Does Metastatic Lymph Node $SUD_{\text{max}}$ Predict Survival in Patients with Esophageal Cancer?

Metastatik Lenf Nodu $SUD_{\text{max}}$ Özofagus Kanserli Hastalarda Sağ Kalım Üzerine Belirleyici midir?

Betül Vatankulu¹, Yasemin Şanlı², Esra Kaytan Sağlam³, Serkan Kuyumcu², Zeynep Güzde Özkan², Ebru Yılmaz², Sevim Puriso⁴, İşık Adalet²

¹Istanbul University Cerrahpaşa Faculty of Medicine, Department of Nuclear Medicine, İstanbul, Turkey
²Istanbul University İstanbul Faculty of Medicine, Department of Nuclear Medicine, İstanbul, Turkey
³Istanbul University Istanbul Faculty of Medicine, Department of Radiation Oncology, Istanbul, Turkey
⁴Istanbul University Istanbul Faculty of Medicine, Department of Biostatistics, İstanbul, Turkey

Abstract

**Objective:** We aimed to investigate the $SUD_{\text{max}}$ of primary tumor and metastatic lymph node in predicting survival in patients with esophageal cancer.

**Methods:** We retrospectively analyzed patients with esophageal cancer between 2009 and 2011 who had FDG positron-emission tomography (PET)/computed tomography (CT). All patients were followed-up to 2013. Clinical staging, $SUD_{\text{max}}$ of primary tumor and metastatic lymph node were evaluated.

**Results:** One hundred seven patients were included in the study. All patients were followed-up between 2 and 49 months. The mean $SUD_{\text{max}}$ of primary tumor and metastatic lymph node were 19.3±8.8 and 10.4±9.1, respectively. Metastatic lymph node $SUD_{\text{max}}$ had an effect in predicting survival whereas primary tumor $SUD_{\text{max}}$ did not have an effect ($p=0.014$ and $p=0.262$, respectively). Multivariate Cox regression analysis showed that clinical stage of the disease was the only independent factor predicting survival ($p<0.001$).

**Conclusion:** Among patients with esophageal cancer, the value of primary tumor $SUD_{\text{max}}$ did not have an effect on survival. Clinical stage assessed with FDG PET/CT imaging was found to predict survival in esophageal carcinoma. Additionally, lymph node $SUD_{\text{max}}$ was identified as a new parameter in predicting survival in the present study.

**Keywords:** Esophageal cancer, FDG positron-emission tomography/computed tomography, survival, lymph node, $SUD_{\text{max}}$

Öz

**Amaç:** Çalışmamızda özofagus kanserli hastalarda primer tümör $SUD_{\text{max}}$ ve metastatik lenf nodu $SUD_{\text{max}}$’ın sağ kalım üzerine olan etkisini araştırmayı amaçladık.

**Yöntem:** 2009 ve 2011 yılları arasında evreleme amacıyla FDG pozitron emisyon tomografisi (PET)/bilgisayarlı tomografi (BT) yapılan özofagus kanser tanılı hastalar retrospektif olarak incelendi. Tüm hastalar Eylül 2013 yılına kadar takip edildi. Histopatoloji, lokalizasyon, klinik evre, primer tümör ve metastatik $SUD_{\text{max}}$ kaydedildi. Tanımlanan parametreler arasındaki ilişkiler ve sağ kalımda univaryant ve multivaryant Cox regresyon analizi ile değerlendirildi.

**Bulgular:** Çalışmaya 107 hasta dahil edildi. Hastaların hepsi 2,49 ay arasında takip edildi. Primer tümör ve metastatik lenf nodu ortalamasına $SUD_{\text{max}}$ sırasıyla 19,3±8,8 ve 10,4±9,1 olarak hesaplandı. Metastatik lenf nodu $SUD_{\text{max}}$ sağ kalım üzerine

Address for Correspondence: Betül Vatankulu MD, Istanbul University Cerrahpaşa Faculty of Medicine, Department of Nuclear Medicine, İstanbul, Turkey
Phone: +90 212 414 20 00 E-mail: bvatankulu@gmail.com Received: 21.06.2015 Accepted: 04.09.2015

Molecular Imaging and Radionuclide Therapy, published by Galenos Publishing.
Introduction
Esophageal cancer constitutes 1.5-2% of all cancers and 5-7% of those in the gastrointestinal tract. It is one of the most lethal of all cancers, and is known to be aggressive, showing significant progression in early stages via metastasis. Long-term survival is low, despite appropriate treatment. The assessment of survival in advance plays an important role in the treatment of the disease (1,2,3,4).

