 patients, and they used the TRG system for treatment response evaluation similar to the present study. They concluded that metabolic and textural parameters could be used to evaluate tumor heterogeneity for the prediction of nCRT response and recurrence in LARC.[16] However, we could not find any significant correlation between FDG-PET/CT parameters and treatment response to nCRT according to the TRG system.

Most recently, Okuno et al.[26] investigated the FDG-PET/CT parameters concerning their contribution to the prediction of pathological complete response or prognosis after nCRT. Ninety-one consecutive patients with LARC were included in their study. They performed both pre- and posttreatment FDG-PET/CT scans. They found that high TLG after nCRT was strongly associated with a worse prognosis for the patients with LARC, and concluded that TLG after treatment might be a promising preoperative predictor of recurrence and death.[26] The current study showed that $MTV \geq 14.65 \text{ cm}^3$ and $TLG \geq 117.00$ on pretreatment FDG-PET/CT were related to worse

The prognostic role of FDG-PET/CT parameters is the other highly evaluated issue for many cancer types. Huang et al.[25] investigated the prognostic value of repeated FDG PET/CT for early prediction of survival in locally advanced non-small cell lung cancer (NSCLC) patients treated with concomitant CRT. They showed that the MTV of the primary tumor has the potential to become a valuable prognostic biomarker for survival outcome in NSCLC patients, and a decrease in MTV

OS in LARC patients treated with nCRT. We could not show any significant relation with the well-known prognostic factors, such as SUVmax and SUVmean. However, MTV and TLG have been developed to calculate the metabolic activity in the whole tumor. MTV is a well-known prognostic factor in various cancers because it represents the dual characteristics of tumor volume and the degree of FDG uptake by the tumor.[27] TLG has been proposed as a more accurate parameter because it considers both SUVmean and MTV.[28] There exists a controversial debate regarding which parameter -MTV or TLG- is superior for predicting prognosis. In the current study, we found that both MTV and TLG were associated with OS in LARC patients, and this finding might be explained that volumetric FDG-PET/CT parameters reflect the metabolic burden of cancer.[29,30] We should consider additional systemic treatments for patients with high metabolic tumor burden.

There are some limitations concerning the usage of FDG-PET/CT as a prediction and/or prognostic tool for patients with LARC. We should interpret the FDG-PET/CT parameters with caution because different cut-off value determination methods were used in the literature and different SUV threshold values for defining MTV and TLG were preferred for those limited number of studies. The optimal cut-off values for SUVmax, SUVmean, MTV and TLG have not yet been established. In our study, we used ROC curve analysis to determine the thresholds as previous studies have been conducted. However, they could not give any exact cut-off value for FDG-PET/CT derived parameters. Despite all uncertainties, it can be concluded that higher MTV and TLG may be a sign of more aggressive behavior for LARC and we should consider more intensive treatment approaches and follow-up schedules for these groups of patients.

Our study has some limitations. The retrospective nature of the study and lack of PET/CT after nCRT are the main limitations. In addition, we measured the tumor size in PET-CT images. Measuring the tumor size in T2-weighted MRI images should be more reliable. However, our findings, which were based on a larger and more homogenous patient population treated with nCRT in modern RT era, and our study cohort, which was considerably larger than those of previous reports, would be more helpful for evaluating the significance of FDG PET/CT metabolic parameters for survival and assessing the correlations of these parameters with other risk factors.

Conclusion

Historically proven prognostic factors, such as stage and concomitant CT applications, are still the most reliable indicators related to the treatment outcomes for the patients with LARC. In our study, we demonstrated that higher MTV and TLG, which reflect tumor burden, is an important issue in terms of treatment outcomes. However, the clinical benefits of using FDG PET/CT metabolic parameters to predict high-risk patients and eventually to change treatment strategy in LARC patients still need further clarification.

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