Role of Pre-therapeutic $^{18}$F-FDG PET/CT in Guiding the Treatment Strategy and Predicting Prognosis in Patients with Esophageal Carcinoma

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Abstract

Objective(s): The present study aimed to evaluate the role of pre-therapeutic $^{18}$fluorine-fluorodeoxyglucose positron emission tomography-computed tomography ($^{18}$F-FDG PET-CT) and maximum standardized uptake value (SUV$_{\text{max}}$) in guiding the treatment strategy and predicting the prognosis of esophageal carcinoma, using the survival data of the patients.

Methods: The present retrospective, cohort study was performed on 40 consecutive patients with esophageal carcinoma (confirmed by endoscopic biopsy), who underwent pre-operative $^{18}$F-FDG PET-CT staging between January 2009 and June 2014. All the patients underwent contrast-enhanced CT and non-contrast $^{18}$F-FDG PET-CT evaluations. The patients were followed-up over 12 months to assess the changes in therapeutic strategies. Survival analysis was done considering the primary tumor SUV$_{\text{max}}$, using the Kaplan–Meier product-limit method.

Results: In a total of 40 patients, $^{18}$F-FDG PET-CT scan led to changes in disease stage in 26 (65.0%) cases, with upstaging and downstaging reported in 10 (25.0%) and 16 (40.0%) patients, respectively. The management strategy changed from palliative to curative in 10 out of 24 patients and from curative to palliative in 7 out of 16 cases. Based on the $^{18}$F-FDG PET-CT scan alone, the median survival of patients in the palliative group was 4.0 (95% CI 3.0-5.0) months, whereas the median survival in the curative group has not been reached, based on the 12-month follow-up. Selection of treatment strategy on the basis of $^{18}$F-FDG PET/CT alone was significantly associated with the survival outcomes at nine months ($P=0.03$) and marginally significant at 12 months ($P=0.05$). On the basis of SUV$_{\text{max}}$, the relation between survival and SUV$_{\text{max}}$ was not statistically significant.

Conclusion: $^{18}$F-FDG PET/CT scan had a significant impact on stage stratification and subsequently, selection of a stage-specific treatment approach and the overall survival outcome in patients with esophageal carcinoma. However, pre-treatment SUV$_{\text{max}}$ failed to establish its usefulness in the assessment of patient prognosis and survival outcome.

Introduction

The incidence of esophageal carcinoma in Malaysia is 1.5 per 100,000 populations (1). Esophageal carcinoma as a relatively rare disease is ranked 17$^{\text{th}}$ and 22$^{\text{nd}}$ most common cancer in Malaysia in males and females, respectively. Despite significant advances in the diagnosis and treatment of esophageal carcinoma, the overall survival remains poor, with a 5-year survival rate of approximately 15% (2). The poor prognosis is predominantly due to the advanced stage at the time of diagnosis, which is often associated with locoregional lymph node involvement and distant metastasis (3). Treatment options for esophageal carcinoma include surgery, radiotherapy, chemotherapy, and targeted therapy. The management strategy is often guided by the presence of nodal and distant metastases, as well as the extent of primary tumor burden (4). Pre-therapeutic imaging, particularly $^{18}$F-FDG PET-CT, can provide valuable information regarding the extent of disease and response to treatment (5). $^{18}$F-FDG PET-CT is a functional imaging modality that can detect tumors based on glucose metabolism, which is increased in malignant cells (6). SUV$_{\text{max}}$ is the maximum standardized uptake value, which is a measure of tumor glucose uptake, and is used to quantify the intensity of FDG uptake (7). SUV$_{\text{max}}$ can be used to assess tumor burden and response to treatment (8). The objective of this study was to evaluate the role of pre-therapeutic $^{18}$F-FDG PET-CT and SUV$_{\text{max}}$ in guiding the treatment strategy and predicting the prognosis of esophageal carcinoma, using the survival data of the patients.