Although the significance of positron-emission tomography/computed tomography (PET/CT) imaging in clinical staging is well known, numerous studies have evaluated the effect of the maximum standard uptake value (SUV max) obtained via PET/CT before surgery on survival. While some authors reported that primary tumor SUV max is associated with survival, others indicated no such association (1,2,3,4,5,6,7,8,9). However, there are no clinical studies on the effect of metastatic lymph node SUV max on survival in esophageal cancer.

The purpose of this retrospective study was to investigate the effect of primary tumor SUV max, metastatic lymph node SUV max, and clinical staging as determined by FDG PET/CT on survival in esophageal cancer.

Materials and Methods
Patients who were histopathologically diagnosed as esophageal cancer and referred to Istanbul University Faculty of Medicine Department of Nuclear Medicine PET/CT Unit for staging by FDG PET/CT imaging between May 2009 and December 2011 were retrospectively evaluated. Clinical follow-up was conducted until March 2013.

The patients were divided into two groups according to their histopathological diagnosis as patients with either squamous cell carcinoma or adenocarcinoma. Tumor localizations were categorized into five groups: cervical, upper thoracic, middle thoracic, lower thoracic, and middle + lower thoracic.

Clinical staging was performed using the tumor-node-metastasis (TNM) staging, a six-stage classification system provided by the American Joint Committee on Cancer (AJCC), after assessment of the results of CT images, endoscopy, pathology reports, and PET/CT imaging as a whole.

Positron-Emission Tomography/Computed Tomography Protocol
Patient Preparation
Patients were instructed to fast for at least 6 h before imaging. The oral anti-diabetic metformine or its derivatives were discontinued in diabetic patients 3 days before the procedure, to prevent colonic uptake. Patients using insulin were allowed to take their long-acting insulin treatment 12 h before FDG injection. Six hours before imaging, patients were administered oral contrast material to delineate the intestine.

The blood glucose level of each patient was measured and then FDG was administered by establishing vascular access for those patients with blood glucose lower than 200 mg dL\(^{-1}\) to prevent extravasations. The dose injected was 0.2 mCi kg\(^{-1}\) body weight F18-FDG After the injection, patients waited for 60-90 min to allow FDG to penetrate the tissues and the PET/CT was then performed.

Examination of the Images
All images obtained were examined on an LCD monitor as both attenuation-corrected and uncorrected multiplanar PET/CT fusion cross-sections (maximum intensity projection=MIP), using the eSOFT software (Siemens).

Assessment of Positron-Emission Tomography Computed Tomography Images
The lesions revealed in PET/CT scans were first evaluated visually. Each focal uptake identified in PET images was searched for in the corresponding CT sections. FDG uptakes that corresponded to the salivary gland, muscle, fatty tissue, and normal lymphoid tissue in CT cross-sections...
were accepted as physiological uptake. On the other hand, focal FDG uptakes corresponding to areas of abnormal soft tissue mass or lymph nodes in CT images were accepted as significant in terms of metastasis.

The point of concern that displayed the most intensive FDG uptake in the primary tumor region was identified and the SUV\text{max}, which is a semi-quantitative measure of FDG uptake, was determined. A SUV\text{max} value greater than 2.5 was used as a cut off for malignancy. The localization of the metastatic lymph node and the highest SUV\text{max} of patients with lymph node metastasis were recorded along with the locations of distant metastasis, if present. Distant organ metastasis and distant lymph node metastasis were identified as distant metastasis (except loco-regional lymph nodes).

**Statistical Analysis**

The normality of the data distribution was assessed with Shapiro-Wilk and one-sample Kolmogorov-Smirnov tests. Parametric data were presented as means ± standard deviation, and non-parametric data as median and minimum-maximum values. Nominal and categorical variables were presented as frequencies and percentages. The parametric distribution was compared with the Student t-test in independent groups, and with the Mann-Whitney U test in the rest. Survival was evaluated by the Kaplan-Meier method. Categorical variables were evaluated with chi-square and Fisher’s exact contingency tests. The Cox multivariate regression model was used to evaluate risk factors, which included gender, age, smoking, primary tumor SUV\text{max}, metastatic lymph node, and stage that could impact survival. The tests were two-sided. P<0.05 was accepted as significant. Statistical analysis was performed with SPSS statistical software, version 17.0 (SPSS Inc, Chicago, Illinois, USA).

