Int J Clin Exp Med 2019;12(3):2690-2696
www.ijcem.com /ISSN:1940-5901/IJCEM0080711

Original Article

Correlation between ^{18}F-FDG PET/CT metabolic parameters and lymph node metastasis of esophageal cancer

Zhiyu Huang[1], Shaoxing Chen[2], Jiancheng Li[1]

[1]Department of Radiation Oncology, Fujian Cancer Hospital Affiliated to Fujian Medical University, Fuzhou, PR China; [2]Department of Radiation Oncology, Provincial Clinical College of Fujian Medical University, Fuzhou, PR China

Received June 2, 2018; Accepted August 4, 2018; Epub March 15, 2019; Published March 30, 2019

Abstract: Objective: The goal of this study was to investigate the correlation between lymph node metastasis and ^{18}F-FDG PET/CT metabolic parameters in primary esophageal patients. Materials and Methods: A total of 82 esophageal cancer patients that were pathologically confirmed and received initial treatment in our hospital from October 2011 to September 2016 were retrospectively analyzed. All patients underwent systemic ^{18}F-FDG PET/CT examination within two weeks before operation but without receiving any anti-tumor treatment before operation. The metabolic parameters of primary lesions and postoperative pathological lymph node metastasis of esophageal cancer patients were recorded. Results: There was strong correlation between metabolic parameters of primary lesion (including SUVmax, SUVmean, MTV, TLG, HF) and lymph node metastasis of esophageal cancer, and TLG of primary lesion had a certain diagnostic value for the lymph node metastasis of esophageal cancer. In addition, ROC curve analysis showed that the minimum TLG for diagnosis of lymph node metastasis of esophageal cancer at the upper and middle segment was 23.06, while the thoracic esophageal cancer at the lower segment was not statistically significant. Conclusion: ^{18}FDG-PET/CT metabolic parameters (SUVmax, SUVmean, MTV, TLG, HF) are closely related to lymph node metastasis of esophageal cancer. The TLG has a certain diagnostic value for the lymph node metastasis of esophageal cancer.

Keywords: Esophageal cancer, lymph node metastasis, PET/CT, metabolic parameter

Introduction

Esophageal cancer is a common malignant tumor with an increasingly high incidence. In China, the incidence of new esophageal cancer was about 47.79% and the mortality rate was about 37.5% in 2015 [1]. Accurate staging and assessment of the range of lesions is the basis for comprehensive diagnosis and surgical treatment of esophageal cancer. In addition, an accurate assessment of the existence of regional lymph node metastasis of esophageal cancer is of great significance to select therapeutic regimens and guide subsequent treatments. At present, lymph node metastasis is mainly identified by imaging techniques such as CT, intracavitary ultrasound and Positron Emission Tomography-Computed Tomography (PET/CT). In recent years, some studies have shown that some new metabolic parameters of ^{18}F-FDG (Fluor-18-fluorodeoxyglucose, ^{18}F-FDG) PET/CT, including MTV (Metabolic Tumor Volume), TLG (Total Lesion Glycolysis), HF (Intratumoral Heterogeneity Factor) have value for the assessment of prognosis of malignant tumors [2-8]. Therefore, whether ^{18}F-FDG PET/CT metabolic parameters can be used to predict the regional lymph node metastasis of esophageal cancer deserved further investigation. The current study aimed to investigate potential correlation between metabolic parameters and lymph node metastasis, diagnostic value of metabolic parameters on lymph node metastasis of esophageal cancer, and the scope of lymph node dissection during operation based on preoperative metabolic parameters of ^{18}F-FDG PET/CT and postoperative pathology results.

Table 1. MTVs corresponding to different percentages of SUVmax in a patient

	40% SUVmax	50% SUVmax	60% SUVmax	70% SUVmax	80% SUVmax
MTV (cm^3)	32.817	25.777	18.792	11.295	4.334

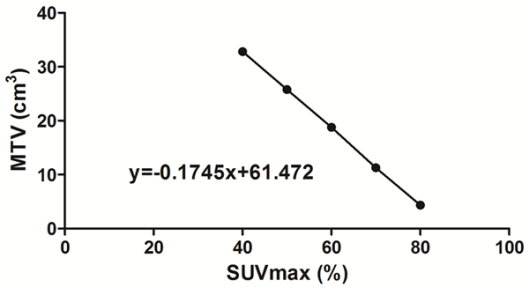

Figure 1. Linear relationship based on **Table 1**. HF value was the slope of the liner function. The slope was negative because of negative correlation between them. In this study, the absolute value was taken, i.e. the HF of the patient was 0.715 (HF = 0.715).