Keywords: Esophageal carcinoma, FDG, PET/CT, Prognosis

Please cite this paper as:
Tan TH, Boey CY, Lee BN. Role of Pre-therapeutic $^{18}$F-FDG PET/CT in Guiding the Treatment Strategy and Predicting Prognosis in Patients with Esophageal Carcinoma. Asia Oceania J Nucl Med Biol. 2016; 4(2): 59-65. doi: 10.7508/aojnmb.2016.02.001

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treatment of this disease, the overall five-year survival remains relatively poor (2). Therefore, accurate pre-therapeutic staging of esophageal carcinoma, which subsequently guides the stage-adapted treatment approach, is critical in optimizing the survival outcomes (3).

The location and depth of tumor involvement, together with the presence of nodal and systemic metastases, are important parameters in guiding treatment approaches such as radical curative surgery, definitive chemoradiotherapy, and palliative therapy (3). In order to fully assess the disease extent, a multimodality approach, comprised of endoscopic ultrasound (EUS), computed tomography (CT), and 18F-fluorine-fluorodeoxyglucose positron emission tomography-CT (18F-FDG PET/CT), is usually adopted.

For the initial tumor (T) staging, EUS has been shown to be the optimal modality in assessing the depth of transmural infiltration (4). Furthermore, this modality facilitates ultrasound-guided biopsy which is associated with a higher histopathological yield. For the evaluation of tumor extension, contrasted CT presents a well-demarcation in depicting local invasion to the adjacent structures and provides some information on peritumoral lymph node involvement (5).

For the evaluation of remote nodal and systemic metastases, which majorly dictate the therapeutic options, 18F-FDG PET/CT scan is particularly useful (6, 7). Furthermore, utility of 18F-FDG PET/CT scan has led to changes in esophageal cancer staging (3-5) and has been found to significantly affect patient management (6, 10).

Several studies have shown the prognostic value of standardized uptake value (SUV) in the overall survival of patients with esophageal carcinoma (11). However, this finding has not been replicated in other studies, and the significant impact of SUV \(_{\text{max}}\) alone on the overall patient survival has not been documented (12, 13). Therefore, the purpose of this study was to evaluate the role of pre-therapeutic 18F-FDG PET/CT and SUV \(_{\text{max}}\) in predicting the treatment strategy and prognosis of patients with esophageal carcinoma, using the survival data of the patients.

**Methods**

The present retrospective, cohort study was performed on 40 consecutive patients with esophageal carcinoma (confirmed by endoscopic biopsy), who underwent pre-operative 18F-FDG PET/CT staging between January 2009 and June 2014. The histological findings, tumor location, prior contrasted CT scan findings, 18F-FDG PET/CT results, SUV \(_{\text{max}}\) of the primary lesion, post-PET/CT treatment, patient follow-up, and survival status of the patients were retrieved, using the hospital database and contacting the patients or their relatives.

The study protocol was approved by the local ethics committee, and informed consents were obtained from the patients through conversations with the patients and their relatives.

**18F-FDG PET/CT imaging protocol**

The patients were required to fast for at least four hours prior to examination. Upon admission, the patients’ body weight was measured and blood glucose level was recorded. Then, 6 MBq/kg of 18F-FDG (range: 285-460 MBq) was intravenously injected, and PET/CT imaging was performed on the dedicated GE® Discovery ST Scanner, equipped with PET and eight-slice CT units. Image acquisition was performed with a whole-body field of view (vertex to mid-thigh), 45-60 min after the injection.

CT transmission images for attenuation correction were captured with exposure factors of 120 kVp, 80 mA, and 0.8 s for all examinations; no intravenous CT contrast was administered. Emission PET images were obtained in a two-dimensional mode at the rate of four min per bed position with a three-slice overlap between consecutive bed positions.

Transaxial PET data were reconstructed using filtered back-projection. The CT data for PET were reconstructed to axial slices with a thickness of 3.3 mm. The images were reviewed on GE Advantage Workstation (version 4.2) by two experienced nuclear medicine physicians. Positive uptakes on PET images were based on non-physiological uptakes greater than liver or SUV \(_{\text{max}}\) > 2.5, corrected for body weight.