**Results**

In this retrospective study, we examined data from 112 patients who underwent FDG PET/CT for staging purposes. The histopathological diagnosis of two patients was leiomyoma. Endoscopic biopsy revealed in situ squamous cell carcinoma in three patients, and no pathologic FDG uptake was identified on their PET/CT scans. The follow-up visits indicated that these patients were disease-free. Within the remaining 107 patients, 48 (44.9%) were female and 59 (55.1%) were male. The age range of patients was 28-85 (56.6±12.3) years. After FDG PET/CT imaging, the patients were monitored for a 2-49 (20.2±2.07) month follow-up period (Figure 1). Most patients had squamous cell carcinoma on histopathology evaluation (Table 1).

Our results showed that esophageal cancer occurred most frequently in the lower thoracic esophagus (45.8%), and 3.7% in the upper thoracic esophagus. In the staging evaluation, only three patients had stage 1 disease, and they were combined with the group of patients with stage 2 disease. Thus, the three staging groups consisted of stages 1-2, 3, and 4 (Table 1).
The SUV_{max} value of the primary tumor was 2–48 in all groups, with a mean of 19.3±8.8. The highest SUV_{max} of metastatic lymph nodes were 2.9-60, with a mean of 10.4±9.1. Seventy patients had lymph node metastases. Lymph node metastases were classified as cervical, thoracic or abdominal, according to their localization. Metastases were detected most frequently in the thoracic area (43%), and least frequently in the cervical area (20.6%). Distant metastasis was present in 31.8% of the patients. Most of these metastases were located in the distant lymph nodes (18.7%) or adrenal gland (2.8%).

There was no significant correlation between tumor localization and survival, tumor localization and primary tumor SUV_{max}, or tumor localization and metastatic lymph node SUV_{max} (p=0.584, p=0.642, and p=0.632, respectively). Tumor localization was a neutral factor with respect to survival.

There was no significant association between the histopathology of the tumor and the primary tumor or metastatic lymph node SUV_{max}. The histopathology of the tumor did not appear to have an effect on survival (Table 2).

Figure 2 shows the correlation between tumor stage and SUV_{max} of the primary tumor. As the tumor stage increased, the SUV_{max} of the primary tumor increased linearly. This increase was more significant in stage 4 patients than in stages 1-2 patients (with p=0.025). The SUV_{max} of the primary tumor was 15.5±7.6 for stages 1-2, 20.3±9.1 for stage 3, and 21.3±8.7 for stage 4.

The mean SUV_{max} of the primary tumor was higher in patients who had died, although not statistically significant (p=0.262).

Fifty percent of the 20 surviving patients had metastatic lymph nodes. Lymph node metastasis was detected in 75% of the 51 patients who died (p=0.003). The metastatic lymph node SUV_{max} were higher in patients who died as compared to those who survived [9 (3.1-60) vs. 5.1 (2.9-25.1), p=0.014]. When patients were grouped according to lymph node SUV_{max} value, patients with higher lymph node SUV_{max} had poorer outcomes. Furthermore, according to the ROC curve analysis, we identified that lymph node SUV_{max} value of 14.2 had a 80.8% sensitivity and 90% specificity for survival rate (p=0.017).

In terms of the correlation between distant metastasis and survival, four of the surviving patients (10%) had distant metastasis. Distant metastasis was also evident in 30 of the patients who died (45%), and its effect on survival was determined to be significant (p=0.001). Our results indicated that lymph node metastases and distant metastases to the liver were related to survival (p=0.005 and p=0.04, respectively).

Cox univariate and multivariate regression analyses were performed for the factors that could impact survival, which included gender, age, smoking, primary tumor SUV_{max}, metastatic lymph node SUV_{max}, the number of metastatic lymph nodes and tumor stage. Lymph node metastasis, lymph node SUV_{max}, and stage were determined to be significant in univariate analyses (p=0.04, p=0.014, and p=0.001, respectively).

