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RESEARCH ARTICLE / ÖZGÜN ARAŞTIRMA

Comparison of Malign Pleural Mesothelioma F-18 Fluorodeoxy Glucose Positron Emission Tomography/ Computed Tomography, Computed Tomography and Teknetium-99m Aerosol Scintigraphy Findings

Malign Plevral Mezotelyoma F-18 FDG PET/BT, BT ve Teknesyum-99m Aerosol Sintigrafisi Bulgularının Karşılaştırılması

[1]Nurşin AGÜLOĞLU
[2]Halil KAYA

[1]Department of Nuclear Medicine, İzmir University of Health Sciences, Dr. Suat Seren Chest Diseases and Surgery Training and Research Hospital, İzmir, Turkey

[2]Department of Nuclear Medicine, İstanbul Aydın University, İstanbul, Turkey

ORCID ID
NA : 0000-0003-3976-2064
HK : 0000-0003-3995-551X

ABSTRACT

Objective: The aim of this study was to examine the relationship between the standard uptake value $(SUV)_{max}$ value obtained from fluorodeoxy glucose positron emission tomography/computed tomography (PET/CT) and the capillary epithelial permeability (CEP) value calculated by diethylenetriamine pentacetic acid (DTPA) aerosol scintigraphy in patients with malignant pleural mesothelioma (MPM).

Material and Methods: Twenty-two MPM diagnosed patients who underwent PET/CT imaging were included in this study. In MPM patients Tc-99m DTPA Aerosol Scintigraphy was performed to determine parenchymal damage. MPM involvement localizations were divided into three areas as upper, middle, and lower. The relationship between tumorSUV_{max}/liverSUV_{max} (SUV_{ratio}), pleural thickening values, and CEP values of each area was examined.

Results: In all areas, a positive correlation was found between SUV_{ratio} and pleural thickening values ($p<0.001$), and a negative correlation was found between SUV_{ratio} and CEP values ($p<0.001$). Furthermore, a negative correlation was found between pleural thickness and CEP values in all 3 areas ($p<0.001$).

Conclusion: In our study, a negative correlation was observed between CEP values and both SUV_{ratio} and the size of pleural thickness. These findings suggest that decreased CEP values may provide information about prognosis.

Keywords: DTPA aerosol scintigraphy, F-18 FDG PET/BT, malignant pleural mesothelioma.

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Correspondence author (Sorumlu yazar): Nurşin AGÜLOĞLU, MD. İzmir Sağlık Bilimleri Üniversitesi, Dr. Suat Seren Göğüs Hastalıkları ve Cerrahisi Eğitim ve Araştırma Hastanesi, Nükleer Tıp Bölümü, İzmir, Turkey.
Tel: +90 232 433 33 33 **e-mail:** aguloglunursin@gmail.com

ÖZ

Amaç: Bu çalışmanın amacı, malign plevral mezotelyoma hastalarında F-18 floro-deoksiglikoz (FDG) pozitron emisyon tomografi/bilgisayarlı tomografi (PET/BT)'den elde edilen SUV_{max} değeri ile DTPA aerosol sintigrafisiyle hesaplanan kapiller epitelyal permeabilite değeri arasındaki ilişkiyi incelemektir.

Gereç ve Yöntemler: Bu çalışmaya, malign plevral mezotelyoma tanısı almış ve PET/BT görüntülemesi yapılmış 22 (13'ü erkek, 9'u kadın) hasta dahil edildi. Malign plevral mezotelyomalı hastalarda parankim hasarını belirlemek amacıyla teknesyum-99m DTPA aerosol sintigrafisi yapıldı. Malign plevral mezotelyoma tutulum lokalizasyonları üst, orta ve alt olmak üzere üç alana ayrılarak her alanın tümör SUV_{max}/karaciğer SUV_{max} ($SUV_{oranı}$) ile plevral kalınlaşma değerleri ve kapiller epitelyal permeabilite değerleri arasındaki ilişki Pearson korelasyon testiyle incelendi.

Bulgular: Her üç alanda $SUV_{oranı}$ ile plevral kalınlaşma değerleri arasında pozitif korelasyon ($p<0,001$), $SUV_{oranı}$ ve kapiller epitelyal permeabilite değerleri arasında negatif korelasyon saptandı ($p<0,001$). Aynı şekilde her üç alanda plevral kalınlık ve kapiller epitelyal permeabilite değerleri arasında negatif korelasyon saptandı ($p<0,001$).

Sonuç: Çalışmada, kapiller epitelyal permeabilite değerleri ile hem $SUV_{oranı}$ hem de plevral kalınlığın boyutu arasında negatif korelasyon izlendi. Azalmış kapiller epitelyal permeabilite değerlerinin prognoz ile ilgili bilgi verebileceği düşünülmektedir.