Materials and methods

Subjects

Esophageal cancer patients treated in our hospital from October 2011 to September 2016 were collected. There were 82 cases meeting inclusion criteria, and all of them were diagnosed with squamous cell carcinoma, including 70 males and 12 females, aged between 41 and 78 years, and medium age of 59 years. None of the patients had a medical history of a tumor, and they underwent systematic ^{18}F-FDG PET/CT examination two weeks before the operation.

The present study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Fujian Provincial Cancer Hospital. Written informed consent was obtained from all participants.

^{18}F-FDG PET/CT equipment and method

The Gemini TF 64 PET/CT instrument (Philips, the Netherlands) was used. ^{18}F-FDGT was generated from Sumitomo Corporation HM-10 cyclotron, with the radiochemical purity greater than 95%. Before the examination, patients were fasted for more than 6 hours, and blood glucose levels were controlled within 3.9~7.5 mmol/L. After intravenous injection of 185~370 MBp (5~10 mCi) ^{18}F-FDG, patients had rest for 60 minutes. After urination, the patients were scanned on the machine in a supine position. CT-scan acquisition parameters were 120 kV, 200 mA, matrix 512 * 512, layer thickness 5 mm. PET images were acquired from the skull base to the upper end of femur at a rate of 1 min/person. The acquisition of images was performed by a three-dimensional model, then attenuation correction was made by CT data. The fusion of PET and CT images was performed on EBW2.0 post-processing workstation, to get the PET, CT and PET/CT fusion images of cross-section, sagittal, and coronal plane. The maximum standard uptake (SUVmax) was measured by ROI (region of interest, ROI).

Acquisition of metabolic parameters

SUVmax refers to the maximum SUV in ROI. SUVmean refers to the mean SUV in ROI. MTV refers to the volume of high metabolic tumor tissue. The volume of lesions was divided according to different bottom-line thresholds, and the MTV values were different. At present, the commonly used thresholds were SUV = 2.5, 40% SUVmax, 50% SUVmax, etc. [9]. The PET Cancer Imaging Guide of 2010 Annual Conference of European Society of Nuclear Medicine recommended 40% SUVmax as the lower threshold of ROI [10]. Therefore, in this study, 40% SUVmax was used as a threshold to measure the images, and the system automatically calculated SUVmean, MTV, TLG = MTV × SUVmean [11].

Measurement of metabolic heterogeneity factor (HF)

Tumor metabolic heterogeneity was determined by primary lesion metabolic volume and volume of adjacent normal tissue [12]. A different percentage of SUVmax had a corresponding MTV, and there was a linear relationship between both of them, and through conversion, the HF value was obtained. It has been reported that when converting HF, the SUVmax that was less than 40% and greater than 80% should be ruled out [12]. For example, the MTVs corresponding to different percentages of SUVmax in a patient are shown in **Table 1** and **Figure 1**.

