^{18}FDG UPTAKE AND THE VALUE OF PET/CT IN STAGE DIAGNOSIS IN ESOPHAGEAL CANCER PATIENTS

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SUMMARY

Objectives: To assess the value of ^{18}FDG PET/CT in stage diagnosis in esophageal cancer patients. Subjects and methods: 32 esophageal cancer patients were performed ^{18}FDG PET/CT for initial stage diagnosis before the treatment. Results: ^{18}FDG uptake of osephageal tumors increased, SUV_{max} increase from 3.1 to 44.8; average value 17.9 ± 9.2; It increased with invasive degree and stage of tumor. The ^{18}FDG PET/CT changed diagnosis of T stage in 2/32 patients (6.3%), of N stage in 15/32 patients (46.8%), detected metastases in 14 patients. After using ^{18}FDG PET/CT, 14/32 patients (43.7%) were upstaged, which included 7/10 patients (70%) of stage I and II and 7/15 patients (46.7%) of stage III. Conclusion: ^{18}FDG PET/CT scan effectively detected nodes, distant metastases, it had great value in stage diagnosis of esophageal cancer patients.

** Keywords: Esophageal cancer; Staging diagnosis; ^{18}FDG PET/CT.*

INTRODUCTION

Esophageal cancer ranks sixth in men, ninth in women in the world. The percentage of men and women varies from 4:1 to 14:1 or higher. According to the World Cancer Research Association, there are about 482,000 new cancer cases each year, of which the mortality rate is very high, 84% of esophageal cancer cases died in 2008.

For effective treatment of esophageal cancer, accurate diagnosis of the stage is very important. The main advantage of ^{18}FDG PET/CT scan is localizing nodal lesions, nodal metastases, mediastinal lymph nodes, and lymph node metastasis are identified with high sensitivity and specificity. ^{18}FDG PET/CT allows for more accurate detection of distant metastatic lesions such as lung metastases, liver metastases, bone metastases that other conventional tests have not yet screened. Thus, based on new lesions detected on ^{18}FDG PET/CT, it helps to diagnose accurately stage of esophageal cancer, which has altered initial treatment in about one-third of patients [3, 5].

At the Oncology Center and Nuclear Medicine, 103 Military Hospital has applied ^{18}FDG PET/CT effectively in the stage diagnosis of many types of cancer. In this topic, we conducted research with the purposes:

- ^{18}FDG uptake characteristics of esophageal cancer.

- Evaluation of the value of ^{18}FDG PET/CT in stage diagnosis in esophageal cancer patients.

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SUBJECTS AND METHODS

1. Subjects.

Patients diagnosed with pathologic esophageal cancer, with indication for ^{18}FDG PET/CT scan prior to treatment for stage diagnosis at the Center for Oncology and Nuclear Medicine, 103 Military Hospital from June 2017 to June 2018.

2. Methods.

- Clinical, uncontrolled, convenient sampling.

- An assessment of disease stage before ^{18}FDG PET/CT scan according to the TNM system (AJCC 2010).

- Procedures for ^{18}FDG PET/CT scan:

+ PET/CT TruFlight Select system of Philips brand. TRUE D software analyzes the results.

+ Radioactive substance: ^{18}FDG (2-fluoro-2-deoxy-D-glucose), dose of 0.15 mCi/kg body weight.

+ Patients must have fast breakfast for 4 - 6 hours, receive a clinical examination, measure height, weight, blood pressure, temperature and blood glucose test before injecting ^{18}FDG (blood sugar should be less than 8 mmol/L or 150 mg/dL).

+ Conduct ^{18}FDG PET/CT scan after 45 minutes of radioactive substance injection. Patients must urinate before scanning.

+ CT 16 scan, 140 kV, 80 mA with a thickness of 3 mm. CT images are reproduced by the 512 x 512 matrix.

+ The results were analyzed, assessed and evaluated by physician majored in nuclear medicine and imaging physician based on CT imaging, PET imaging and PET/CT inter-imaging under histopathological and histological diagnosis: ^{18}FDG uptake increased on PET/CT. Determination of the semi-quantitative indices of ^{18}FDG SUV_{max} uptake for primary tumor lesions, metastatic lesions, and lymph nodes.

RESULTS AND DISCUSSION

1. Characteristics of ^{18}FDG uptake of tumors, lymph nodes, distant metastatic lesions in esophageal cancer patients.

Table 1: ^{18}FDG (SUV_{max}) uptake by tumor position.

Tumor location	Number of patients	SUV_{max}			p
		Min	Max	X ± SD	
1/3 upper (1)	4	3.1	30.9	16.8 ± 13.3	$p_{1,2} = 0.49$ $p_{1,3} = 0.38$ $p_{2,3} = 0.24$
1/3 middle (2)	13	4.5	24.8	16.8 ± 6.6	
1/3 lower (3)	15	5	44.8	19.1 ± 10.4	
Total	32			17.9 ± 9.2	

Most of the malignant tumors in the esophagus were strongly increased glucose uptake. Therefore, PET/CT with ^{18}FDG is very valuable in the initial stage diagnosis of esophageal cancer. In the research group, ^{18}FDG uptake increased, SUV_{max} from 3.1 to 44.8; average value 17.9 ± 9.2; which was about 6 - 7 times higher than the standard diagnosis (2.5).

