^{18}F-fluorodeoxyglucose positron emission computed tomography for monitoring tumor response in esophageal carcinoma treated with concurrent chemoradiotherapy

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Abstract. The aim of the present study was to explore the value of ^{18}F-fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET) in monitoring the early tumor response of esophageal squamous cell carcinoma (ESCC) treated with concurrent chemoradiotherapy (CRT). A total of 48 patients with pathologically proven ESCC were retrospectively analyzed. All patients underwent two serial ^{18}F-FDG PET scans at baseline (pre-CRT) and 40 Gy/4 weeks of starting radiation therapy (inter-CRT). All patients received intensity-modulated radiotherapy (with a total radiation dose of 59.6 Gy) concurrently with cisplatin-based chemotherapy. The maximum standardized uptake value (SUV_{max}) and metabolic tumor volume (MTV) were measured using ^{18}F-FDG PET. The percentage changes (Δ) in SUV_{max} and MTV between two serial scans were calculated and were revealed to be associated with the objective tumor response (oTR), according to the Response Evaluation Criteria in Solid Tumors 1.1. Among the 48 patients, 20.8% achieved a complete response, 68.8% exhibited a partial response and the oTR rate was 89.6%. On the pre-CRT PET scans, the mean SUV_{max} and MTV were 14.1±5.8 and 58.2±25.4 cm^3, respectively. Following 40 Gy irradiation over 4 weeks, the mean SUV_{max} and MTV significantly decreased to 4.3±3.5 and 19.0±12.1 cm^3, respectively (P<0.001). A significantly higher ΔSUV_{max} and ΔMTV was observed in the responders compared with that in the non-responders [0.71±0.16 vs. 0.51±0.26 (P=0.015); and 0.64±0.13 vs. 0.42±0.09 (P=0.001), respectively]. Univariate analysis revealed that ΔSUV_{max} and ΔMTV were significantly associated with oTR (P=0.010 and P=0.001, respectively). ΔMTV was used as a predictor and a cut-off value of 54% discriminated responders from non-responders with a sensitivity of 69.8% and a specificity of 100% (P=0.001). The area under the receiver operating characteristic curve was 0.837 (95% confidence interval, 0.702-0.928). The results of the present study indicated that interim ^{18}F-FDG PET scans may provide early prognostic value for determining oTR in patients with ESCC undergoing treatment with CRT.

Introduction

Esophageal squamous cell carcinoma (ESCC) is the 4th most common cause of cancer-associated mortality and the fifth most frequently diagnosed cancer type in China (1). ESCC is a highly aggressive malignancy with a poor prognosis due to the fact that the majority of tumors are asymptomatic until they have reached advanced stages (1). At present, concurrent chemoradiotherapy (CRT) has been established as an important approach for patients with locally advanced carcinoma of the esophagus (2). This treatment schedule is also appropriate for patients who are either medically unfit for surgery or unwilling to undergo surgery (3). The ability to predict which patients respond to CRT or develop resistance would be invaluable for individualizing therapeutic approaches, as early modifications in therapy regimens for non-responders may improve treatment outcomes.

Conventional anatomic imaging modalities, such as computed tomography, evaluate tumor response as changes in tumor size only after weeks or months following therapy, and are not ideally suitable for early prediction for treatment response. ^{18}F-fluorodeoxyglucose positron emission computed tomography (^{18}F-FDG PET) as a functional imaging technique has demonstrated potential value for monitoring early response to neoadjuvant CRT in esophageal cancer (4-8), as metabolic variation of the tumor occurs prior to any anatomical structure changes. However, there is no study to date has examined

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Table I. Patient characteristics.

Characteristics	Responder	Non-responder	Total no. (%)	P-value
Sex				0.833
Male	36	4	40 (83.3)	
Female	7	1	8 (16.7)	
Age, years				0.645
Range	40-75	61-75	40-75	
Median	60	64	61	
Tumor length, cm				0.361
Range	2-15	6.4-11	2-15	
Median	5.6	7.8	6	
Tumor location				0.626
Cervical	4	0	4 (8.3)	
Upper thoracic	17	1	18 (37.5)	
Middle thoracic	18	3	21 (43.8)	
Lower thoracic	4	1	5 (10.4)	
TNM stage				0.689
II_a	7	0	7 (14.6)	
II_b	3	0	3 (6.3)	
III	20	3	23 (47.9)	
IV_a	13	2	15 (31.2)	
Chemotherapy				0.943
Cisplatin + 5-FU	20	2	22 (45.8)	
Cisplatin + pemetrexed	14	2	16 (33.4)	
Cisplatin + capecitabine	9	1	10 (20.8)	

TNM, tumor-node-metastasis; 5-FU, fluorouracil.

interim treatment ^{18}F-FDG PET for monitoring response to definitive CRT.