**Determination of disease stage**

All patients had undergone contrasted CT evaluation prior to 18F-FDG PET/CT scan. The median interval between CT and PET/CT scan was one month. Due to suboptimal spatial resolution on PET with noncontrast CT, no attempt was made to define local invasion or peritumoral lymphadenopathy during PET/CT interpretation. Therefore, on the basis of 18F-FDG PET/CT alone, information on T stage and N1 was not available, and consequently, the American Joint Committee on Cancer (AJCC) staging system was not adopted (14).

Based on 18F-FDG PET/CT alone, the disease extent was classified as follows: 1) tumor without nodal or distant metastasis; 2) tumor with nodal metastasis and no distant metastasis; and 3)
tumor with nodal and distant metastases. To determine the actual clinical approach based on surgical resectability, the overall disease stage was re-categorized into curative (localized tumor + resectable nodal metastasis) and palliative (tumor + unresectable distant nodal metastasis ± distant metastasis), based on contrast CT findings and PET/CT reports.

**Survival follow-up**

The overall survival was used as the primary endpoint to evaluate the prognostic significance. The overall survival was measured from the date of diagnosis of esophageal carcinoma to the date of patient’s death by any cause. The surviving patients were followed-up for at least 12 months. Among 40 patients, nine cases missed the survival data.

**Statistical analysis**

SPSS version 19.0 was used for the statistical analysis. The mean SUV\(_{\text{max}}\) was analyzed, using unpaired t-test and ANOVA test. Survival after follow-up was analyzed, using the Kaplan–Meier product-limit method. P-value less than 0.05 was considered statistically significant.

### Results

#### Baseline characteristics

Distribution of the characteristics of patients and tumors is summarized in Table 1. The median age of the subjects was 61 years (range: 42-78 years), and the male-to-female ratio was 24/16. Contrary to the reports in the United States, squamous cell carcinoma was the predominant histological subtype in the present study (15).

In the AJCC staging manual (seventh edition), the previously classified esophagogastric junction (EGJ) tumor was re-categorized as lower third esophageal tumor. By this re-classification, the lower esophagus became the primary site of esophageal tumors (14).

#### Correlation between SUV\(_{\text{max}}\) and tumor characteristics

The SUV\(_{\text{max}}\) of \(^{18}\text{F}-\text{FDG}\) in the primary lesion was high with the mean value of 12.6±7.1 (Table 2). A higher SUV\(_{\text{max}}\) was demonstrated in the proximal esophagus, compared to middle and lower regions (P=0.04). Expectedly, the squamous cell type predominantly exhibited higher SUV\(_{\text{max}}\) compared to adenocarcinoma cell type (P=0.02).

With regard to the classification of disease spread, Table 2 shows the correlation between SUV\(_{\text{max}}\) and tumor characteristics. As demonstrated, the localized tumor + resectable nodal metastasis showed lower SUV\(_{\text{max}}\) compared to localized tumor + unresectable distant nodal metastasis ± distant metastasis (P=0.03).

### Table 1.

Distribution of the characteristics of patients and tumors

| Parameters     | Characteristics | N  | % |
|----------------|-----------------|----|---|
| Sex            |                 |    |   |
| Male           |                 | 24 | 60.0 |
| Female         |                 | 16 | 40.0 |
| Histology      |                 |    |   |
| Adenocarcinoma |                 | 15 | 37.5 |
| Squamous cell carcinoma | | 19 | 47.5 |
| Not available  |                 | 6  | 15.0 |
| Tumor location |                 |    |   |
| Upper third    |                 | 3  | 7.5 |
| Middle third   |                 | 9  | 22.5 |
| Lower third    |                 | 28 (16 EGJ*) | 70.0 |

