RESEARCH ARTICLE

Potential Impact of Atelectasis and Primary Tumor Glycolysis on F-18 FDG PET/CT on Survival in Lung Cancer Patients

Zekiye Hasbek[1]*, Birsen Yucel[2], Ismail Salk[3], Bulent Turgut[1], Taner Erselcan[1], Nalan Akgul Babacan[4], Turgut Kacan[5]

Abstract

Background: Atelectasis is an important prognostic factor that can cause pleuritic chest pain, coughing or dyspnea, and even may be a cause of death. In this study, we aimed to investigate the potential impact of atelectasis and PET parameters on survival and the relation between atelectasis and PET parameters. Materials and Methods: The study consisted of patients with lung cancer with or without atelectasis who underwent ^{18}F-FDG PET/CT examination before receiving any treatment. ^{18}F-FDG PET/CT derived parameters including tumor size, SUVmax, SUVmean, MTV, total lesion glycosis (TLG), SUV mean of atelectasis area, atelectasis volume, and histological and TNM stage were considered as potential prognostic factors for overall survival. Results: Fifty consecutive lung cancer patients (22 patients with atelectasis and 28 patients without atelectasis, median age of 65 years) were evaluated in the present study. There was no relationship between tumor size and presence or absence of atelectasis, nor between presence/absence of atelectasis and TLG of primary tumors. The overall one-year survival rate was 83% and median survival was 20 months (n=22) in the presence of atelectasis; the overall one-year survival rate was 65.7% (n=28) and median survival was 16 months (p=0.138) in the absence of atelectasis. With respect to PFS; the one-year survival rate of AT+ patients was 81.8% and median survival was 19 months; the one-year survival rate of AT- patients was 64.3% and median survival was 16 months (p=0.159). According to univariate analysis, MTV, TLG and tumor size were significant risk factors for PFS and OS (p<0.05). However, SUVmax was not a significant factor for PFS and OS (p>0.05). Conclusions: The present study suggested that total lesion glycolysis and metabolic tumor volume were important predictors of survival in lung cancer patients, in contrast to SUVmax. In addition, having a segmental lung atelectasis seems not to be a significant factor on survival.

Keywords: Atelectasis - lung cancer - ^{18}F-FDG - PET/CT - total lesion glycolysis

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Introduction

Lung cancer is the most common cancer in terms of incidence and mortality both in men and women in the world (Zhang et al., 2013). Clinical and pathologic staging is critical in the selection of appropriate treatment modalities. The choice of therapy, with the options including surgery, radiation therapy and chemotherapy, used alone or in combination with other treatments, is based on the tumor stage. Accurate staging subscribes both prediction of response to treatment and determines the treatment options (De Leyn et al., 2007; Abramyuk et al., 2012). Computed tomography (CT) is the most widely available and commonly used non-invasive imaging method for diagnosis and staging of patients with lung cancer. Recently, ^{18}F-FDG PET/CT (Positron Emission Tomography/Computerized Tomography) is used for initial staging in lung cancer and it is the most advanced imaging technique in the world with three-dimensional (3D) screening in identification of metabolic characterisation of tumor (Pauwels et al., 2013). PET has the potential to distinguish viable tumor and non-malignant tissue (Shyn, 2013). Maksimum Standardized Uptake Value (SUVmax) which was acquired by PET is commonly used in clinical practice as a criterion for malignancy, which is defined as ratio of activity in tissue per milliliter to the activity in the injected dose per kilogram patient body weight. A high SUV value is commonly accepted as a poor prognostic factor (Zhu et al., 2013). Due to the development of software programs, recent studies have shown that metabolic tumor volume (MTV) and total lesion glycolysis (TLG) may be useful quantitative parameters for the prognostic evaluation (Arslan et al., 2011; Liao et al., 2012; Zhang et al., 2013). Viable tumor volume could be easily estimated by those programs. These parameters could potentially

*[1]Department of Nuclear Medicine, [2]Department of Radiation Oncology, [3]Department of Radiology, [5]Department of Medical Oncology, Faculty of Medicine, Cumhuriyet University, Sivas, [4]Department of Medical Oncology, Pendik Training and Research Hospital, Marmara University, Istanbul, Turkey *For correspondence: hasbekz@yahoo.com*

have clinical value in response to treatment evaluation and disease prognostication.