The present study aimed to investigate the prognostic value of interim ^{18}F-FDG PET in order to determine the objective tumor response (oTR) in patients with ESCC who received only definitive CRT.

Patients and methods

Patients. Between August 2011 and January 2015, 48 consecutive patients with biopsy-proven locally advanced ESCC were enrolled in the present study. The study protocol was approved by the Shandong Tumor Hospital Ethics Committee (Shandong, China) and written informed consent was obtained from all patients. Among the 48 patients, there were 40 (83.3%) male and 8 (16.7%) female, with a median age of 61 years (range, 40-75 years). Pretreatment investigations included a complete blood count, measurement of serum electrolytes, a chest radiograph, a computed tomography (CT) scan of the chest and abdomen, barium swallow radiography and an upper gastroesophageal endoscopy.

Patients who had undergone ^{18}F-FDG PET scans prior to CRT (pre-CRT) and 40 Gy/4 weeks of starting radiation therapy (inter-CRT) were included in the present study. Other inclusion criteria were as follows: i) Patient age was <76 years and the Karnofsky score was >70 without any previous treatment; ii) the absence of distant metastasis; iii) no contraindications to radiotherapy or chemotherapy; and iv) no signs of infection or diagnosis of diabetes at the time of the PET scan. The characteristics of the enrolled patients are listed in Table I. Of the 48 patients treated with definitive CRT, 10 were diagnosed with clinical stage II cancer and did not undergo surgery due to patient refusal, poor cardiopulmonary function or advanced age.

PET scanning. All patients fasted and rested for >6 h prior to consuming 500 ml water and were then administered with 7-11 mCi radioactive tracer. Patient serum glucose levels were confirmed to be <6.6 mmol/l. All patients were examined on a dedicated PET/CT scanner (GE Healthcare Life Sciences, Little Chalfont, UK). Subsequently, the emission scans were acquired from the level of the calvaria to the thigh for 4 min per position. Each patient received a scan lasting 24-28 min in total covering 14.5 cm at an axial sampling thickness of 4.25 mm per slice. The non-contrast spiral CT component was performed with a slice thickness of 4.25 mm and a rotation speed of 0.8 sec per rotation. PET images were reconstructed with CT-derived attenuation correction using the ordered-subset expectation maximization algorithm. The attenuation-corrected PET images, CT images and fused PET/CT images displayed as coronal, sagittal and transaxial slices were viewed on a GE Xeleris 2 workstation

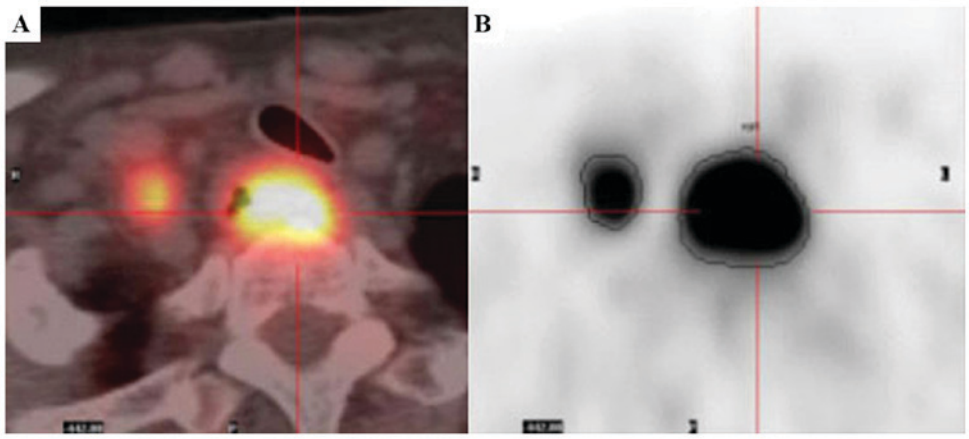

Figure 1. (A) Abnormal fluorodeoxyglucose uptake in esophageal carcinoma of a 65-year-old female. (B) Automatic region-of-interest (primary tumor and lymph node) was contoured with a standardized uptake value threshold of 2.5. The automatic delineation was inspected visually and corrected manually if non-tumor areas were included in the segmentation volume.