EGJ= Esophagogastric junction

### Table 2.

Correlation between maximum standardized uptake value (SUV\(_{\text{max}}\)), tumor characteristics, and tumor spread

| Factors | Mean SUV\(_{\text{max}}\) (95% CI) | P-value |
|---------|----------------------------------|---------|
| Tumor location |                                |         |
| Upper (n=3)      | 21.3 (14.2, 28.3) | 0.04    |
| Middle (n=9)     | 13.6 (8.4, 18.7)  |         |
| Lower (n=28)     | 11.1 (8.7, 14.2)  |         |
| Histology        |                                |         |
| Adenocarcinoma   | 9.7 (6.4, 13.0)   | 0.02    |
| Squamous cell cancer | 15.1 (12.0, 18.3) |         |
| T T + N involvement: tumor without nodal or distant metastasis (n=18) | 10.6 (7.6, 13.7) | 0.11    |
| T T + N + M involvement: tumor with nodal and distant metasesases (n=15) | 15.7 (11.3, 20.0) |         |
| T + N involvement: tumor with nodal metastasis but no distant metastasis (n=7) | 11.4 (5.4, 17.3) |         |
| Tumor + resectable nodal metastasis (n=21) | 10.4 (7.7, 13.1) | 0.03    |
| Tumor + unresectable distant nodal metastasis ± distant metastasis (n=19) | 15.1 (11.4, 18.9) |         |

T = tumor, N = nodal, M = distant metastasis
extension, the mean SUV$_{\text{max}}$ progressively increased from localized tumors to nodal metastases and subsequently to distant metastases, although this finding was not statistically significant. However, when the tumor stage was re-classified on the basis of surgical resectability, the unresectable group had a significantly higher SUV$_{\text{max}}$, compared to the resectable group.

**Management impact of pre-therapeutic $^{18}$F-FDG PET/CT**

Among 40 patients, $^{18}$F-FDG PET/CT led to a change in disease stage in 26 patients, with upstaging and downstaging reported in 10 and 16 cases, respectively (Table 3). Also, among 24 patients with palliative care as their initial treatment strategy, 10 cases were re-classified in the curative group on the basis of $^{18}$F-FDG PET/CT scan. On the other hand, management modification from curative to palliative was observed in 7 out of 16 patients (Table 3).

Among 19 patients in the curative group, only eight cases underwent surgical resection with or without neoadjuvant chemoradiation, two patients opted for only chemoradiation, two patients refused treatment, and seven cases missed the follow-ups. On the other hand, in the palliative group, 12 out of 21 patients received chemoradiation therapy, seven patients refused treatment, and two patients missed the follow-ups. In 5 out of 24 patients, the management strategy was modified from palliative to curative, while in 5 out of 16 patients, the strategy changed from curative to palliative. Figures 1 and 2 shows two examples of treatment change.

Based on $^{18}$F-FDG PET/CT alone, the median survival of patients in the palliative group was 4.0 (95% CI: 3.0-5.0) months, whereas the median survival of patients in the curative group has not been reached in the 12-month follow-up (Figure 3). The treatment strategy on the basis of $^{18}$F-FDG PET/CT alone was significantly associated with survival outcomes at nine months ($P=0.03$) and marginally significant at twelve months ($P=0.05$).

**Table 3. Impact of $^{18}$F-FDG PET/CT on modifications in disease stage and therapy**

| Findings                | N=40 | Percentage |
|-------------------------|------|------------|
| PET impact on disease stage | 26   | 65.0%      |
| Upstaging               | 10   | 25.0%      |
| Downtstaging            | 16   | 40.0%      |
| PET impact on disease management | 17/40 | 42.5%     |
| From palliative to curative | 10/24 | 41.7%    |
| From curative to palliative | 7/16  | 43.8%     |