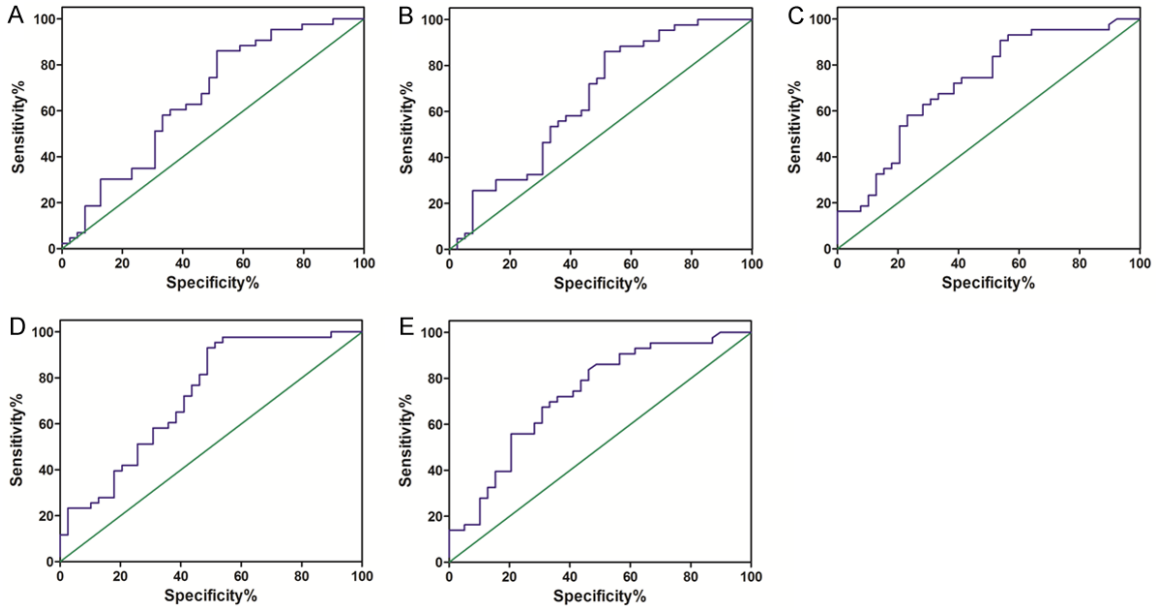

Figure 2. ROC analysis for the correlation of PET/CT metabolic parameters and lymph node metastasis. A. Relationship of SUVmax and lymph node metastasis of esophageal carcinoma. B. Relationship of SUVmean and lymph node metastasis of esophageal carcinoma. C. Relationship of MTV and lymph node metastasis of esophageal carcinoma. D. Relationship of TLG and lymph node metastasis of esophageal carcinoma. E. Relationship of HF and lymph node metastasis of esophageal carcinoma.

Statistical analysis

Data analysis was performed by SPSS for Windows 17.0 software. ROC curve analysis was conducted to calculate the AUC, sensitivity, specificity. Logistic binary regression analysis was performed, and $P < 0.05$ was considered statistically significant.

Results

Correlation of PET/CT metabolic parameters and lymph node metastasis: ROC curve analysis

The correlation between metabolic parameters and lymph node metastasis was investigated by ROC (Receiver Operating Characteristic Curve, ROC) analysis. As shown in **Figure 2**, the AUC of SUVmax was 0.657, cutoff value was 7.350, $P = 0.014$. The AUC of SUVmean was 0.655, cutoff value was 4.399, $P = 0.016$. The AUC of MTV was 0.719, cutoff value was 5.375, $P = 0.001$. The AUC of TLG was 0.722, cutoff value was 24.080, $P = 0.001$. The AUC of HF was 0.727, cutoff value was 0.1385, $P = 0.001$. These data suggested that there was correlation between metabolic parameters and lymph node metastasis of esophageal cancer.

Univariate analysis of PET/CT metabolic parameters and lymph node metastasis

As shown in **Table 2**, the PET/CT metabolic parameters were divided into two groups, including SUVmax (cutoff value 7.350, divided into two groups: SUVmax ≥ 7.350, SUVmax < 7.350), SUVmean (cutoff value 4.399, divided into two groups: SUVmean ≥ 4.399, SUVmean < 4.399), MTV (cutoff value 5.375, divided into two groups: MTV ≥ 5.375, MTV < 5.375), TLG (cutoff value 24.080, divided into two groups: TLG ≥ 24.080, TLG < 24.080), and HF (cutoff value 0.1385, divided into two groups: HF ≥ 0.1385, HF < 0.1385). The univariate analysis of PET/CT metabolic parameters and lymph node metastasis was performed by logistic binary regression and the results showed that, all metabolic parameters were statistically significant ($P = 0.001$, $P = 0.001$, $P = 0.001$, $P < 0.001$, $P = 0.001$, respectively), suggesting that there was a correlation between metabolic parameters and lymph node metastasis of esophageal cancer.