(GE Healthcare Life Sciences, Little Chalfont, UK). Pre-CRT scans were performed 1-5 days prior to commencing CRT and inter-CRT scans were acquired following 40 Gy/4 weeks of starting radiation therapy.

Treatment

Radiotherapy. All patients were placed in a supine position with thermoplastic immobilization prior to the CT simulation and each daily radiotherapy (RT). All patients received intensity-modulated radiotherapy (IMRT) with six MV X-rays and a two-phase irradiation protocol. The first phase was administered as conventionally fractionated RT with a total of 40 Gy in 20 fractions (fx) in 4 weeks, which irradiated the gross tumor volume (GTV), including that of the primary tumor (GTV_p) and that of the metastatic lymph nodes (GTV_n). The planning target volume was defined as GTV_p with the addition of 3-5 cm margins superiorly and inferiorly, 1 cm margins laterally, and with the addition of a 1 cm margin for GTV_n. The second phase was delivered to the boost volume as an additional dose of 19.6 Gy twice a day in 14 fx over 7 days at 1.4 Gy/fx, with a 6 h minimal interval between fractions. The total dose administered to the clinical tumor was 59.6 Gy and 34 fx over 35 days.

Chemotherapy. All patients were scheduled to receive two cycles of concurrent chemotherapy, which began on the first day of RT. The chemotherapeutic regimens in the present study consisted of intravenous cisplatin 25 mg/m^2/day on days 1-3 plus 500-600 mg/m^2 fluorouracil (5-FU) every 24 h by continuous infusion for 120 h, plus 1,000 mg capecitabine twice daily with a 12 h interval on days 1-14 or plus 400-500 mg/m^2 pemetrexed on day 1 of a 21-day cycle.

Metabolic parameters. The pre- and inter-CRT PET images were analyzed by two experienced and independent nuclear medicine physicians. Semi-quantitative analysis of the SUV was corrected by the injected dose and body weight (g) and was calculated as follows: Tissue activity concentration (Bq/ml)/[administered activity (Bq)/weight (g)]. Metabolic and volumetric parameters were measured using PET-Volume Computer-Assisted Reading software (AW4.5 Platform; GE Healthcare, Chicago, IL, USA), which provides an automatically delineated volume of interest using an isocontour threshold method based upon the SUV. SUV_{max} was defined as the SUV on the highest pixel image in the tumor region. MTV was defined as the volume of interest of tumor segmented by a threshold of 2.5 (Fig. 1) (9,10). The percentage changes (Δ) of metabolic parameters (P) between pre- and inter-CRT were calculated and expressed as a ratio, and were marked for ΔP, which was calculated as follows: $\Delta P = [(P_{pre\text{-}CRT} - P_{inter\text{-}CRT})/P_{pre\text{-}CRT}] \times 100\%$.

Response evaluation. The oTR evaluation was performed ≥4 weeks after the end of therapy based upon the Response Evaluation Criteria in Solid Tumors 1.1 (RECIST 1.1) (11), outlined as follows: Complete response (CR), disappearance of all target lesions; partial response (PR), ≥30% decrease from baseline; progressive disease (PD), ≥20% increase over smallest sum observed or appearance of new lesions; and stable disease (SD), neither PR nor PD criteria met. The assessment of oTR included repeated endoscopy, barium swallow and contrast-enhanced CT scan. Response was assessed by two experienced radiologists who were blinded to the outcomes of the PET scans. Patients with an outcome of CR or PR were defined as responders and those with an outcome of SD, or PD were classed as non-responders.

Statistical analysis. Descriptive analyses are expressed as the mean ± standard deviation. Statistical comparisons between responders and non-responders were performed using independent Student's t-tests. Parameter comparisons between pre- and inter-CRT were calculated using paired Student's t-tests. Associations between parameters and the oTR were analyzed using univariate analysis. Receiver-operating characteristic (ROC) curve analysis was used to evaluate the predictive ability of parameters. All statistical analysis was performed using SPSS version 20.0 (IBM Corp., Armonk, NY, USA) and MedCalc version 15.2 (MedCalc Software bvba, Ostend, Belgium). All tests were two-tailed and $P<0.05$ was considered to indicate a statistically significant difference.