**Table 4. Correlation between SUV$_{\text{max}}$ and 12-month survival based on the treatment strategy**

| Treatment strategy        | Median survival (month) (95% CI) | $P$  |
|---------------------------|----------------------------------|------|
| Surgical resection        |                                  |      |
| SUV$_{\text{max}}$$\leq$10 (n=3) | NR                               | 0.36 |
| SUV$_{\text{max}}$$>10$ (n=5)     | 10.0 (1.4, 18.6)                 |      |
| Chemoradiotherapy         |                                  |      |
| SUV$_{\text{max}}$$\leq$10 (n=5) | 4.0 (NA, NA)                    | 0.90 |
| SUV$_{\text{max}}$$>10$ (n=6)     | 12.0 (NA, NA)                   |      |
| No treatment              |                                  |      |
| SUV$_{\text{max}}$$\leq$10 (n=4) | 6.0 (0.1, 11.9)                 | 0.47 |
| SUV$_{\text{max}}$$>10$ (n=5)     | 4.0 (2.2, 5.8)                  |      |

NR = not reached, NA = not available
Relationship between SUV\textsubscript{max} and survival outcomes

In 31 patients with available survival data, the median SUV\textsubscript{max} of the primary tumor was 10.1±4.9 (Table 4). Therefore, SUV\textsubscript{max} of 10 was selected as the cut-off point while analyzing the survival outcomes in comparison with treatment factors and SUV\textsubscript{max}. Overall, the link between survival and SUV\textsubscript{max} in surgically treated, chemoradiation, and non-treatment groups was not statistically significant. Moreover, it is interesting to note that in the chemoradiation group, a higher median survival was observed in patients with SUV\textsubscript{max} above 10.

Discussion

Over the past few years, $^{18}$F-FDG PET/CT has shown increasing efficacy in pre-operative staging of esophageal carcinoma, particularly in the detection of remote nodal and systemic metastatic diseases (16, 18). $^{18}$F-FDG PET/CT has an accuracy of 83.7\% in detecting nodal metastases, while CT scan alone exhibits an accuracy of 76.6\% (6). Furthermore, the accuracy of $^{18}$F-FDG PET/CT scan in detecting distant metastases supersedes CT scan (96.43\% vs. 78.57\%) (7). This level of accuracy is crucial, as 20-30\% of patients with esophageal carcinoma with demonstrable metastatic disease at the time of initial diagnosis are precluded from high-risk curative surgeries (8).

In the present study, non-contrasted $^{18}$F-FDG PET/CT was used as an additional modality following conventional contrasted CT scan and EUS to further stage the disease, based on lymph node involvement (N) and distant metastasis (M) criteria. As a result, changes in disease stage were observed in 65.0\% of patients with upstaging and downstaging in 25.0\% and 40.0\% of cases, respectively.

In addition, in the present study, the impact of $^{18}$F-FDG PET/CT scan on therapeutic changes was tremendous. In total, 41\% of patients with the initial palliative strategy were re-classified in the curative group, whereas an opposite trend was reported in 31.3\% of patients. These findings have clear implications for treatment decision-making, as nearly one-third of the patients were re-classified as either candidates who will benefit from curative surgery or prevented from unnecessary high-risk surgery.

In the present study, the high percentage of $^{18}$F-FDG PET/CT-induced changes in the management strategy is comparable with previous studies (10, 19-22). However, such results tend to overlook the fact that 27.5\% of patients in this study were referred for confirmatory $^{18}$F-FDG PET/CT due to initial equivocal CT findings (e.g., solitary subcentimeter pulmonary nodule and small hypodense hepatic lesion).

As the frequency of patient referrals based on indeterminate CT findings increases, the likelihood of stage change after $^{18}$F-FDG PET/CT may be increased. Moreover, in this study, patients with T1 or T2 cancer were excluded from $^{18}$F-FDG PET/CT evaluation, as previous studies have revealed the insignificant diagnostic yield of PET in the detection of unsuspected metastatic disease at early stages (23).

In summary, such selective referrals are likely to contribute to sampling bias. Nonetheless, despite such potential bias, the change in management strategy is inevitable, based on correct staging in the majority of patients.