Anahtar kelimeler: DTPA aerosol sintigrafi, F-18 FDG PET/BT, malign plevral mezotelyoma.

INTRODUCTION

Malignant pleural mesothelioma (MPM) is a rare but aggressive tumor of mesothelial origin that is strongly associated with asbestos exposure.[1] Patients with MPM have a poor prognosis, and the median survival is 20–29 months despite treatment with three modalities including surgery, chemotherapy, and radiotherapy.[2] Although computed tomography (CT) images are effective in localizing the regions, it is insufficient to determine the presence of pleural fibrosis after treatment and to differentiate benign and/or malignant lesions is well known.[3]

It has been reported in various studies that F-18 fluorodeoxyglucose positron emission tomography/CT (F18-FDG PET/CT) is a useful method in distinguishing whether pleural pathologies are malignant or not, and in determining the extent of tumor in malignant pathologies. In addition, it has been shown that patients with a high standard uptake value (SUV), a semi-quantitative value reflecting the FDG uptake rate of the lesions, have a worse prognosis and have a shorter life expectancy than those with low levels.[4] In many studies, it has been reported that the degree of F18-FDG uptake in the pleura and the qualitative evaluation of pleural thickening enable the differentiation of benign pleural plaques and inflammatory conditions from malignant pleural formations.[5]

Tc 99m diethylenetriamine pentacetic acid (DTPA) aerosol scintigraphy is used to show the damage in the alveolocapillary area due to asbestosis in the early period.[6] It has been shown that the Tc 99m DTPA clearance rate, which is an indicator of pulmonary epithelial membrane permeability, increases in pulmonary-epithelial membrane damage caused by various reasons. The clearance rate of Tc 99m DTPA is a sensitive indicator that determines alveolar damage in interstitial lung diseases and other lung pathologies as in asbestosis.[7]

The aim of this study was to determine the relationship between tumorSUV_{max}/liverSUV_{max} (SUV_{ratio}) values calculated with F-18 FDG PET-CT and pleural thickness size and capillary epithelial permeability (CEP) values in patients diagnosed with MPM due to asbestos exposure.

MATERIAL AND METHODS

Patients

Twenty-two histopathologically MPM diagnosed patients with PET/CT imaging were included in this study. Patients with MPM were evaluated for PET/CT uptake and staged according to the International Mesothelioma Interest Group (IMIG) system. Stage 1-2 patients were taken as the first group and Stage 3-4 patients as the second group. Demographic and clinical information of all patients were evaluated retrospectively. Patients with pleural effusion were excluded from the study. DTPA Aerosol Scintigraphy was performed to determine parenchymal damage in patients with MPM who underwent PET/CT imaging.

The size of the pleural thickening area in the diseased hemithorax on PET/CT in MPM patients was measured in centimeters (cm). The SUV_{max} value of the same region was calculated. Standard values were obtained by proportioning SUV_{max} values with liver SUV_{max}. The relationship between pleural thickening size and SUV_{ratio} values was compared. CEP value was calculated in patients with MPM. The relationship between CEP value and pleural thickening size and

SUV_{ratio} values were compared. This study was conducted with the approval of the Dicle University Faculty of Medicine Medical Ethics Committee (Date: 27.08.2010, number: 118).

PET-CT Imaging

PET-CT examinations were performed with PET-CT device (Siemens Biograph 6 knoxville, TN) in the Nuclear Medicine Department of Diyarbakır State Hospital. Before the radiopharmaceutical injection, finger blood glucose was measured with a glucometer in well-hydrated patients who were fasting for at least 4 h before the procedure. Patients with blood glucose levels below 150 mg/dL were intravenously injected with 296–555 MBq (8-15 mCi) FDG. Following the FDG injection, the patients were rested for 60 min in a calm and comfortable environment, motionless, in order to achieve ideal tumor involvement. At the end of the waiting period, the patient was asked to empty her/his bladder, and then the patient was placed on the PET-CT scanner bed in the supine position. Transmission images were taken for 15 s with attenuation correction CT (100 mAs, 130 kV) before scanning. Then, body parts from the vertex to the upper third of the thigh were imaged sequentially with IV non-contrast low-dose CT followed by PET. The examinations of 7-8 bed positions were completed in approximately 25 min. In these images, the lung was divided into three equal areas, upper, middle and lower, and thickness size, SUV_{max}, and SUV_{ratio} values were calculated from the widest area of the pleural thickening region.

DTPA Aerosol Imaging

DTPA Aerosol Scintigraphy was performed with a Toshiba GCA 601 E serial number digital camera at Dicle University Faculty of Medicine, Department of Nuclear Medicine. In DTPA Aerosol scintigraphy, 25 mCi Tc-99m DTPA aerosol was inhaled by mouth with tidal respiration while the patient was in a sitting position with a nebulizer. Planar images were taken in the supine position under a gamma camera in a 30-min posterior projection with a 30-s/section period. By using a low-energy general purpose parallel-hole collimator, 60 images of 30 s were dynamically acquired in a 64× 64 matrix, with both lungs entering the image. From these images, the CEP values for a total of 6 areas of interest from the upper, middle, and lower parts of both lungs were calculated as the decreasing activity percentage per minute ($\%min^{-1}$).