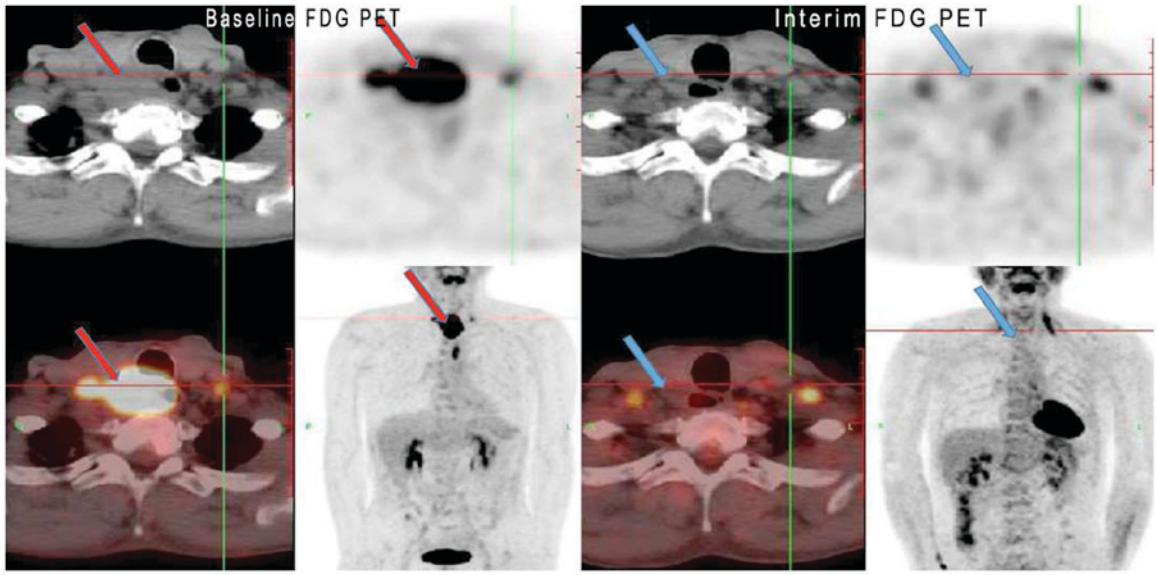

Figure 2. ^{18}F-FDG PET scan of a 58-year-old male with cervical esophageal squamous cell carcinoma. The red arrow indicates the primary tumor at baseline ^{18}F-FDG PET scan, the maximum standardized uptake value was 21.2 and the metabolic tumor volume was 36.8 cm^3. The blue arrow indicates the primary tumor after 40 Gy/4 weeks of starting radiation therapy, tumor FDG uptake had ceased with a final tumor complete response. ^{18}F-FDG PET, ^{18}F-fluorodeoxyglucose positron emission tomography.