![Figure 2](image)

**Table 2. Correlation between localization, histopathological type, SUV_{max} and survival rate**

| Localization (n, %)      | Adenocarcinoma (n=19) | Squamous cell carcinoma (n=88) | p-value |
|--------------------------|-----------------------|--------------------------------|---------|
| Cervical                 | 0                     | 16 (18.2)                      |         |
| Upper thoracic           | 0                     | 5 (5.7)                        |         |
| Mid thoracic             | 0                     | 28 (31.8)                      | 0.001   |
| Lower thoracic           | 17 (89.5)             | 32 (36.4)                      |         |
| Mid+lower thoracic       | 2 (10.5)              | 7 (8)                          |         |
| SUV_{max} of primary tumor (mean ± SD) | 17.9±6.2   | 19.6±9.3                       | 0.435   |
| SUV_{max} of metastatic lymph nodes (mean ± SD) | 10.9±6.9   | 10.3±9.6                       | 0.822   |
| Survival rate (n, %)     | 7 (36.8)              | 33 (37.5)                      | 0.957   |

SD: Standard deviation
respectively). However, multivariate analysis determined that disease stage was the only independent variable associated with survival, which was notably significant in stages 3 and 4 (p=0.001). Compared with stage 1-2, stage 3 was associated with a 4.6-fold greater risk, and stage 4, an 8.2-fold greater risk mortality. The chi-square test indicated that the correlation between survival and cancer stage was significant (p=0.001) (Table 3) (Figure 3).

Discussion

Our findings suggest that the SUV\textsubscript{max} of the primary tumor as determined by FDG PET/CT imaging that is used for staging patients with esophageal cancer is not predictive of survival. Our results indicated that the staging system currently used in clinical practice is effective regarding the survival of patients with esophageal cancer. Additionally, the lymph node SUV\textsubscript{max} of patients with lymph node and distant metastasis had predictive value with regard to survival.

Esophageal cancer is aggressive and progresses rapidly in early stages via metastasis; thus, the long-term survival rate is low despite appropriate treatment (10). A review of the literature indicates a 5-year survival rate of 12% (11). Hong et al. (12) showed that patients followed-up for 5-25 months survived for a mean of 17.3 months. In another study, the mean survival was reported as 15.7 months over a 24-52-month follow-up period (6). In our study, patients followed-up for 2-49 months after FDG PET/CT staging survived for 20.2 months, in line with previous findings.

In many studies, squamous cell-type esophageal cancer was related to poor prognosis (5,13); however, several studies reported that histopathologic type was not related to prognosis (4,6,14,15). In these studies, high SUV\textsubscript{max} were attributed to increased Glut-1 expression (5,13). In our study, although the SUV\textsubscript{max} were generally high, we observed that there was no difference according to histopathologic types. Moreover, histopathologic type was not associated with survival in our study; however, the squamous cell carcinoma subtype was over-represented in our patients.

Assessment of survival in advance plays an important role in the treatment of the disease (16). Classical staging has been shown to be associated with survival, and tumor tissue should be excised either surgically or by other methods, such as endoscopic.

In clinical practice, there is a need for less invasive and more accessible techniques to determine prognosis. The most frequently used approach is FDG PET/CT imaging. FDG PET/CT is a noninvasive imaging method used to quantify tumor metabolism and guide pre-treatment staging by identifying distant metastasis (10). The SUV\textsubscript{max} in FDG PET/CT imaging has predictive value for survival, particularly in head-neck and lung cancer patients (17,18,19). In light of this information, many recent studies have cited SUV\textsubscript{max} as an effective means of predicting survival in esophageal cancer patients (1,2,3,4,5,6,7,8,9).

Fukunaga et al. (4) and Kato et al. (5) determined that a high SUV\textsubscript{max} value in the primary tumor was more effective in determining survival of patients with esophageal cancer as compared to low SUV\textsubscript{max}. However, the most important
deficiency of these two studies was that multivariate analysis was not performed, making the significance of their findings uncertain. In a study of patients with esophageal carcinoma, the primary tumor SUV\(_{\text{max}}\) was associated with survival (9); however, most of the patients were in early stages of the disease that was assessed clinically and pathologically.