Atelectasis and post-obstructive pneumonia, caused by bronchial compression or involvement, responsible for large percentage of death in lung cancer patients. Atelectasis and tumors both appear as solid dense shadows on computed tomography, so differentiation can be difficult. Differentiation between tumor and atelectasis is crucial in order to determine the area of atelectasis and the creation of appropriate size portals during radiation therapy planning (Ding et al., 2012; Yin et al., 2013). Besides, differentiation of the tumor from atelectasis is important for CT-guided biopsy. This separation is easy by PET/CT which helps also avoiding unnecessary irradiation.

In this study, we investigated the value of PET related parameters of SUVmax and TLG, together with tumor volume and tumor size for predicting of survival in lung cancer. Our aim also was to reveal the relationship between TLG of primary tumor and presence of atelectasis and its prognostic significance in patients with lung cancer.

Materials and Methods

Patients

Hospital registration of 50 consecutive patients with lung cancer (22 with atelectasis, 28 without atelectasis) were evaluated between April 2012 and September 2013 in the present study. All patients had baseline ^{18}F-FDG PET/CT scan for initial staging. Patients were divided into two groups: patients with CT features suggestive of atelectasis (AT+) and without atelectasis (AT-). Patients had other tumors before, received prior chemotherapy or radiotherapy, with no definitive histologic diagnosis, and a blood glucose level greater than 150 mg/dL were excluded from the study. The study was performed in accordance with the principles of the Declaration of Helsinki.

Clinical, histopathological and treatment data were obtained from hospital registry. Patients were staged according to the TNM system, based on the 7th edition of the American Joint Committee on Cancer (AJCC) TNM classification. Patients with early stages were treated by surgery. Patients with locally advanced stage were treated with combined concurrent chemoradiotherapy. Those with the extensive disease received chemotherapy or radiotherapy as palliative treatment. Mostly used chemotherapeutic agents were cisplatin, etoposide and taxotere.

The treatment response was evaluated every 3 months. Patients were followed with clinical and CT of thorax, abdomen and/or ^{18}F-FDG PET/CT. Overall survival (OS) was calculated from date of diagnosis to the date of either last follow-up or death. The progression-free survival (PFS) was defined as the time elapsed from the date of diagnosis to the date of first evidence of disease progression or last follow-up.

Imaging acquisitions/analysis

Positron Emission Tomography imaging was performed before the begining of any treatment and images were acquired using a combined PET/CT scanner (Discovery600 PET/CT GE Medical Systems, USA). Each patient fasted for at least 6 h before imaging. After ensuring that blood glucose was <150 mg/dl, approximately 370 MBq 18F- FDG were administered i.v. 1 h before image acquisition. Oral contrast agent was used for enhancement in the CT scan. Attenuation correction of PET images with the CT data was performed. The CT scan was performed firstly. Right after the CT acquisition, a standard PET imaging protocol was taken from the cranium to the mid-thigh with an acquisition time of 3 min/bed in 3-dimensional mode. All PET studies were acquired in 3-D mode. CT images were acquired with 70 mA, 120 kV, axial slice thickness of 3.75 mm. CT and PET images were matched and fused into transaxial, coronal and saggital images. The data were transferred via the Digital Imaging and Communications in Medicine (DICOM) protocol to a processing Workstation (AW Volume Share5 GE Medical Systems S.C.S, France). And then visual and semi-quantitative analysis were performed. Tumor and atelectasis area size (three maximum diameters) were measured. SUVmax, SUVmean and MTV were calculated from attenuation-corrected ^{18}F-FDG PET images for tumor mass. The SUVmax computed by standard methods from the activity in the most intense voxel in the three dimensional tumor region from the transaxial whole body images. SUVmean was determined from the average voxel counts within the tumor region. Automatic VOI using an isocontour threshold method was placed over the primary tumor. TLG was then calculated as: "TLG=SUVmean X MTV". And the volume of in the atelectasis area was calculated by measuring the three maximum diameters according to the ellipsoid volume formula: ($V=\pi/6\times width\times length\times thickness$).