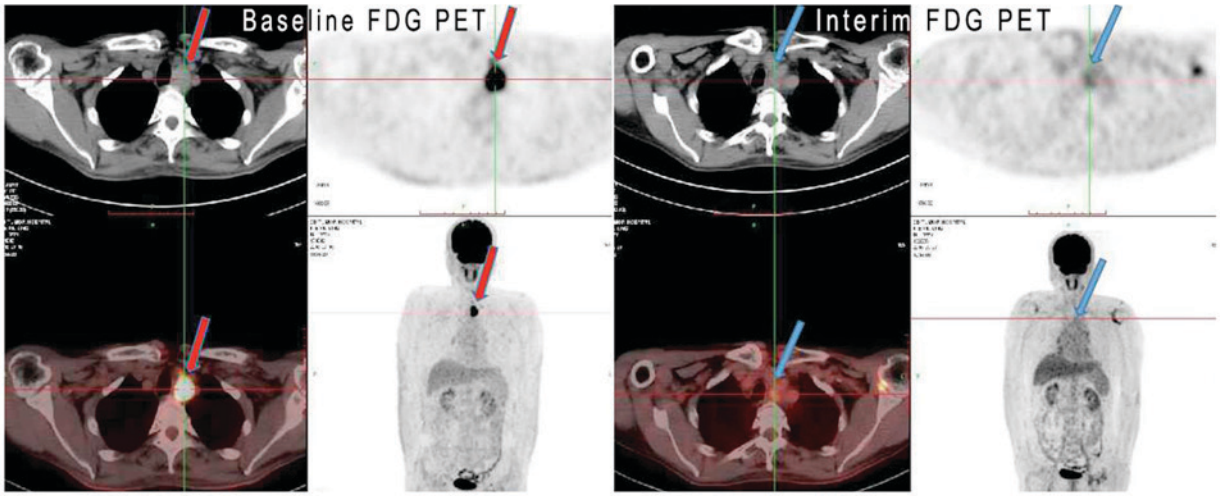

Figure 3. ^{18}F-FDG PET scan of a 70-year-old male with upper thoracic esophageal squamous cell carcinoma. The red arrow indicates the primary tumor at the baseline 18F-FDG PET scan. The SUV_{max} was 14.6 and the MTV was 19.2 cm^3. The blue arrow indicates the primary tumor after 40 Gy/4 weeks of starting radiation therapy. The tumor FDG uptake had decreased to an SUV_{max} of 2.8 and an MTV of 4.1 cm^3, with a final tumor partial response. ^{18}F-FDG PET, ^{18}F-fluorodeoxyglucose positron emission tomography; SUV_{max}, maximum standardized uptake value; MTV, metabolic tumor volume.

Results

Treatment response. There were 10 (20.9%) patients with stage II disease, 23 (47.9%) with stage III disease and 15 (31.2%) with stage IV_a disease, according to the American Joint Committee on Cancer 7th staging system (12). The median tumor length was 6.0 cm (range, 2.0-15.0 cm). Following the completion of treatment, 10 patients (20.8%) attained a CR, 33 (68.8%) exhibited a PR and 5 (10.4%) had SD, with no cases of PD. The overall oTR rate was 89.6% (43/48). No significant differences in patient characteristics between responders and non-responders were observed (Table I; all P>0.05). Figs. 2 and 3 show two representative cases of clinical CR and PR, respectively.

FDG uptake by tumors. All 48 patients had abnormal FDG uptake in their primary tumors or lymph nodes on pre-CRT PET scans, with a mean SUV_{max} of 14.1±5.8 and a mean MTV of 58.2±25.4 cm^3. However, following 40 Gy irradiation over 4 weeks and 1-2 cycles of concurrent chemotherapy, FDG uptake by tumors in the interim PET scans was significantly decreased, with a mean SUV_{max} of 4.3±3.5 and a mean MTV of 19.0±12.1 cm^3 (Table II; P<0.001). Fig. 4 demonstrates the changes in MTV and SUV_{max} in 5 non-responders between pre- and inter-CRT PET scans compared with the changes in responders. The metabolic and volumetric parameters of FDG PET were all decreased steadily from baseline to interim treatment in responders, and non-responders. However, the reduction rate of MTV between pre- and inter-CRT in

Table II. Comparisons of fluorodeoxyglucose positron emission tomography parameters between the baseline (pre-CRT) and 4 weeks after starting concurrent chemoradiotherapy (inter-CRT).

Parameter	Pre-CRT	Inter-CRT	P-value
MTV, cm^3	58.2±25.4	19.0±12.1	<0.001
SUV_{max}	14.1±5.8	4.3±3.5	<0.001

Data are presented as the mean ± standard deviation. CRT, chemoradiotherapy; SUV_{max}, maximum standardized uptake value; MTV, metabolic tumor volume.

Table III. Differences in fluorodeoxyglucose positron emission tomography parameters between responders and non-responders.

Parameter	Responder	Non-responder	P-value
ΔMTV	0.64±0.13	0.42±0.09	0.001
ΔSUV_{max}	0.71±0.16	0.51±0.26	0.015

Data are presented as the mean ± standard deviation. SUV_{max}, maximum standardized uptake value; MTV, metabolic tumor volume.

Table IV. Associations between parameters and objective tumor response.

Parameter	Threshold value[a]	χ^2	P-value
MTV_{pre}, cm^3	50.6	0.81	0.367
MTV_{inter}, cm^3	20.4	4.16	0.041
ΔMTV	0.54	11.0	0.001
SUV_{pre}	12.5	0.59	0.442
SUV_{inter}	3.4	3.65	0.056
ΔSUV_{max}	0.57	9.32	0.010
Age (years)	-	1.26	0.461
Sex	-	0.08	0.778
Tumor location	-	3.20	0.361
Tumor diameter	-	2.25	0.086
TNM stage	-	2.87	0.412
Chemotherapy	-	0.21	0.712

[a]Threshold value was determined by receiver operating characteristic curve analysis. SUV_{max}, maximum standardized uptake value; MTV, metabolic tumor volume; TNM, Tumor-Node-Metastasis.

responders was 0.64±0.13 vs. 0.42±0.09 in non-responders, a difference that was statistically significant (P=0.001). A similar difference was observed for ΔSUV_{max}, (0.71±0.16 in responders vs. 0.51±0.26 in non-responders; P=0.015; Table III).