Evaluation of Images

The right and left lungs are divided into 3 parts, upper, middle, and lower. CEP values of six areas were calculated separately. In patients with MPM, the diseased hemithorax observed on PET/CT was divided into three equal areas as upper, middle, and lower. The size of the region with the highest pleural thickening in each area was measured and SUV_{max} values were calculated. In PET/CT images, both lungs were divided into three equal areas and the region of interest (ROI) was drawn from the region of pleural thickening from the upper, middle, and lower areas. In addition, a large ROI was drawn from the homogeneous liver region (segment VIII) and the values were normalized by proportioning to each other.

The size of the pleural thickening area in the diseased hemithorax on PET/CT in MPM patients was measured in centimeters (cm). The SUV_{max} value of the same region was calculated. SUV_{max} values were proportional to liver SUV_{max} and standard values were obtained (SUV_{ratio}). The relationship between pleural thickening size and SUV_{ratio} values was compared. CEP value was calculated in patients with MPM and compared with pleural thickening size and SUV_{ratio} values.

Statistical Analysis

Analyzes were performed with SPSS software v 25.5 (IBM, NY, USA). After performing descriptive statistics, Shapiro-Wilk and Kolmogorov-Smirnov tests of normality were used to determine whether the continuous data were normally distributed. The results of these analyzes were presented as mean±standard deviation, median, and minimum-maximum values. Chi-square and Fisher's exact tests were used to compare categorical data between groups. Results were given as numbers and percentages (%). Pearson Correlation test was used to examine the relationship between continuous variables. $p<0.05$ was considered statistically significant.

RESULTS

A total of 22 patients, 13 (59%) male, and 9 (41%) female, were included in the study. The mean age of the patients with MPM was 54.6±13.2 (range 31–83 years).

MPM involvement localizations were divided into three areas as upper, middle, and lower, and SUV_{ratio} and pleural thickening values of each area were determined (Table 1). When the relationship between these two parameters was examined, a highly significant positive correlation was found between SUV_{ratio} and pleural thickening in the upper area ($r=0.733$; $p<0.001$). A moderately significant positive correlation was determined between SUV_{ratio} and pleural thickening in the midfield ($r=0.528$; $p<0.05$). A highly significant positive correlation was found between SUV_{ratio} and pleural thickening in the lower area ($r=0.753$; $p<0.001$) (Table 2).

When the relationship between SUV_{ratio} and CEP values in 3 areas of MPM involvement localizations was examined, a highly significant negative correlation was determined between SUV_{ratio} and CEP values in the upper area ($r=–0.830$; $p<0.001$). A moderately significant negative correlation was found between SUV_{ratio} and CEP values in the middle and lower areas ($r=–0.772$, $p<0.001$ and $r=–0.640$; $p<0.001$, respectively) (Table 2).

In addition, the relationship between pleural thickening values in 3 areas of MPM involvement localizations and CEP values was also examined. A high level of statistically significant negative correlation was found between pleural thickening and CEP values in all 3 areas (Upper area $r=–0.723$; $p<0.001$, middle area $r=–0.740$; $p<0.001$, lower area $r=–0.691$; $p<0.001$) (Table 2). Patients with MPM were evaluated for PET/CT uptake and staged according to the IMIG system. When the mean CEP values between the groups were compared, no statistically significant difference was found ($p>0.05$).

DISCUSSION

F-18 FDG PET/CT, which reveals the metabolic activity of the disease rather than the morphological structure, is quite successful in the differentiation of benign and malignant lesions, in the staging of

Table 1: Demographic and clinical characteristics of patients with MPM

Variable	Mean±SD	n	%
Age (years) (min-max)	54.6±13.2 (31.0–83.0)		
Gender			
Male		13	59.0
Female		9	41.0
Stage			
I-II		13	59.0
III-IV		9	41.0
SUV_{max}			
Upper area	10.2±1.9		
Middle area	10.1±1.9		
Lower area	8.4±1.0		
Pleural thickening (cm)			
Upper area	2.2±1.0		
Middle area	2.3±1.3		
Lower area	3.3±1.8		
CEP (min^{-1})			
Upper area	0.264±0.14		
Middle area	0.245±0.13		
Lower area	0.210±0.12		
SUV_{max}/Liver SUV_{max}			
Upper area	4.05±3.16		
Middle area	3.96±2.86		
Lower area	3.46±1.81		

MPM: Malignant pleural mesothelioma, SUV: Standard uptake value, CEP: Capillary epithelial permeability.