Statistical analysis

SPSS 15.0 software was used for statistical analysis. The chi-square and frequencies test were applied to evaluate the statistical significance of the parameters. Significance levels were presented as p values. It was assumed that the observed differences were statistically significant at the $p<0.05$ levels. The median values of SUVmax, average SUV, MTV, TLG and tumor size were used as cut-offs to divide the patients into two groups. Survival outcomes were characterized using the Kaplan-Meier method, and were compared using log-rank tests. The prognostic significance of SUVmax, MTV, TLG and other clinical variables were assessed by univariate and multivariate analyses using a Cox proportional hazards regression model.

Results

Patients characteristics

A total of 50 consecutive patients were analyzed. The median age was 65 years (range: 48-81). Forty four patients (88%) were male, 6 patients (12%) were female. Eight (16%) patients were nonsmokers and 42 (84%) patients were smokers. Among these 50 patients, 31 (62%) were noted to have masses in the right lung, 19 (38%) were noted to have masses in the left lung. According to the histopathological results; 35 (70%) patients had

squamous cell carcinoma, 15 (30%) patients had adeno carcinoma. TNM classification was IA in 4 patients, IB in 7 patients, IIA in 7 patients, IIB in 4 patients, IIIA in 15 patients, IIIB in 7 patients and IV in 6 patients. Patients with distant metastatic disease in our study were regarded because of their involvement of only axillary and cervical lymph node. Demographic characteristics of patients are given in Table 1.

Complete resection was performed in 10 (20%) patients. Adjuvant chemoradiotherapies were administered to 20 (40%) patients. Radiotherapy were performed in 8 (16%) patients, chemotherapy were performed in 22 (44%) patients.

The median tumor size was 4.95 cm (range 2-11.4 cm). The median tumor volume was 33 cm3 (range: 5-377 cm3). The median tumor SUVmax was 16.9 (range: 4.4-42.9). The median tumor TLG was 372 (range: 26-3317). The median atelectasis area volume was 106 cm3 (range: 5-463) and SUVmax was 2.75 (1.4-3.8). There was no significant relation between AT+/AT- and tumor size (p=0.204). The mean TLG was 650 in AT- patients and 415 in AT+ patients. The results show that, there is no statistically significant relation between TLG and AT+ and AT- patients (p=0.186). The SUVmax in the atelectasis area was lower than tumor tissue (2.7±0.6 and 17.4±8.5, respectively) but higher than normal lung tissue (0.89±0.8) (p<0.05). When we compare the levels of SUVmax and TLG between stages, only the TLG level of stage IV patients was statistically significantly different from level of stage I patients (p=0.053).

Survival analysis

We also evaluated the relationships among different PET parameters and between primary tumor size, atelectasis volume and PET parameters. Strong positive correlation was found between TLG and primary tumor size (r=0.839, p=0.0001). There was no correlation between SUVmax and primary tumor size (r=0.221, p=0.123), between SUVmax and atelectasis volume (r=0.128, p=0.601), between TLG and atelectasis volume (r=0.371, p=0.117). Weak correlation was found between TLG and SUVmax (r=0.280, p=0.049).

The median follow-up time of all patients was 11 (1-24) months. At the time of the last follow-up visit, 37 (74%) patients were alive, and 13 (26%) patients were dead. The overall median survival, the overall 1 year survival and the progression-free one-year survival were 20 months, 73% and 71.5% for all cases respectively.