Associations between clinical characteristics and tumor response. Univariate analysis revealed that ΔSUV_{max} and

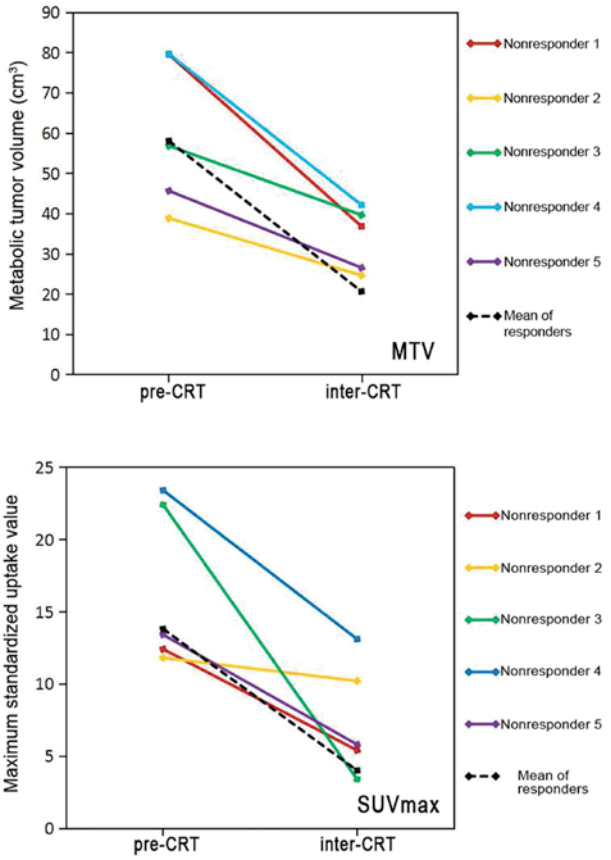

Figure 4. MTV and SUV_{max} of fluorodeoxyglucose positron emission tomography at baseline (pre-CRT) and interim treatment (inter-CRT) in non-responders vs. responders. MTV, metabolic tumor volume; SUV_{max}, maximum standardized uptake value; CRT, chemoradiotherapy.

ΔMTV were significantly associated with oTR (P=0.010 and P=0.001, respectively). An association between interim MTV (MTV_{inter}) and oTR was also observed (P=0.041), while no significant association was observed between interim SUV_{max} and oTR (P=0.056). Age, sex, tumor location, tumor diameter, chemotherapy and clinical tumor-node-metastasis (TNM) stage were not significantly associated with oTR (Table IV; all P>0.05). ROC curve analysis (Table V and Fig. 5) revealed that ΔSUV_{max} (cut-off, 57%) displayed an area under the ROC curve (AUC) of 0.744 [95% confidence interval (CI), 0.544-0.890], with a sensitivity of 0.761 and a specificity of 0.800 (P=0.057). However, a threshold of 54% ΔMTV divided the responders from the non-responders with a sensitivity of 0.698, a specificity of 1.000 and an AUC of 0.837 (95% CI, 0.702-0.928; P=0.001).

Discussion

ESCC is a highly heterogeneous type of cancer where patients at the same TNM stage and undergoing the same treatment regimens, exhibit different treatment responses and survival rates. Therefore, it is necessary to obtain a reliable tool to identify the treatment-resistant patients and to develop individualized treatment strategies, which may be an effective way to improve the survival of patients.

A previous study reported that clinical parameters (age, sex, TNM stage, tumor location and pathology) were unable

Table V. ROC curve analysis of metabolic parameters for treatment response prediction.

Parameter	AUC	95% CI of AUC	Sensitivity	Specificity	P-value
ΔMTV	0.837	0.702-0.928	0.698	1.000	0.001
ΔSUV_{max}	0.744	0.544-0.890	0.761	0.800	0.057

ROC, receiver operating characteristic; AUC, area under the ROC curve; CI, confidence interval; SUV_{max}, maximum standardized uptake value; MTV, metabolic tumor volume.