Although the significant role of $^{18}$F-FDG PET/CT in therapeutic changes does not necessarily translate to survival benefit, several studies have shown the efficacy of this modality in providing prognostic information in esophageal carcinoma (22, 24). This finding was also highlighted in the current study, where PET-CT-guided treatment plan was significantly associated with 12-month survival outcomes.

The difference in survival outcomes between curative and palliative groups was obvious at nine months, based on $^{18}$F-FDG PET/CT alone. However, despite the fact that the median survival in the curative group has not been reached at 12-month follow-up, the survival outcomes in this period between the two groups were marginally different due to the convergence of both curves after nine months (P=0.05). This convergence might be related to the improved outcomes of patients who subsequently responded to the definitive chemoradiation regimens (25); however, longer...
duration of follow-ups is needed to confirm this finding.

Various studies with controversial results have been published on the relationship between SUV\textsubscript{max} and survival outcomes in esophageal carcinoma (26). The median SUV\textsubscript{max} values in various studies range from 0.26 to 17.2, as summarized by Taan et al. (26). In the current study, the mean value of SUV\textsubscript{max} (12.6) was higher than the majority of conducted studies.

Also, the present findings were in agreement with the results reported by Taan et al., indicating the significantly higher value of SUV\textsubscript{max} in squamous cell carcinoma subtype, which was predominantly located in the upper esophageal region (26). However, these results remain unexplained and assessment of the possible link between the biological factors of two cellular subtypes and glucose metabolism is an interesting subject for future research.

Furthermore, in the present study, similar to the findings reported by Taan et al., SUV\textsubscript{max} was significantly elevated in the primary tumor as the disease burden (disease stage) increased (26). This finding was consistent with the notion that a large tumor burden is probably associated with a high tumoral proliferative rate and aggressiveness, which are in turn closely related to high glucose metabolism (27).

A meta-analysis by Pan et al. reported a hazard ratio of 1.86 by evaluating the prognostic value of SUV for the overall survival of patients with esophageal carcinoma (11). Interestingly, despite the close relationship between SUV\textsubscript{max} and disease stage, the findings of this study showed a poor association between survival outcomes and SUV\textsubscript{max} among surgically treated, chemoradiation, and non-treatment groups. Although these results were contrary to the findings reported by Pan et al., they were in line with other studies, showing that pre-treatment SUV\textsubscript{max} is of limited use in prognostic stratification (28-31).

The main reason for the poor correlation between pre-treatment SUV\textsubscript{max} and disease prognosis, as suggested by Taan et al., is the overriding effect of stage-based prognostic factor, which directly influences the therapeutic approach (26). Therefore, pre-treatment SUV\textsubscript{max} does not provide relevant information, influencing the actual clinical decision-making. Other parameters such as functional tumoral length, functional tumor volume, and total lesion glycolysis may be relevant prognosticators for survival outcomes (28-32), which may be of interest in future studies.

The major limitations of the present study included the small sample size hindering multivariate analysis, significant missing data due to the retrospective design of the study, and disease misclassification bias (due to intrinsic limitation of PET/CT instrumentation, as well as 18F tracer). The use of contrasted agents during CT acquisition on 18F-FDG PET/CT could be useful in making direct comparisons with the initial contrasted CT findings too.

**Conclusion**

18F-FDG PET/CT had a significant impact on stage stratification and subsequently, determination of the stage-stratified treatment approach in patients with esophageal carcinoma. Such stage-guided treatment strategies could improve the overall survival outcomes. However, pre-treatment SUV\textsubscript{max} failed to be of use in the prognostic assessment and survival outcomes.

**Conflicts of interest**

The author’s declare none conflicts of interest.

**Acknowledgments**

We would like to thank Kean-Ghee Lim for his valuable advice on manuscript writing and all the staff for their assistance. We also extend our gratitude to the Director General of Health in Malaysia for granting permission to publish this paper.