^{18}FDG uptake in tumor not only reflects the benign tumor/melanoma border but also partly reflects the intrinsic biology of the tumor, so many SUVs are not only valuable for cancer diagnosis but it is also worth prolonging the life expectancy, treatment results, etc. There was a significant difference in treatment outcomes in patients with "low" SUVs and "high" SUVs, so many studies have shown interest in glucose uptake characteristics of tumors, nodes, metastasis, showing that ^{18}FDG SUV_{max} may be a biomarker with assessment value of tumor malignancy, direction for treatment... [3, 5].

Table 2: ^{18}FDG uptake by T invasive degree of tumor.

T invasive degree	Number of patients	SUV_{max}	p
T1 (1)	4	7.9 ± 4.4	$p_{1,2} = 0.06$; $p_{1,3} = 0.003$ $p_{1,4} = 0.0005$; $p_{2,3} = 0.12$ $p_{2,4} = 0.01$; $p_{3,4} = 0.04$
T2 (2)	8	14.1 ± 8.7	
T3 (3)	12	18.5 ± 6.1	
T4 (4)	8	25.8 ± 9.4	
Total	32	17.9 ± 9.2	

SUV_{max} increased with invasive degree of tumors, low in patients with tumor retention (T1), SUV_{max} = 7.9 ± 4.4. When invasive degree increased to T2, the SUV_{max} increased with an average of 14.1 ± 8.7 and continued to increase in T3, T4.

Table 3: ^{18}FDG uptake of tumor by node group.

Node	Number of patients	SUV_{max}		p
N0 (1)	3	11.3 ± 8.5		$p_{1,2} = 0.29$; $p_{1,3} = 0.1$ $p_{1,4} = 0.08$; $p_{2,3} = 0.18$ $p_{24} = 0.07$; $p_{3,4} = 0.13$
N1 (2)	6	14.4 ± 7.2	18.6 ± 9.1	
N2 (3)	13	17.7 ± 7.3		
N3 (4)	10	22.3 ± 11.5		

SUV_{max} of tumors with metastatic nodules (including N1, N2 and N3) was 18.6 ± 9.1; higher than in the non-detectable nodal metastasis on ^{18}FDG PET/CT. It can be seen that when esophageal cancer patients in progress, with metastatic nodules, the tumor metabolism is increasing sharply, the more metastatic nodules (N1 to N2, to N3), ^{18}FDG uptake at tumor continuously increased (from 14.4 ± 7.2 of the N1 group increased to 17.7 ± 7.3 in the N2 group and 22.3 ± 11.5 in esophageal cancer group N3).

Table 4: ^{18}FDG uptake of tumor in patients with and without metastase.

Metastasis (on PET/CT)	Number of patients	SUV_{max}	p
Non-metastasis	18	18.8 ± 9.7	p = 0.26
Metastasis	14	16.7 ± 8.7	

However, the difference was not statistically significant. It is possible that in the late stage of distant metastasis, in the primary tumor, there was even necrosis, the tumor metabolism did not continue to increase.

Table 5: ^{18}FDG uptake by metastase stage.

Stage	Number of patients	SUV_{max}	p
I - II (1)	5	11.4 ± 9.5	$p_{1,2} = 0.08$ $p_{1,3} = 0.25$ $p_{2,3} = 0.11$
III (2)	13	20.9 ± 9.3	
IV (3)	14	16.7 ± 8.7	
Total	32	17.9 ± 9.2	

^{18}FDG (SUV_{max}) uptake was low when the patient was in stages I - II, and then increased from stage III. In stage IV with distant metastase, SUV_{max} tended to decrease.

2. Diagnosis of tumors, nodes of esophageal cancer by ^{18}FDG PET/CT.

PET/CT scan with ^{18}FDG detected esophageal cancer in 100% of patients. ^{18}FDG uptake increased sharply, SUV_{max} from 3.1 to 44.8; average value of 17.9 ± 9.2, which means 6 to 7 times higher than the normal diagnosis threshold and thus 100% was positive.

- Diagnosis of invasive tumors (T):

After ^{18}FDG PET/CT, the diagnosis result by T (invasive) classification in 1 patient before ^{18}FDG PET/CT was T1, after ^{18}FDG PET/CT was T2 and 1 patient from T3 after ^{18}FDG PET/CT was T4 due to tracheal invasion.

- Diagnosis of nodes (N):

Before ^{18}FDG PET/CT scan, on CT, 14 upper lymph nodes and 62 lymph nodes of the lung-mediastinum were detected in 27/32 patients. 5 patients were diagnosed with nodal (N0). Results on ^{18}FDG PET/CT revealed lymphadenopathy in 29/32 patients (90.6%), including supraclavicular lymphadenopathy (16 lymph nodes/10 patients), lymph node (77 nodes/27 patients) and, in particular, ^{18}FDG PET/CT detected lymphadenopathy (25 nodes/14 patients). A total of 118 lymph nodes were identified, more than CT at 2 patients and 42 lymph nodes, which changed the diagnosis of lymphadenopathy in 15/32 patients (46.8%).