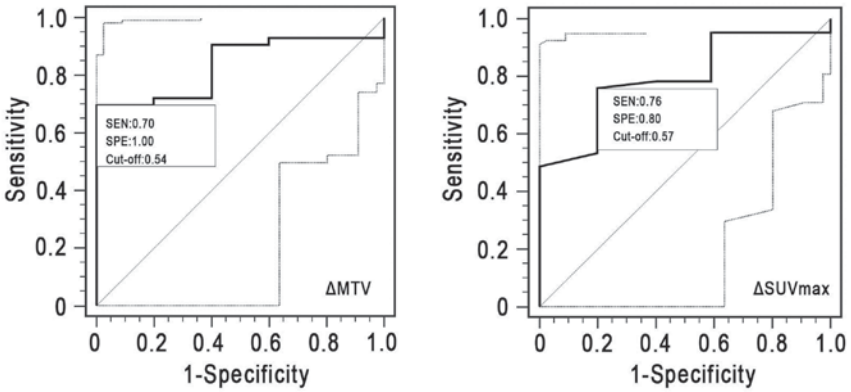

Figure 5. The ΔMTV and the ΔSUV_{max} for tumor response prediction by receiver-operating characteristic curve analysis. MTV, metabolic tumor volume; ΔSUV_{max}, maximum standardized uptake value; SEN, sensitivity; SPE, specificity.

to predict response to CRT (13). Certain studies have focused on biological markers to estimate possible treatment responses to CRT; however, these promising biomarkers require further validation with larger high-quality clinical trials (14,15). Previous studies have suggested that ^{18}F-FDG PET is a non-invasive method for monitoring pathological response and prognosis for carcinomas of the esophagus during or following neoadjuvant CRT (4-8). Monjazeb *et al* (16) reviewed 163 patients with esophageal cancer receiving neoadjuvant CRT with or without resection. ^{18}F-FDG PET scans were performed and analyzed pre- and post-CRT. In a study undertaken by Monjazeb *et al* (16), for patients treated with definitive CRT, the median survival time and the 2-year overall survival (OS) rate for the patients achieving complete response was 38 months, and 71% vs. 11 months and 11% for those patients who had not achieved a complete response. Multivariate analysis indicated that PET complete response is the strongest independent prognostic factor for esophageal cancer [survival hazard ratio (HR), 9.82; P<0.01; local failure HR, 14.13; P<0.01].

As a semi-quantitative parameter of ^{18}F-FDG PET, SUV, which may reflect the intensity of metabolic activity of the tumor, has been suggested as a prognostic marker for the histopathological response of esophageal carcinoma (4-8,17-20). For example, Wieder *et al* (7) reported that, for histopathological responders, the decrease in SUV between baseline and 2 weeks after initiation of therapy was 44%, but was only 21% in the non-responders (P=0.0055). At the preoperative scan (3-4 weeks after CRT), tumor metabolic activity had decreased by 70% in histopathological responders and by 51% in histopathological non-responders. Lordick *et al* (5) reported that the median event-free survival time was 29.7 months (95% CI, 23.6-35.7 months) in metabolic responders vs. 14.1 months (95% CI, 7.5-20.6 months) in non-responders (HR, 2.18; P=0.002). Chhabra *et al* (18) observed that with a cut-off value of a 35% decrease in SUV_{max} between baseline and post-CRT, the 3-year OS rate for responders (ΔSUV ≥35%) was 64%, while that for non-responders (ΔSUV <35%) was only 15% (P=0.004). Another study undertaken by Huang *et al* (19) revealed that ΔSUV was significantly associated with OS and disease-free survival rates. The 3-year OS rate of the ΔSUV >60% group was 71% and that of the ΔSUV ≤60% group was 40.7% (P=0.045). In the present study, the SUV_{max} of tumor(s) decreased steadily from baseline to interim treatment in responders and non-responders, and the reduction rates of SUV_{max} (ΔSUV_{max}) were significantly different between the responders and the non-responders. However, a threshold of 57% ΔSUV_{max} was unable to divide the responders from the non-responders successfully, with an AUC of 0.744 (95% CI, 0.544-0.934; P=0.057).