**References**

1. Omar ZA, Ali ZM, Tamin NS. Malaysian cancer statistics—data and figure peninsular Malaysia 2006. National Cancer Registry: Ministry of Health Malaysia; 2006.
2. Rankin S. The value of [18F]fluorodeoxyglucose-PET/CT in oesophageal cancer. Cancer Imaging. 2011;11(1A):S156-60.
3. Berry MF. Esophageal cancer: staging system and guidelines for staging and treatment. J Thorac Dis. 2014; 6(Suppl 3):S289–97.
4. Bruzzi JF, Munden RF, Truong MT, Marom EM, Sabloff BS, Gladish GW, et al. PET/CT of esophageal cancer: its role in clinical management. Radiographics. 2007;27(6):1635-52.
5. Hong SJ, Kim TJ, Nam KB, Lee IS, Yang HC, Cho S, et al. New TNM staging system for esophageal cancer: what chest radiologists need to know. Radiographics. 2014;34(6):1722-40.
6. Williams RN, Ubhi SS, Sutton CD, Thomas AL, Entwistle J, Bowrey DJ. The early use of PET-CT alters the management of patients with esophageal cancer. J Gastrointest Surg. 2009;13(5):868-73.
7. Kim K, Park SJ, Kim BT, Lee KS, Shim Y. Evaluation of lymph node metastases in squamous cell carcinoma of the esophagus with positron emission to-
mography. Ann Thorac Surg. 2001;71(1):290-4.
8. Quint LE, Hepburn LM, Francis IR, Whyte RJ, Orringer MB. Incidence and distribution of distant metastases from newly diagnosed esophageal carcinoma. Cancer. 1995;76(7):1120–5.
9. Kumar P, Damle NA, Bal C. Role of 18F-FDG PET/CT in the Staging and Restaging of Esophageal Cancer: a Comparison with CECT. Indian J Surg Oncol. 2011;2(4):343-50.
10. Chatterton BE, Ho Shon I, Baldey A, Lenzo N, Parikeos A, Kelley B, et al. Positron emission tomography changes management and prognostic stratification in patients with oesophageal cancer: results of a multicentre prospective study. Eur J Nucl Med Mol Imaging. 2009;36(3):354-61.
11. Pan L, Gu P, Huang G, Xue H, Wu S. Prognostic significance of SUV on PET/CT in patients with esophageal cancer: a systematic review and meta-analysis. Eur J Gastroenterol Hepatol. 2009;21(9):1008–15.
12. Brown C, Howes R, Jamieson GG, Barhalomeusz D, Zingg U, Sullivan TR, et al. Accuracy of PET-CT in predicting survival in patients with esophageal cancer. World J Surg. 2012;36(5):1089-95.
13. Hong D, Lunagomez S, Kim EE, Lee JH, Bresalier RS, Swisher SG, et al. Value of baseline positron emission tomography for predicting overall survival in patient with nonmetastatic esophageal or gastroesophageal junction carcinoma. Cancer. 2005;104(8):1620-6
14. Edge SB, Byrd DR, Compton CC, Fritz A, Greene FL, Trotti A. AJCC cancer staging manual. 7th ed. Berlin, Germany: Springer; 2010. P. 117-26.
15. Howlader N, Noone AM, Krapcho M, Neyman N, Aminou R, Waldron W, et al. SEER cancer statistics review, 1975-2008. Bethesda, MD: National Cancer Institute; 2011.
16. Van Vliet EP, Heijenbrok-Kal MH, Hunink MG, Kuijpers EJ, Siersma PD. Staging investigations for oesophageal cancer: a meta-analysis. Br J Cancer. 2008;98(3):547–57.
17. Roedl JB, Blake MA, Holalkere NS, Mueller PR, Cullen RR, Harisinghani MG. Lymph node staging in esophageal adenocarcinoma with PET-CT based on a visual analysis and based on metabolic parameters. Abdom Imaging. 2009;34(5):610–7.