Table 1. Patient Characteristics

Patients characteristics		No.	%
Age (years)	Median	65±9	
	Range	48-81	
Gender	Male	44	88
	Female	6	12
Histology	Squamous cell carcinoma	35	70
	Adeno carcinom	15	30
Smoking status	Smoker	42	84
	Nonsmoker	8	16
Stage	I	11	22
	II	11	22
	III	22	44
	IV	6	12

Table 2. Parameters for Survival?

Parameters		N	Progressive-free survival 1-year rate (%)	Median (months)	p value	Overall survival 1-year rate (%)	Median (months)	p value
Presence of atelectasis								
Absent		28	64.3	16	0.159	65.7	16	0.138
Present		22	81.8	19		83	20	
PET parameters								
TLG	≤372	25	83.2	-	0.015*	83.6	-	0.023*
	>372	25	56.7	13		61.2	16	
MTV	≤33	25	83.7	19	0.011*	84	20	0.016*
	>33	25	52.3	13		57.1	13	
SUV max								
	≤16.9	25	87.5	-	0.071	88	-	0.087
	>16.9	25	56.8	13		60.4	16	
Tumor size (cm)								
	≤5	26	86.6	19	0.016*	87.4	20	0.017*
	>5	24	54.2	13		56.6	13	

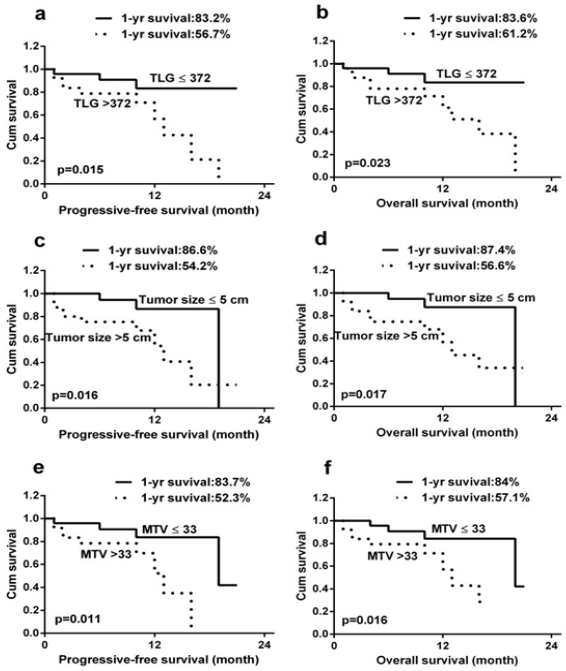

Figure 1. Kaplan-Meier Analysis of Progression Free Survival And Overall Survival for Lung Cancer Patients. a and b0 TLG ≤372 versus > 372; c and d) tumor size ≤ 5 cm versus > 5 cm; and e and f) MTV ≤ 33mL versus > 33 mL

The overall one-year survival rate of 22 patients with presence of atelectasis was 83% and the median survival was 20 months; the overall one-year survival rate of 28 patients with absent of atelectasis was 65.7% and the median survival was 16 months (p=0.138). With respect to PFS; the one-year survival rate of with AT+ patients was 81.8% and median survival was 19 months; the one-year survival rate of with AT- patients was 64.3% and median survival was 16 months (p=0.159). Table 2 demonstrates the univariate analysis of patients.

According to univariate analysis, MTV, TLG and tumor size were significant risk factors for PFS and OS (p<0.05) (Figure 1). However, as it can be seen in Table 2 SUVmax was not a significant factor the univariate analysis of patients.

All of the variables that were significantly associated

with PFS or OS in the univariate analysis, including the PET parameters were entered into the multivariate Cox model. But important independent risk factor could not be determined in multivariate analysis.