Multivariate analysis of PET/CT metabolic parameters and lymph node metastasis

The above univariate analysis on PET/CT metabolic parameters showed that SUVmax,

Table 2. Correlation between lymph node metastasis and PET parameters

Variable	Range	Number of cases with lymph node metastasis	Number of cases without lymph node metastasis	*P* value	95% CI	
					Lower limit	Upper limit
SUVmax	≥ 7.350	37	20	0.001	2.016	17.027
	< 7.350	6	19			
SUVmean	≥ 4.399	37	20	0.001	2.016	17.027
	< 4.399	6	19			
MTV	≥ 5.375	39	21	0.001	2.501	27.923
	< 5.375	4	18			
TLG	≥ 24.080	40	20	< 0.001	3.348	47.927
	< 24.080	3	19			
HF	≥ 0.1385	36	18	0.001	2.152	16.732
	< 0.1385	7	21			

Table 3. Multivariate analysis of lymph node metastasis and PET parameters

Variable	*P* value	95% CI	
		Lower limit	Upper limit
SUVmax	0.798	0.074	7.430
MTV	0.561	0.181	23.316
TLG	0.027	1.433	446.928
HF	0.503	0.341	18.860

SUVmean, MTV, TLG, and HF were statistically significant, then we conducted multivariate analysis on all parameters (SUVmax, SUVmean, MTV, TLG, HF) and found that only TLG was statistically significant, P = 0.027 (**Table 3**). The correlation between TLG and lymph node metastasis was analyzed by ROC curve. Its AUC was greater than 0.7. When the cutoff value was 24.080, the sensitivity was 93.0%, specificity was 51.3%, and Youden index was 0.443, P = 0.001, suggesting that TLG of primary lesion has diagnostic value for lymph node metastasis of esophageal cancer, and the minimum TLG for diagnosis of lymph node metastasis of esophageal cancer was 24.08. In addition, according to different sites of primary lesion of esophageal cancer, ROC curve analysis on TLG of the thoracic esophageal cancers at the upper and middle segment and the lower segment was performed, and it was found that the thoracic esophageal cancers at the upper and middle segment were statistically significant. When TLG > 23.06, its AUC was 0.755, the sensitivity was 96.7%, specificity was 51.7%, and Youden index was 0.484, P = 0.001, while the thoracic esophageal cancer at the lower segment was not statistically significant, suggesting that the minimum TLG for diagnosis of lymph node metastasis of esophageal cancer at the upper and middle segment was 23.06.

Discussion

Esophageal cancer is a common malignant tumor, and current treatment is mainly focused on the comprehensive treatment. The existence of lymph node metastasis plays a decisive role for the choice of surgical approaches and the extent of lymph node dissection, so it is important to assess lymph node metastasis before surgery. The commonly-used lymph node examination methods such as CT, MRI, intracavity ultrasound belong to anatomical structure imaging with some limitations. It was found that, the PET/CT diagnosis of esophageal cancer lymph node metastasis was more accurate than the enhanced CT [11]. In addition, another research study by van Vliet and his group [13] conducted the meta-analysis with the results showing that, both sensitivity and specificity of PET/CT for diagnosis of regional lymph node of esophageal cancer were superior to CT and intra-cavity ultrasound. At present, the PET/CT diagnosis of lymph node metastasis of esophageal cancer should be subject to the locally high metabolic lesions in the lymphatic drainage area observed by naked eyes. A number of lymph node metastases were found after operations that were not found before operation. The PET/CT metabolic parameters were correlated with the lymph node metastasis, but whether it can be used to predict lymph node metastasis needs to be further studied.