In a study of 47 patients by Hong et al., (12) the SUV\(_{\text{max}}\) was not related to survival; only the quantity of abnormal uptake on FDG PET/CT imaging appeared to have an association. We should note that in our study clinical staging was not included in survival analysis, and that there were fewer early-stage than advanced-stage patients. A study conducted by van Westreenen et al. (20) reported that high SUV\(_{\text{max}}\) was related with poor prognosis but not survival in patients with esophageal carcinoma. Choi et al. (2) showed that tumor volume and presence of lymph nodes displaying FDG uptake were independently associated with survival while SUV\(_{\text{max}}\) was not. In a study of 40 patients with distal esophageal cancer, the SUV\(_{\text{max}}\) of the primary tumor was not related to survival; this outcome was attributed to the histopathology, which only included adenocarcinoma (21). In all these studies, the SUV\(_{\text{max}}\) was determined to predict survival by univariate analysis, with the exception of the following two studies; using univariate analysis of survival could be the most important deficiency in these studies. Two large, multi-centered, randomized, prospective studies reported that the SUV\(_{\text{max}}\) of the primary tumor was not associated with survival (8,22). However, as these two studies only involved patients suitable for curative treatment, the debate on this issue continues. A recent study indicated that tumor volume, tumor length and total lesion glycolysis were significant prognostic factors for overall survival, but SUV\(_{\text{max}}\) was not (23). We did not evaluate PET/CT parameters such as tumor volume and total lesion glycolysis in the present study. However, our data indicated no correlation between the SUV\(_{\text{max}}\) of the primary tumor and survival, according to both univariate and multivariate analyses. The higher number of patients with advanced-stage disease as compared to early-stage patients in our study, and histopathologically, the fewer adenocarcinomas as compared to squamous cell carcinomas may have prevented identification of a correlation between survival and the SUV\(_{\text{max}}\) of the primary tumor. In those studies showing a relationship between SUV\(_{\text{max}}\) and survival, the SUV\(_{\text{max}}\) varied between 3 and 12 (4,6,7). The much higher mean SUV\(_{\text{max}}\) in our study was attributed to the high rate of squamous cell carcinoma and the high proportion of advanced-stage patients.

Another important finding of our study is that the presence of metastatic lymph node and distant metastasis are predictive of survival. The high SUV\(_{\text{max}}\) of the metastatic lymph nodes were negatively associated with survival. We found that lymph node SUV\(_{\text{max}}\) had high sensitivity and specificity for survival rate. A review of previous studies indicated that many factors have been investigated in terms of prediction of survival in patients with esophageal cancer; however, the correlation between the SUV\(_{\text{max}}\) of metastatic lymph nodes and survival is reported herein for the first time.

Cheze-Le Rest et al. (6) determined that while the existence of two or more local lymph nodes with FDG uptake affected survival, distant organ and/or lymph node uptake did not. When the methodology of this study was reviewed, it is seen that distant organ and/or lymph node metastasis was not stated separately; uptake in more than one field in FDG PET imaging was considered as distant metastasis. Many studies have reported that lymph node uptake is an independent predictive factor for survival (2,3,6,7).

In our study, consistent with these previous reports, lymph node uptake was predictive of survival as indicated by univariate analysis. Additionally, distant organ metastasis was independently negatively associated with survival. Distant organ metastasis, particularly those to the liver, had the greatest influence on survival, consistent with previous reports (24).

In many studies, pathological and clinical staging was independently associated with survival (2,3,8). However, several others have reported that clinical staging was not associated with survival (6,25). In the latter two studies, in which no relationship between staging and survival was determined, FDG PET was not used as the quantitative method and conventional methods were used for staging. In our study, consistent with the literature, pathological and clinical staging had an independent predictive value for survival in patients with advanced-stage disease. Furthermore, the SUV\(_{\text{max}}\) of the primary tumor was high in advanced stages of the disease, and this elevation was significant, particularly in stages 1-2 and stage 4.

**Limitations**

The retrospective nature of this study may be the most important limitation. The heterogeneity of the patient group, in terms of stage and histopathology, represents another limitation. Additionally, because most patients did not undergo surgery, pathological staging of these patients could not be assessed. It is well known that the false positivity and false negativity rates of lymph node SUV\(_{\text{max}}\) value are high in detecting lymph node metastasis, due to accompanying inflammatory disease and microscopic metastasis (26). In other words, lymph node SUV\(_{\text{max}}\) does not necessarily indicate a true lymph node metastasis, without confirmation by pathological evaluation. Nevertheless, in the present study, pathological assessment of lymph nodes was not performed. There were two reasons for this; first, most patients were treated without surgery due to advanced stage disease with
distant organ metastasis, and second the retrospective design of the study did not allow performing additional pathological evaluation. Another limitation of the present study was lack of follow-up of treatment regimens and treatment center of the patients. We also did not evaluate PET/CT parameters such as metabolic tumor volume and total lesion glycolysis.