Discussion

Atelectasis can be developed with both benign and malignant etiology. However, most of atelectasis are malignant origin. Benign obstructive lesions showed lower FDG uptake than malignant obstructions (Cho et al., 2011). Sahin et al. (2011) found that the rate of hilar fullness, consolidation and atelectasis were higher in SCLC and epidermoid carcinoma with radiological examination. Similar to our study, FDG uptake in the atelectasis area is higher than in normal lung parenchyma, and generally lower than in tumor tissue (Gerbaudo and Julius, 2007). It could be related to the hypoxia in collapsed lung parenchyma. Because hypoxia induces an adaptive response of increasing cellular glucose uptake. Proximal tumors in the airway frequentlty lead to bronchial obstruction with atelectasis.

Atelectasis is an important prognostic factor that can be cause pleuritic chest pain, cough or dyspnea even may cause death. Chen et al. (2010) reported that, tumor-associated atelectasis had no influence upon survival of superficial endobronchial lung cancer patients. Solely, according to Bulbul et al. (2010) and Dediu et al. (2009) atelectasis was associated with prolonged survival in locally advanced NSCLC and it might be related to decreased intratumoral blood flow and nutrition due to shunts in the neighboring atelectatic area (Bulbul et al., 2005). Ou et al. (2008) reported that, visceral pleura invasion, hilar atelectasis, or obstructive pneumonitis in Stage IB non-small cell lung cancer is dependent on tumor size. They found that, the 5-year survival rate and the median survival time of Stage IB patients with tumors ≤3 cm in size were similar to the patients with Stage IA NSCLC. It makes tumor T3 to be existed obstructive atelectasis of the entire lung. Whereas, if the tumor which extends to the hilar region is associated with atelectasis or obstructive pneumonitis but does not involve the entire lung, that tumor is T2 (AJCC). In our preliminary study, atelectasis was the type of post-obstructive, however it was not involving the entire lung except one patient. Although not statistically significant, we were found that, atelectasis associated with prolonged survival in our study (PFS; AT+: 19 months, AT-:16 months and OS; AT+:20 months, AT-:b16 months). There was no significant relation between AT+/AT- and tumor size (p=0.204). However, according to univariate analysis, tumor size were significant risk factors for PFS and OS.

^{18}F-FDG PET/CT can improve the accuracy of the clinical stage and provides the basis for patients to choose the correct treatment approach, assessment of treatment response as a prognostic factor. PET/CT may improve evaluation of tumor by combining both anatomic information and functional information. Mutlu et al. [18] reported that, staging with PET/CT has better results in terms of survival staging. Some studies have reported that tumor SUVmax was a significant prognostic factor in the survival analysis and high SUV are generally more aggressive and have a poorer prognosis (Billè et al., 2013).

Metabolic tumor volume or total lesion glycolysis may provide additional valuable information with regards to prognostic value as well as the treatment response monitoring. Several studies suggested that, there may not be a distinct relation between poor prognosis of tumor and SUVmax, and because of the tumor heterogenity, SUVmax may not reflect tumor prognosis completely in some tumors (Moon et al., 2013; Abd El-Hafez et al., 2013). Because the SUVmax can depend upon partial volume effect, body composition, lenght of uptake period, level of plasma glucose or mixed effect. Whereas, TLG is less affected by the performance of the camera and it combines the volumetric and metabolic information (Obara et al., 2013). Lee et al. (2007) reported in their study that, semi-automatically measured total body MTV is better than SUVmax and SUVmean for prediction of prognosis in 18 NSCLC and 1 SCC patients. Similarly, Liao et al. (2012) demonstrated that TLG and MTV is a better predictor of survival than SUVmax and SUVmean. Some investigations have been suggested that TLG is a better prognostic indicator than SUVmax in some tumors as nasopharyngeal cancer, oesophageal cancer, endometrium cancer (Roedl et al., 2008; Cheng et al., 2012; Liu et al., 2012; Abd El-Hafez et al., 2013). Zaizen et al. (2012) reported that, TLG may be more useful than SUVmean and SUVmax for predicting PFS and OS in NSCLC patients receiving chemotherapy.