Accurate preoperative staging played an important role in the development of surgical proce-

dures for esophageal cancer. It was found that, for patients receiving surgery of esophageal cancer, the 5-year survival rate of patients with lymph node metastasis was less than 15% (< 15%), while the 5-year survival rate of patients without lymph node metastasis was more than 40% (> 40%) [14]. Because PET/CT examination is expensive, it is mainly used for clinical examination of esophageal cancer with distant metastasis, and the CT examination mainly used for of esophageal cancer without lymph node metastasis. At present, fewer studies on the correlation between PET metabolic parameters and lymph node metastasis have been reported. In earlier studies, for example, retrospective analysis on 49 patients with esophageal squamous cell carcinoma examined by PET/CT before operation showed that, SUVmax and MTV were correlated with lymph node metastasis [15]. Another retrospective analysis was conducted on 51 esophageal cancer patients by preoperative PET/CT examination and found that there was correlation between metabolic parameters (SUVmax, MTV, TLG, HF) and lymph node metastasis, and further multivariate analysis showed that only HF was statistically significant [16]. It was also found that MTV, SUVmax were correlated with the lymph node metastasis of esophageal cancer [17]. ^{18}F-FDG PET/CT metabolic parameters were proportional to the glucose metabolism of tissues, and most tumors were highly metabolic [9]. The larger the metabolic parameters, the more advanced the tumor, and the higher degree of malignancy, and therefore, the higher possibility the occurrence of regional lymph node metastasis. In this study, PET/CT metabolic parameters and lymph node metastasis were studied using ROC curve, and all *P* values were less than 0.05, suggesting that there was a correlation between PET/CT metabolic parameters (including SUVmax, SUVmean, MTV, TLG, HF) and lymph node metastasis of esophageal cancer. Then logistic univariate regression analysis also suggested that there was such correlation, in which, SUVmax (P = 0.001), SUVmean (P = 0.001), MTV (P = 0.001), TLG (P < 0.001), and HF (P = 0.001).

At present, the clinical diagnosis of lymph node metastasis of esophageal cancer is still mainly based on CT. A general consensus achieved is the following diagnostic criteria in lymph node metastasis of esophageal cancer: mediastinal lymph node short-axis diameter > 1 cm and the diameter of tracheal esophageal bypass, pericardium and abdominal lymph node long-axis diameter > 0.5 cm on the CT images. The PET/CT metabolic parameters are mainly used to evaluate whether tumors are benign or malignant. Currently, at SUVmax > 2.5, malignancy is suspected. It was difficult to identify the regional lymph node metastasis of esophageal cancer by the SUVmax value [18]. For other parameters, a small number of studies have suggested a correlation with the lymph node metastasis of esophageal cancer [17-21], but its diagnostic value on lymph node metastasis of esophageal cancer was rarely mentioned. TLG is the product of SUVmean and MTV, which combines two factors namely SUV and MTV, so theoretically its application value is higher than other metabolic parameters. In this study, the logistic univariate regression analysis showed that, there was a correlation between PET/CT metabolic parameters (SUVmax, SUVmean, MTV, TLG and HF) and lymph node metastasis of esophageal cancer, all *P* values were less than 0.01. The further logistic multivariate regression analysis on each metabolic parameter found that, TLG was statistically significant, P = 0.027, suggesting that TLG had diagnostic value for the lymph node metastasis of esophageal cancer. In addition, by studying the TLG and lymph node metastasis of esophageal cancer through ROC curves, it was found that when TLG = 24.08, its AUC was 0.722, the sensitivity was 93.0%, the specificity was 51.3%, P = 0.001. The results show that TLG had a certain diagnostic value for lymph node metastasis of esophageal cancer, and the minimum TLG was 24.08 for the diagnosis. According to the different sites of primary lesions of esophageal cancer, ROC curve analysis was conducted for TLG of the thoracic esophageal cancers at the upper and middle segment and the lower segment. The results show that the thoracic esophageal cancers at the upper and middle segment were statistically significant. When TLG > 23.06, its AUC was 0.755, the sensitivity was 96.7%, specificity was 51.7%, P = 0.001, while the thoracic esophageal cancer at the lower segment was not statistically significant, suggesting that the minimum TLG for diagnosis of lymph node metastasis of esophageal cancer at the upper and middle segment was 23.06.