- Distant metastatic diagnosis:

Before PET/CT scan, distant metastases were detected in 7 patients. On ^{18}FDG PET/CT, 14/32 patients (43.6%) had distant metastases to the lung, liver and bones, ranging from 1 to 2 different organs per patient, with a total of 26 metastatic lesions (in the lungs of 7 patients with 8 lesions; in the bones of 4 patients with 6 lesions and in the liver of 5 patients with 12 lesions). Thus, ^{18}FDG PET/CT detected further distant metastases in 7 patients (3 patients with pulmonary metastases, 1 patient with bone metastases, 1 patient with liver metastases, 2 patients with liver and bone metastases).

3. Change of staging after PET/CT scan.

Table 6: Change of staging after ^{18}FDG PET/CT scan.

Before PET/CT		Stage after ^{18}FDG PET/CT scan						
Stage	Number of patients	I	IIa	IIb	IIIa	IIIb	IIIc	IV
I	3	1	-	1	-	-	-	1
IIa	1	-	-	1	-	-	-	-
IIb	6	-		2	1	1	1	1
IIIa	6				4			2
IIIb	3	-	-	-	-	1	2	-
IIIc	6	-	-	-	-	-	3	3
IV	7							7
Total	32	1	0	4	5	2	6	14

There was a change in the diagnostic results after ^{18}FDG PET/CT in 14/32 patients (43.7%):

+ 1 patient in stage I transfered to stage IIb and 1 patient from stage I transfered to stage IV.

+ 1 patient in stage IIa transfered to stage IIb; 3 patients from stage IIb transfered to stage III (1 IIIa; 1 IIIb and 1 IIIc).

+ 1 patient in stage IIb before ^{18}FDG PET/CT, after ^{18}FDG PET/CT changed and transferred to stage IV.

+ 2 patients from stage IIIa transferred to stage IV.

+ 2 patients from stage IIIb transferred to stage IIIc.

+ 3 patients in stage IIIc before ^{18}FDG PET/CT, after ^{18}FDG PET/CT ranked stage IV.

^{18}FDG PET/CT changed the diagnosis result of T invasive, N node, and distant metastatic M compared to prior to ^{18}FDG PET/CT scan, thus the stage diagnosis has been changed in esophageal cancer patients.

Table 7: Change of staging after ^{18}FDG PET/CT.

Stage before ^{18}FDG PET/CT	Number of patients	Change of staging after ^{18}FDG PET/CT			
		Unchangeable	Reduction of stage	Increase in stage	
				Number of patients	%
I	3	1	-	2	66.6
II	7	2	-	5	71.4
III	15	8	-	7	46.7
IV	7	7	-	-	-
Total	32	18	-	14	43.7

Significant changes in patients prior to 18FDG PET/CT were classified as stage I, II (7/10 patients, 70%). 14 patients changed in staging diagnosis, original treatment of 9 patients (28.1%) including 7 patients with stage IV metastases and 2 patients with stage IIb transferred to stage IIIb and IIIc must be changed.

Authors such as Rankin S (2011) [5], Ali Dervim K, Michael A.B (2012) [2], Akira Tangoku, Yota Yamamoto (2012) [1] showed that there were many modern imaging diagnostics such as endoscopic ultrasound combined with small needle biopsy, chest and abdominal CT, PET. Each method has its own advantages and disadvantages. Endoscopic ultrasonography is the preferred method for detecting primary tumors and regional lymph nodes, but no lesions are detected distant from esophageal tumor 5 cm. CT is commonly applied for stage diagnosis, however, accuracy is affected when some malignant nodules are small in size or when inflammatory lesions or benign pathologies. 18FDG PET/CT will detect nodal changes that CT does not detect. The main advantage of 18FDG PET/CT is to detect distal metastases in the liver, bones, and lungs for accurate stage diagnosis [4].

CONCLUSSION

^{18}FDG uptake in esophageal cancer was high, SUV_{max} of 3.1 - 44.8; average value of 17.9 ± 9.2; increased in invasive degree of tumor. It was low in patients in the focal period (T1), SUV_{max} = 7.9 ± 4.4, and increased in T2 (14.1 ± 8.7) continuously increased in T3, T4. SUVmax was low when the patient was still in stage I - II, then rose from stage III. SUVmax in stage IV was in the direction of decrease.

^{18}FDG PET/CT screening detected 29/32 patients (90.6%) with lymphadenopathy, a total of 118 nodes including 16 superior lymph nodes, 77 lung neoplasia lymph nodes, 25 lymph nodes. Distant metastatic found in 7 patients. ^{18}FDG PET/CT results changed the staging diagnosis according to T in 2/32 patients (6.3%), according to N in 15/32 patients (46.8%). The overall result after 18FDG PET/CT screening had 14/32 patients (43.7%) with stage-change 7/10 patients (70%) in stage I, II; and 7/15 patients (46.7%) in stage III.

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