In the present study, we found which of the TLG could be useful for predicting PFS or OS in with or without atelectasis lung cancer patients. Also, our results suggested that over 373 TLG of tumor can be used as the cut-off point for patient risk stratification. Also, we found that, MTV >33 mL was a significant risk factor for the PFS and OS of the lung cancer. However, SUVmax was not significant for PFS and OS. So, we think that, metabolic tumor burden plays a more important role in survival than SUVmax which shows glucose metabolism rate.

Our study has some limitations. Firstly the number of patients was small and follow-up period was short. Another potential limitation is that, treatment protocols, TNM staging, histological sub-group were heterogenous in this study. For this reason, this study should require evaluation in large-scale prospective studies for the optimal cut-off values.

In conclusion, our preliminary study showed that, total lesion glycolysis and metabolic tumor volume are more important predictors of survival than SUVmax in lung cancer patient. Survival was not different in patients with atelectasis and without atelectasis, and there was not relationship between tumor size and presence or absent of atelectasis. Also, we found that, there are no relationship between presence/absence of atelectasis and TLG of primary tumor.

References

Abd El-Hafez YG, Moustafa HM, Khalil HF, et al (2013). Total lesion glycolysis: a possible new prognostic parameter in oral cavity squamous cell carcinoma. *Oral Oncol*, **49**, 261-8.

Abramyuk A, Appold S, Zöphel K, et al (2012). Quantitative modifications of TNM staging, clinical staging and therapeutic intent by FDG-PET/CT in patients with non-small cell lung cancer scheduled for radiotherapy-a retrospective study. *Lung Cancer*, **78**, 148-52.

Arslan N, Tuncel M, Kuzhan O, et al (2011). Evaluation of outcome prediction and disease extension by quantitative 2-deoxy-2[18F] fluoro-D-glucose with positron emission tomography in patients with small cell lung cancer. *Ann Nucl Med*, **25**, 406-13.

Billè A, Okiror L, Skanjeti A, et al (2013). The prognostic significance of maximum standardized uptake value of primary tumor in surgically treated non-small-cell lung cancer patients: analysis of 413 cases. *Clin Lung Cancer*, **14**, 149-56.

Bulbul Y, Oztuna F, Topbas M, Ozlu T (2005). Survival analyses of patients with thoracic complications secondary to bronchial carcinoma at the time of diagnosis. *Respiration*, **72**, 388-94.

Bulbul Y, Eris B, Orem A, et al (2010). Pulmonary atelectasis and survival in advanced non-small cell lung carcinoma. *Ups J Med Sci*, **115**, 176-80.

Chen C, Zheng H, Gao W, et al (2010). Prognosis and staging of superficial endobronchial lung cancer: the impact of invasion depth, tumor diameter, and coexistent pneumonitis or atelectasis. *Chin Med J*, **123**, 1505-9.

Cheng NM, Chang JT, Huang CG, et al (2012). Prognostic value of pretreatment ^{18}F-FDG PET/CT and human papillomavirus type 16 testing in locally advanced oropharyngeal squamous cell carcinoma. *Eur J Nucl Med Mol Imaging*, **39**, 1673-84.

Cho A, Hur J, Kang WJ, et al (2011). Usefulness of FDG PET/CT in determining benign from malignant endobronchial obstruction. *Eur Radiol*, **21**, 1077-87.

Dediu M, Crisan E, Radut M, et al (2009). The favorable prognostic significance of atelectasis in patients with advanced non-small cell lung cancer: results of a prospective observational study. *Lung Cancer*, **63**, 271-6.

De Leyn P, Lardinois D, Van Schil PE, et al (2007). ESTS guidelines for preoperative lymph node staging for non-small cell lung cancer. *Eur J Cardiothor Surg*, **32**, 1-8.

Ding XP, Zhang J, Li BS, et al (2012). Feasibility of shrinking field radiation therapy through ^{18}F-FDG PET/CT after 40 Gy for stage III non-small cell lung cancers. *Asian Pac J Cancer Prev*, **13**, 319-23.