At present, lymph node dissection of esophageal cancer surgery mainly includes chest and

stomach, or neck, chest, abdomen. There is no consensus on prognosis of the two surgical procedures. It was found that, the 1-year, 2-year and 5-year survival rates of esophageal cancer patients who underwent three-field lymph node dissection were higher than those who underwent two-field lymph node dissection [21]. But it was also reported that there was no statistical difference in the postoperative survival time between the two kinds of surgical procedures [20]. Due to the complex anatomical structure around the cervical lymph nodes, it was easy to cause injury of recurrent laryngeal nerves, anastomotic fistula and respiratory complications during dissection. Therefore, not all esophageal cancer patients should choose the neck, chest, and abdominal lymph node dissection, instead, we should conduct assessment on the lymph node metastasis before operation and select appropriate surgical procedures. For patients who were highly suspicious of lymph node metastasis with high TLG of primary lesions found in preoperative PET/CT examination, the possibility of metastasis was high, and neck, chest, abdominal lymph node dissection should be performed to achieve better prognosis. For patients who were suspicious of lymph node metastasis with low TLG of primary lesions found in preoperative PET/CT examination, the possibility of metastasis was low. Therefore, considering tumor sites, we should avoid the neck, chest, abdominal lymph node dissection to reduce the surgical complications.

Conclusion

The current study found a correlation between ^{18}FDG-PET/CT metabolic parameters (SUVmax, SUVmean, MTV, TLG, HF) and lymph node metastasis of esophageal cancer patients, which could provide a reference basis for the diagnosis of esophageal cancer. The parameter TLG had a certain diagnostic value for lymph node metastasis of esophageal cancer, and the minimum TLG for diagnosis of lymph node metastasis of esophageal cancer was 24.08, and the minimum TLG for diagnosis of lymph node metastasis of esophageal cancer at the upper and middle segment was 23.06. It was preferred that the three-field lymph node dissection was performed for patients with high possibility of metastasis, especially for those with esophageal cancers at upper and middle thoracic segments.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Jiancheng Li, Department of Radiation Oncology, Fujian Cancer Hospital Affiliated to Fujian Medical University, 420 Fuma Road, Fuzhou 350014, Fujian, PR China. Tel: +86-13906900190; Fax: +86-591-83928767; E-mail: docjianchengli@sina.com

References

[1] Chen W, Zheng R, Baade PD, Zhang S, Zeng H, Bray F, Jemal A, Yu XQ and He J. Cancer statistics in China, 2015. CA Cancer J Clin 2016; 66: 115-132.

[2] Chang S and Kim SJ. Prediction of recurrence and mortality of locally advanced esophageal cancer patients using pretreatment F-18 FDG PET/CT parameters: intratumoral heterogeneity, SUV, and volumetric parameters. Cancer Biother Radiopharm 2016; 31: 1-6.

[3] Liu XQ, Zhou HZ and Du J. Prognostic value of metabolic tumor volume measured by ^{18}F-FDG PET/CT imaging in preoperative breast cancer patients. J Clin Med Pract 2014; 18: 55-59.

[4] Chung MK, Jeong HS, Park SG, Jang JY, Son YI, Choi JY, Hyun SH, Park K, Ahn MJ, Ahn YC, Kim HJ, Ko YH and Baek CH. Metabolic tumor volume of [F-18]-Fluorodeoxyglucose positron emission tomography/computed tomography predicts short-term outcome to radiotherapy with or without chemotherapy in pharyngeal cancer. Clin Cancer Res 2009; 15: 5861-5868.

[5] Hyun SH, Choi JY, Shim YM, Kim K, Lee SJ, Cho YS, Lee JY, Lee KH and Kim BT. Prognostic value of metabolic tumor volume measured by 18F-fluorodeoxyglucose positron emission tomography in patients with esophageal carcinoma. Ann Surg Oncol 2010; 17: 115-122.

[6] Xie YT, Zheng R, Wu N, Zhang WJ, Liang Y, Liu Y, Li XM, Liang M and Xiao ZF. Prognostic value of FDG PET-CT metabolic parameters before treatment in patients with esophageal cancer receiving radiotherapy. Chin J Radiat Oncol 2016; 25: 452-456.

[7] Yildirim F, Yurdakul AS, Ozkaya S, Akdemir UO and Ozturk C. Total lesion glycolysis by ^{18}F-FDG PET/CT is independent prognostic factor in patients with advanced non-small cell lung cancer. Clin Respir J 2017; 11: 602-611.