Conclusion

According to our findings, the SUV max of the primary tumor did not have a predictive value in terms of survival in patients with esophageal cancer. Consistent with previous studies, the predictive value of staging by FDG PET/CT imaging in determining survival of esophageal cancers was found to be reliable, making this method feasible for clinical practice. Although the negative effect of lymph node metastasis on survival of patients with esophageal cancer is well known, the negative effect of high lymph node SUV max on survival is a new parameter, which should be considered for clinical practice.

At least two professional editors, both native speakers of English, have checked the English in this document. For a certificate, please see: http://www.textcheck.com/certificate/zfj1td.

Ethics Committee Approval: The study were approved by the Istanbul University Istanbul Medical Faculty of Local Ethics Committee, Informed Consent: Consent form was filled out by all participants, Concept: Betül Vatankulu, İlk Adalet, Design: Betül Vatankulu, İlk Adalet, Yasemin Şanlı, Data Collection or Processing: Betül Vatankulu, Serkan Kuyumcu, Ebru Yılmaz, Analysis or Interpretation: Betül Vatankulu, Sevim Purisa, Esra Kaytan Sağlam, Literature Search: Zeynep Gözde Özkan, Writing: Betül Vatankulu, Peer-review: Externally peer-reviewed, Conflict of Interest: No conflict of interest was declared by the authors, Financial Disclosure: The authors declared that this study has received no financial support.