18. Roedl JB, Prabhalaker HB, Mueller PR, Blake MA. Prediction of metastatic disease and survival in patients with gastric and gastroesophageal junction tumors: the incremental value of PET-CT over PET and the clinical role of primary tumor volume measurements. Acad Radiol. 2009;16(2):219-26.
19. Berrissford RG, Wong WL, Day D, Toy E, Napier M, Mitchell K, et al. The decision to operate: role of integrated computed tomography positron emission tomography in staging oesophageal and oesophagogastric junction cancer by the multidisciplinary team. Eur J Cardiothorac Surg. 2008;33(6):1112-6.
20. Gananantha S, Hazebroek EJ, Leibman S, Berry H, Osgood I, Shon IH, et al. The utility of FDG-PET in the preoperative staging of esophageal cancer. Dis Esophagus. 2008;21(5):389-94.
21. Salahudeen HM, Balan A, Naik K, Mirsadraee S, Scarsbrook AF. Impact of the introduction of integrated PET-CT into the preoperative staging pathway of patients with potentially operable oesophageal carcinoma. Clin Radiol. 2008;63(7):765-73.
22. Barber TW, Duong CP, Leong T, Bressel M, Brummond EG, Hicks RJ. 18F-FDG PET/CT has a high impact on patient management and provides powerful prognostic stratification in the primary staging of esophageal cancer: a prospective study with mature survival data. J Nucl Med. 2012;53(6):864-71.
23. Kim TJ, Kim HY, Lee KW, Kim MS. Multimodality assessment of esophageal cancer: preoperative staging and monitoring response to therapy. Radiographics 2009;29(2):403-21.
24. Luketich JD, Fiedman DM, Weigel TL, Meehan MA, Keenan RJ, Townsend DW, et al. Evaluation of distant metastases in esophageal cancer: 100 consecutive positron emission tomography scans. Ann Thorac Surg. 1999;68(4):1133-6.
25. Monjazeb AM, Riedlinger G, Aklila M, Geisinger KR, Mishra I, Isom S, et al. Outcomes of patients with esophageal cancer staged with 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) can postchemoradiation therapy PET-PET predict the utility of resection? J Clin Oncol. 2010;28(31):4714-21.
26. Al-Taan OS, Elweri A, Sharpe D, Rodgers PM, Ubhi SS, Bowrey DJ. Prognostic value of baseline FDG uptake on PET-CT in esophageal carcinoma. World J Gastrointest Oncol. 2014;6(5):139-44.
27. Shimoda W, Hayashi M, Murakami K, Oyama T, Sunagawa M. The relationship between FDG uptake in PET scans and biological behavior in breast cancer. Breast Cancer. 2007;14(3):260-8.
28. Hatt M, Visvikis D, Albaughch NM, Tixier F, Pradi er O, Cheze-le Rest C. Prognostic value of 18F-FDG PET image-based parameters in esophageal cancer and impact of tumour delineation methodology. Eur J Nucl Med Mol Imaging. 2011;38(7):1191-202.
29. Van Westreenen HL, Plukker JT, Cobben DC, Verhoogt CJ, Groen H, Jager PL. Prognostic value of the standardized uptake value in esophageal cancer. AJR Am J Roentgenol. 2005;185(2):436-40.
30. Cerfolio RJ, Bryant AS. Maximum standardized uptake values on positron emission tomography of esophageal cancer predicts stage, tumor biology, and survival. Ann Thorac Surg. 2006;82(2):391–4.
31. Cheze-le Rest C, Metges JP, Teyton P, Jestin-Le Tal lec V, Lozac'h P, Volant A, et al. Prognostic value of initial fluorodeoxyglucose-PET in esophageal cancer: a prospective study. Nucl Med Commun. 2008;29(7):628–35.
32. Choi JY, Jang HJ, Shim YM, Kim K, Lee KS, Choi Y, et al. 18F-FDG PET in patients with esophageal squamous cell carcinoma undergoing curative surgery: prognostic implications. J Nucl Med. 2004;45(11):1843-50.