The ability of SUV_{max} to predict oTR remains controversial and is influenced by a variety of factors, including the total dose of FDG injected, the time between the injection and scanning, noise and image reconstruction. Furthermore, a number of biological and technological factors influence the measurement of SUV_{max} (21). Therefore, the exploration of other metabolic parameters is required. MTV and total lesion glycolysis (TLG) are volume-based parameters that represent metabolic tumor burden. A number of previous studies have reported the effectiveness of MTV and/or TLG as prognostic factors in esophageal carcinoma (6,22-24). Roedl *et al* (24) reported that a decrease in MTV between

pre- and post-treatment PET scans was a better predictor of histopathological response, and survival in comparison with a decrease in the SUV or the clinical response evaluation based on the RECIST 1.1 in adenocarcinomas of the esophagus. Kim *et al* (6) revealed that a threshold of 25.5% ΔMTV divided the responders from the non-responders with a sensitivity of 80%, a specificity of 76.3% and an AUC of 0.731 (95% CI, 0.591-0.843; P=0.0027). The present study observed that MTV decreased steadily from baseline to interim treatment in responders and non-responders. Furthermore, the reduction rate of MTV was significantly higher in responders compared with that in non-responders. Univariate analysis demonstrated that ΔMTV was significantly associated with oTR. A threshold of 54% ΔMTV divided the responders from the non-responders with an AUC of 0.837 (95% CI 0.702-0.928), a sensitivity of 0.698 and a specificity reaching 1.000 (P=0.001). One retrospective multi-center study demonstrated that the MTV defined by a physician significantly decreased from PET1 (pre-CRT) to PET2 (3 weeks from the start of CRT), whereas the MTV defined as 40% of the SUV_{max} did not decrease significantly (25). The MTV from PET1 or PET2 was significantly lower in patients with CR at 3 months, while the SUV_{max} was not.

The reasons for certain discrepancies in the aforementioned studies may be explained by differences in the pathological types of cancer, treatment regimens or criteria used to evaluate the tumor response. In Western countries, the most common pathological type of esophageal cancer is esophageal adenocarcinoma, which may be more suited for neoadjuvant CRT followed by surgery at locally advanced stages. The pathological CR may be used to assess treatment response. However, in China, a substantial proportion of newly diagnosed esophageal carcinomas were squamous cell carcinomas and were not suitable for surgery (26). For these patient, CRT was an important treatment option. Therefore, the patients enrolled in the present study all received definitive CRT. The aim of the present study was to identify a reliable predictor to permit the early identification of patients who may or may not respond to CRT. The RECIST criteria is recommended to evaluate the solid tumor response using the changes in tumor size on CT images. Due to radiation-induced inflammation, edema may remain present in the esophageal wall of certain patients, even >8 weeks after radiotherapy (27). When using metabolic parameters of FDG PET, OTR may be assessed 4 weeks from the start of CRT (after 40 Gy irradiation), as in the present study. However, it must be accounted for that FDG PET may have difficulty in differentiating between complete responses and residual disease or post-treatment inflammation (28), as glucose accumulates in tumor and inflammatory cells, and inflammatory cells are common in irradiated esophageal tissue. Therefore, uptake on an ^{18}F-FDG PET scan may represent either residual tumor or esophagitis. For example, Yue *et al* (29) recruited 21 patients with inoperable locally advanced ESCC who underwent a serial 3'-deoxy-3'-(18)F-fluorothymidine (^{18}F-FLT) PET scan during radiotherapy. Among the 19 patients, 2 patients who had undergone scans following completion of the entire radiotherapy course exhibited no tumor uptake on the ^{18}F-FLT PET scan, but high uptake on the ^{18}F-FDG PET scan. Pathological examination of these regions revealed inflammatory infiltrates, but no residual tumor (29). The aforementioned study suggests that ^{18}F-FLT PET may discriminate tumor from esophagitis more effectively than ^{18}F-FDG PET, which may have important clinical applications.

The present study has a number of limitations that must be taken into account. To begin with, the study was retrospective in design and comprised a small population. Additionally, ^{18}F-FDG PET scan results were compared with objective therapeutic responses according to the RECIST 1.1 and not with the pathological response to treatment. According to the pathological criteria, pathological T (primary tumor) and N (lymph nodes) were assessed according to the percentage of viable residual tumor cells within the postoperative cancerous tissues. In the present study, it was not possible to acquire the postoperative pathological tissues. Future prospective studies with a larger study population may be able to accurately identify the association between ^{18}F-FDG PET scan results and oTR.

In conclusion, given the aforementioned limitations, the present study provides clinical evidence that interim ^{18}F-FDG PET scans may exhibit early prognostic value for determining oTR in patients with ESCC. The findings of the present study suggest that ΔMTV may be a useful parameter to assess clinical oTR to definitive CRT, which may permit early identification of CRT responders and non-responders.

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