[8] Son SH, Kim DH, Hong CM, Kim CY, Jeong SY, Lee SW, Lee J and Ahn BC. Prognostic implica-

tion of intratumoral metabolic heterogeneity in invasive ductal carcinoma of the breast. BMC Cancer 2014; 14: 585.

[9] Hu N, Wu YG, Xiao LZ, Tan YL and Wang YH. Metabolic parameters of ^{18}F-FDG PET/CT and their application in lymphoma. Int J Radiat Med Nucl Med 2015; 39: 342-347.

[10] Boellaard R, O'Doherty MJ, Weber WA, Mottaghy FM, Lonsdale MN, Stroobants SG, Oyen WJ, Kotzerke J, Hoekstra OS, Pruim J, Marsden PK, Tatsch K, Hoekstra CJ, Visser EP, Arends B, Verzijlbergen FJ, Zijlstra JM, Comans EF, Lammertsma AA, Paans AM, Willemsen AT, Beyer T, Bockisch A, Schaefer-Prokop C, Delbeke D, Baum RP, Chiti A and Krause BJ. FDG PET and PET/CT: EANM procedure guidelines for tumour PET imaging: version 1.0. Eur J Nucl Med Mol Imaging 2010; 37: 181-200.

[11] Tan R, Zhu RJ, Ge QX, Lu BY, Yao SZ, Li X and Liu QW. The application of ^{18}F-FDG PET/CT and contrast enhanced MSCT in detecting metastatic lymph nodes in esophageal cancer. Chin J Nucl Med 2007; 27: 356-359.

[12] Kidd EA and Grigsby PW. Intratumoral metabolic heterogeneity of cervical cancer. Clin Cancer Res 2008; 14: 5236-5241.

[13] van Vliet EP, Heijenbrok-Kal MH, Hunink MG, Kuipers EJ and Siersema PD. Staging investigations for oesophageal cancer: a meta-analysis. Br J Cancer 2008; 98: 547-557.

[14] Tanaka T, Matono S, Mori N, Shirouzu K and Fujita H. T1 squamous cell carcinoma of the esophagus: long-term outcomes and prognostic factors after esophagectomy. Ann Surg Oncol 2014; 21: 932-938.

[15] Zhu WQ, Yu JM, Sun XR, Xing LG, Xie P, Sun XD, Guo HB, Yang GR and Kong L. The prognostic value of metabolic tumor volume in FDG PET/CT evaluation of post-operative survival in patients with esophageal squamous cell cancer. Chin J Nucl Med 2011; 31: 378-381.

[16] Kim SJ, Pak K and Chang S. Determination of regional lymph node status using (18)F-FDG PET/CT parameters in oesophageal cancer patients: comparison of SUV, volumetric parameters and intratumoral heterogeneity. Br J Radiol 2016; 89: 20150673.

[17] I HS, Kim SJ, Kim IJ and Kim K. Predictive value of metabolic tumor volume measured by ^{18}F-FDG PET for regional lymph node status in patients with esophageal cancer. Clin Nucl Med 2012; 37: 442-446.

[18] Tangoku A, Yamamoto Y, Furukita Y, Goto M and Morimoto M. The new era of staging as a key for an appropriate treatment for esophageal cancer. Ann Thorac Cardiovasc Surg 2012; 18: 190-199.

[19] Jung JH, Kim CY, Son SH, Kim DH, Jeong SY, Lee SW, Lee J and Ahn BC. Preoperative prediction of cervical lymph node metastasis using primary tumor SUVmax on ^{18}F-FDG PET/CT in patients with papillary thyroid carcinoma. PLoS One 2015; 10: e0144152.

[20] Igaki H, Tachimori Y and Kato H. Improved survival for patients with upper and/or middle mediastinal lymph node metastasis of squamous cell carcinoma of the lower thoracic esophagus treated with 3-field dissection. Ann Surg 2004; 239: 483-490.

[21] Soydal C, Yuksel C, Kucuk NO, Okten I, Ozkan E and Doganay Erdogan B. Prognostic value of metabolic tumor volume measured by ^{18}F-FDG PET/CT in esophageal cancer patients. Mol Imaging Radionucl Ther 2014; 23: 12-15.