References

1. Kato H, Kuwano H, Nakajima M, Miyazaki T, Yoshikawa M, Ojima H, Tsukada K, Onouchi N, Endo K. Comparison between positron emission tomography and computed tomography in the use of the assessment of esophageal carcinoma. Cancer 2002;94:921-928.
2. Choi JY, Jang HJ, Shim YM, Kim K, Lee KS, Lee KH, Choi Y, Choe YS, Kim BT. 18F-FDG PET in patients with esophageal squamous cell carcinoma undergoing curative surgery: prognostic implications. J Nucl Med 2004;45:1843-1850.
3. Choi JY, Jang HJ, Shim YM, Kim K, Ahn G, Lee KH, Choi Y, Choe YS, Kim BT. Prognostic significance of vascular endothelial growth factor expression and microvessel density in esophageal squamous cell carcinoma: comparison with positron emission tomography. Ann Surg Oncol 2006;13:1054-1062.
4. Fukunaga T, Okazumi S, Koide Y, Isono K, Imazeki K. Evaluation of esophageal cancers using fluorine-18-fluorodeoxyglucose PET. J Nucl Med 1998;39:1002-1007.
5. Kato H, Takita J, Miyazaki T, Nakajima M, Fukai Y, Masuda N, Fukuchi M, Manda R, Ojima H, Tsukada K, Kuwano H, Onouchi N, Endo K. Concentration of 18F-fluorodeoxyglucose (FDG) accumulation with glucose transporter (Glut-1) expression in esophageal squamous cell carcinoma. Anticancer Res 2003;23:3263-3272.
6. Cheze-Le Rest C, Metges JP, Teyton P, Jastin-Le Tallec V, Lozac'h P, Volant A, Visvikis D. Prognostic value of initial fluorodeoxyglucose-PET in esophageal cancer: a prospective study. Nucl Med Commun 2008;29:628-635.
7. Makino T, Doki Y, Miyata H, Yasuda T, Yamasaki M, Fujiiwara Y, Takiguchi S, Higuchi I, Hatazawa J, Monden M. Use of (18)F-fluorodeoxyglucose-positron emission tomography to evaluate responses to neo-adjuvant chemotherapy for primary tumor and lymph node metastasis in esophageal squamous cell carcinoma. Surgery 2008;144:793-802.
8. Omloo JM, Slooff GW, Boelard R, Hoekstra OS, Jager PL, van Dullemen HM, Fockens P, Plukker JT, van Lanschot JJ. Importance of fluorodeoxyglucose-positron emission tomography (FDG-PET) and endoscopic ultrasonography parameters in predicting survival following surgery for esophageal cancer. Endoscopy 2008;40:464-471.
9. Rizk N, Downey RJ, Akhurst T, Gonen M, Bains MS, Larson S, Rusch V. Preoperative 18F-fluorodeoxyglucose positron emission tomography standardized uptake values predict survival after esophageal adenocarcinoma resection. Ann Thorac Surg 2006;81:1076-1081.
10. Omloo JM, van Heijl M, Hoekstra OS, van Berge Henegouwen MI, van Lanschot JJ, Slooff GW. FDG-PET parameters as prognostic factor in esophageal cancer patients: a review. Ann Surg Oncol 2011;18:3338-3352.
11. Pickens A, Orringer MB. Geographical distribution and racial disparity in esophageal cancer. Ann Thorac Surg 2003;76:1367-1369.
12. Hong D, Lunagomez S, Kim EE, Lee JH, Bresalier RS, Swisher SG, Wu TT, Morris J, Liao Z, Komaki R, Ajani JA. Value of baseline positron emission tomography for predicting overall survival in patient with nonmetastatic esophageal or gastroesophageal junction carcinoma. Cancer 2005;104:1620-1626.
13. Phay JE, Hussain HB, Moley JE. Strategy for identification of novel glucose transporter family members by using internet-based genomic databases. Surgery 2000;128:946-951.
14. Brown C, Howes B, Jamieson GG, Bartholomew M, Zingg U, Sullivan TR, Thompson SK. Accuracy of PET-CT in predicting survival in patients with esophageal cancer. World J Surg 2012;36:1089-1095.
15. Menzel Ch, Döbert N, Rieker O, Kneist W, Mose S, Teising A, Junginger TR, Böttcher HD, Bartenstein P, Grünwald F. 18F-deoxyglucose PET for the staging of oesophageal cancer: influence of histopathological subtype and tumour grading. Nuklearmedizin 2003;42:90-93.
16. Hoekstra CJ, Hoekstra OS, Stroobants SG, Vansteenkiste J, Nuyts J, Smit EE, Boers M, Twisk JW, Lammersma AA. Methods to monitor response to chemotherapy in non-small cell lung cancer with 18F-FDG PET. J Nucl Med 2002;43:1304-1309.
17. Greven KM, Williams DW 3rd, McGuirt WF Sr, Harkness BA, D’Agostino RB Jr, Keyes JW Jr, Watson NE Jr. Serial positron emission tomography scans following radiation therapy of patients with head and neck cancer. Head Neck 2001;23:942-946.
18. Jadvar H, Conti PS. Diagnostic utility of FDG PET in multiple myeloma. Skeletal Radiol 2002;31:690-694.
19. Rose DM, Delbeke D, Beauchamp RD, Chapman WC, Sandler MP, Sharp KW, Richards WO, Wright JK, Fresex ME, Pinson CW, Leach SD. 18F-fluorodeoxyglucose-positron emission tomography in the management of patients with suspected pancreatic cancer. Ann Surg 1999;229:729-737.
20. 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;185:436-440.
21. Stahl A, Stoffluss J, Ott K, Wieder H, Fink U, Schwaiger M, Weber WA. FDG PET and CT in locally advanced adenocarcinomas of the distal oesophagus. Clinical relevance of a discordant PET finding. Nuklearmedizin 2005;44:249-255.
22. Chatterton BE, Ho Shon I, Baldey A, Lenzo N, Patrikeos A, Kelley B, Wong D, Ramshaw JE, Scott AM. 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;36:354-361.

23. Hatt M, Visvikis D, Albarghach NM, Tixier F, Pradier O, Cheze-le Rest C. Prognostic value of 18F-FDG PET image-based parameters in oesophageal cancer and impact of tumour delineation methodology. Eur J Nucl Med Mol Imaging 2011;38:1191-1202.

24. Quint LE, Hepburn LM, Francis IR, Whyte RI, Orringer MB. Incidence and distribution of distant metastases from newly diagnosed esophageal carcinoma. Cancer 1995;76:1120-1125.

25. Duong CP, Demetriou H, Weih L, Thompson A, Williams D, Thomas RJ, Hicks R. Significant clinical impact and prognostic stratification provided by FDG PET in the staging of oesophageal cancer. Eur J Nucl Med Mol Imaging 2006;33:759-769.

26. Perigaud C, Bridji B, Roussel JC, Sagan C, Mugniot A, Duveau D, Baron O, Despins P. Prospective preoperative mediastinal lymph node staging by integrated positron emission tomography-computerised tomography in patients with non-small-cell lung cancer. Eur J Cardithorac Surg 2009;36:731-736.