Table 2: Evaluation of the correlation between SUV_{ratio}, pleural thickening values, and CEP values according to the localization of involvement in patients with MPM

Variable	Upper area	Middle area	Lower area
SUV_{max}/liver SUV_{max} versus pleural thickening	r=0.733	r=0.528	r=0.753
	p<0.001	p=0.012	p<0.001
SUV_{max}/liver SUV_{max} versus CEP	r=–0.830	r=–0.772	r=–0.640
	p<0.001	p<0.001	p<0.001
Pleural thickening versus CEP	r=–0.723	r=-0.740	r=–0.691
	p<0.001	p<0.001	p<0.001

SUV: Standard uptake value, CEP: Capillary epithelial permeability, MPM: Malignant pleural mesothelioma.

the metabolic response to the treatment applied to MPM, and in the evaluation of its prognosis, and in the diagnosis of malignant pleural involvement.[8] The fact that MPMs have high FDG affinity mostly due to their increased glucose metabolism increases the effectiveness of FDG PET in diagnosis.[9]

Benard et al.,[10] evaluated the diagnostic significance of FDG-PET in 28 patients with MPM. They found that the SUV value of the malignant group was significantly higher than the SUV value in the benign group. They detected hypermetabolic lymph nodes in 9 of 12 patients who appeared normal on CT. They found that the sensitivity

was 92%, specificity 75%, and accuracy 89% in patients with MPM. Using semiquantitative analyzes, they concluded that in cases where the SUV value is >2.0, the discrimination between benign and malignant has 91% sensitivity, 100% specificity, and 92% accuracy. In our study, the calculated SUV_{max} value of patients with a histopathologically definite diagnosis of MPM was found to be 2.1 lowest while the highest value was 38.0. We found that the patients in our study had metabolically very high SUV_{max} values.

In our study, the thickened pleural surfaces of the disease usually showed up with moderate/high FDG accumulation in PET-CT images of our patients. Furthermore, as pleural thickening increased, SUV_{max} values in that region increased proportionally and there was a strong positive correlation between the size of pleural thickening and SUV_{ratio} values. In a study by Tessonnier et al.,[11] they reported that benign tumors have smaller sizes, low CT density, low SUV_{max}, and low SUV_{ratio}. They found that the SUV_{ratio} was the most precise parameter in distinguishing the tumor, and the sensitivity and specificity reached 100% when the tumor SUV_{ratio} was 1.8.

The National Heart, Lung and Blood Institute concluded at 1988 that the lung clearance rate of Tc-99m DTPA aerosol scintigraphy is an index of lung epithelial permeability in the evaluation of alveolar microvascular injuries of the lung. The increase in pulmonary epithelial permeability as a result of inflammation in interstitial lung disease and diseases such as pneumoconiosis increase the DTPA clearance rate. On the other hand, thickening of the alveolar epithelium reduces diffusion and decreases DTPA clearance. A normal clearance indicates the absence of inflammation in the lung. In the studies, although DTPA clearance findings are not specific to the disease, it was concluded that this method could be applicable since it could provide clinical information about alveolo-capillary permeability and parenchymal damage. DTPA lung clearance measurement is very sensitive for early diagnosis, prognosis and treatment of the disease, noninvasive, inexpensive method that can be applied in all nuclear medicine centers and has very low patient radiation exposure.[3] Studies have shown that Tc-99m DTPA has diagnostic value in the detection of minimal endothelial cell lesions.[12]

In the study of Harrison et al.,[13] CT, bronchoalveolar lavage and DTPA clearance were found to be abnormal in asymptomatic patients with normal chest X-ray. Furthermore, while CT was normal, elevated DTPA clearance and bronchoalveolar lavage helped diagnose lung disease at an early stage. In the study of Kaya et al.,[14] the CEP value in MPM patients was found to be statistically significantly lower than the control group. As a result, they concluded that pulmonary epithelial permeability is significantly reduced in MPM cases caused by contact with asbestos, and Tc-99m DTPA aerosol scintigraphy is a useful parameter in showing the extent of lesions.

The small sample size and retrospective design are the main limitations of this study. However, to our knowledge, our study contributes to the literature as it is one of the rare studies evaluating the correlation between SUV_{ratio} and CEP values in MPM patients. However, to evaluate the importance and results of this study, it is necessary to compare it with larger series studies.

Conclusion

In this study, unlike other studies, PET/CT parameters and CEP values of MPM patients were compared. In our study, a negative correlation was observed between CEP values and both the SUV_{ratio} and the size of the pleural thickness. It suggests that decreased CEP values can provide information about prognosis.

Disclosures

Ethics Committee Approval: The study was approved by The Dicle University Faculty of Medicine Medical Ethics Committee granted approval for this study (date: 27.08.2010, number: 118).

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