Gerbaudo VH, Julius B (2007). Anatomo-metabolic characteristics of atelectasis in F-18 FDG-PET/CT imaging. *Eur J Radiol*, **64**, 401-5.

Lee P, Weerasuriva DK, Lavori PW, et al (2007). Metabolic tumor burden predicts for disease progression and death in lung cancer. *Int J Radiat Oncol Biol Phys*, **69**, 328-33.

Liao S, Penney BC, Zhang H, et al (2012). Prognostic value of the quantitative metabolic volumetric measurement on ^{18}F-FDG PET/CT in stage IV nonsurgical small-cell lung cancer. *Acad Radiol*, **19**, 69-77.

Liu FY, Chao A, Lai CH, et al (2012). Metabolic tumor volume by ^{18}F-FDG PET/CT is prognostic for stage IVB endometrial carcinoma. *Gynecol Oncol*, **125**, 566-71.

Moon SH, Choi JY, Lee HJ, et al (2013). Prognostic value of 18F- FDG PET/CT in patients with squamous cell carcinoma of the tonsil: comparisons of volume-based metabolic parameters. *Head Neck*, **35**, 15-22.

Mutlu H, Buyukcelik A, Erden A, et al (2013). Staging with PET-CT in patients with locally advanced non small cell lung cancer is superior to conventional staging methods in terms of survival. *Asian Pac J Cancer Prev*, **14**, 3743-6.

Obara P, Pu Y (2013). Prognostic value of metabolic tumor burden in lung cancer. *Chin J Cancer Res*, **25**, 615-22.

Ou SH, Zell JA, Ziogas A, Anton-Culver H (2008). Prognostic significance of the non-size-based AJCC T2 descriptors: visceral pleura invasion, hilar atelectasis, or obstructive pneumonitis in stage IB non-small cell lung cancer is dependent on tumor size. *Chest*, **133**, 662-9.

Pauwels EK, Coumou AW, Kostkiewicz M, Kairemo K (2013). [F]Fluro-2-Deoxy-D-Glucose positron emission tomography/computed tomography imaging in oncology: initial staging and evaluation of cancer therapy. *Med Princ Pract*, **22**, 427-37.

Roedl JB, Colen RR, Holalkere NS, et al (2008). Adenocarcinomas of the esophagus: response to chemoradiotherapy is associated with decrease of metabolic tumor volume as measured on PET-CT. Comparison to histopathologic and clinical response evaluation. *Radiother Oncol*, **89**, 278-86.

Sahin F, Yıldız P (2011). Radiological, bronchoscopic and histopathologic characteristics of patients with primary lung cancer in Turkey (2006-2009). *Asian Pac J Cancer Prev*, **12**, 1947-52.

Shyn PB (2013). Interventional positron emission tomography/computed tomography: state-of-the-art. *Tech Vasc Interv Radiol*, **6**, 182-90.

Yin LJ, Yu XB, Ren YG, et al (2013). Utilization of PET-CT in target volume delineation for three-dimensional conformal radiotherapy in patients with non-small cell lung cancer and atelectasis. *Multidiscip Respir Med*, **8**, 21.

Zaizen Y, Azuma K, Kurata S, et al (2012). Prognostic significance of total lesion glycolysis in patients with advanced non-small cell lung cancer receiving chemotherapy. *Eur J Radiol*, **81**, 4179-84.

Zhang H, Wroblewski K, Appelbaum D, Pu Y (2013). Independent Prognostic Value of Whole-body Metabolic Tumor Burden from FDG-PET in Non-Small Cell Lung Cancer. *Int J Comput Assist Radiol Surg*, **8**, 181-91.

Zhu SH, Zhang Y, Yu YH, et al (2013). FDG PET-CT in non-small cell lung cancer: relationship between primary tumor FDG uptake and extensional or metastatic potential. *Asian Pac J Cancer Prev*, **14**, 2925-9.