



doi • 10.5578/tt.67947

Tuberk Toraks 2019;67(1):8-14

Geliş Tarihi/Received: 24.09.2018 • Kabul Ediliş Tarihi/Accepted: 06.02.2019

KLİNİK ÇALIŞMA
RESEARCH ARTICLE

The F-18 FDG PET/CT and CT evaluation of pleural plaques

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Cite this article as: Koç ZP, Özcan Kara P, Balci Y, Örekici G, Bozdoğan Arpacı R, Sercan Özgür E. The F-18 FDG PET/CT and CT evaluation of pleural plaques. Tuberk Toraks 2019;67(1):8-14.

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SUMMARY

The F-18 FDG PET/CT and CT evaluation of pleural plaques

Introduction: Pleural plaques have the possibility of bearing malignancy thus investigation of this entity is important and the most important indicator of malignancy in general is fluorodeoxyglucose (FDG) accumulation in radiological appearance. However there is discrepancy between results of previous studies in the literature about this subject. The aim of this study is to analyze the standardized uptake value of pleural plaques and the cut off levels for malignancy in comparison with computed tomography (CT).

Materials and Methods: Seventy one patients were included in the study (27F, 44M; mean: 59.9 ± 13.1 years). Oncologic F-18 FDG positron emission tomography/computed tomography (PET/CT) was performed to all the subjects for a different primary tumor. Pleural plaques were identified in all patients in CT component of PET/CT examination. Contrast enhanced and nonenhanced CT images were evaluated by a Radiology Physician independently according to the gold standard pathology.

Results: The diagnostic sensitivity, specificity of CT was; 39%, 79% respectively and if the cut-off SUV_{max} level was accepted "4.8" the diagnostic sensitivity and specificity of PET was 71%, and 63% respectively.

Conclusion: According to the results and ROC curves determined in the study the cut-off level for evaluation of pleural plaques in PET examination was "4.8". The sensitivity and accuracy of PET was higher compared to CT with this cut-off value.

Key words: Pleural plaques, FDG, PET, CT

ÖZET

Plevral plakların F-18 FDG PET/CT ve CT ile değerlendirilmesi

Giriş: Plevral plakların malign olma olasılığı vardır ve bu antitenin araştırılması çok önemli olup en önemli radyolojik belirteç genel olarak florodeoksiglukoz (FDG) tutulumudur. Ancak bu konu ile ilgili daha önceki çalışmalar ve literatür bilgileri arasında uyumsuzluklar vardır. Bu çalışmanın amacı plevral plaklarda standardize tutulum değeri (SUD) ve malignite açısından kesim değerinin analizi ve bulguların bilgisayarlı tomografi (BT) ile karşılaştırılmasıdır.

Materyal ve Metod: Yetmiş bir hasta (27 K, 44 E; ortalama yaş: 59.9 ± 13.1) çalışmaya dahil edilmiştir. Onkolojik amaçlı F-18 FDG PET/BT tüm hastalara uygulanmıştır. Pozitron emisyon tomografi/bilgisayarlı tomografi (PET/BT) görüntülerinin BT kısmından elde edilen görüntülerde tanımlanan plevral plaklar bağımsız bir Radyoloji Uzmanı tarafından kontrastlı veya kontrastsız BT görüntüleri üzerinden değerlendirilmiş ve sonuçlar altın standard patoloji olmak üzere karşılaştırılmıştır.

Bulgular: Tanısal sensitivite, spesifisite BT için %39, %79 sırasıyla ve SUV_{max} için kesim değeri 4.8 kabul edildiğinde PET için %71 ve %63 sırasıyla bulunmuştur.

Sonuç: Bizim çalışmamızın sonuçlarına göre ROC eğrileri ile belirlenen plevral plaklar için malignite için en uygun kesim değeri 4.8 olarak hesaplanmıştır. Bu kesim değeri kabul edildiğinde PET/BT'nin sensitivite ve doğruluğu BT'ye göre yüksek bulunmuştur.

Anahtar kelimeler: Plevral plaklar, FDG, PET, CT

INTRODUCTION

Pleural plaques are one of the manifestations of asbestosis related pleural disease. In the end of this spectrum the patients may develop malignant mesothelioma; a rare and highly mortal malignancy. The first line imaging modality is computed tomography (CT) which can determine the extent of disease (invasion to adjacent structures; mediastinal or diaphragmatic) and accompanying parenchyma or nodal involvement. However CT or magnetic resonance (MR) imaging cannot differentiate malignant and benign pleural plaques sufficiently (1).

F-18 fluorodeoxyglucose (FDG) positron emission tomography-computed tomography (PET/CT) is a discriminative imaging modality in various types of malignant tumors. It has been investigated whether PET/CT can differentiate malignant and benign pleural disease previously and the diagnostic accuracy of this modality is documented in staging of malignant mesothelioma (2). However the FDG uptake of the pleural plaques was not considered an important determinant

previously and there is no documented and/or accepted cut-off value already for malignant/benign plaque discrimination (3).

The aim of this study is to evaluate the discriminative role of FDG uptake in pleural plaques and to determine a cut-off level for malignant plaques in comparison with CT.

MATERIALS and METHODS

Patients

The study was approved by the Institutional Research Ethics Committee. Seventy one patients were subject of this study (27F, 44M; mean: 59.9 ± 13.1 years). The patients were referred to PET/CT examination due to different kinds of malignant tumors or suspicious malignant findings (cancer of primary unknown, solitary pulmonary nodule or pleural malignancy) (Table 1). The patients were informed about the examination and informed consents were obtained. The study was conducted according to the Helsinki Declaration revised in 2010.

Table 1. The summary of the number of primary tumors of the patients included in the study

| | Lung | Pleura | CUP | SPN | Breast | Larynx | Colon | Bladder | RCC | Testis | Tongue | PC | NHL | Thymus |
|---|------|--------|-----|-----|--------|--------|-------|---------|-----|--------|--------|----|-----|--------|
| N | 26 | 16 | 6 | 5 | 4 | 3 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |

CUP: Cancer of unknown primary, SPN: Solitary pulmonary nodule, RCC: Renal cell cancer, PC: Peritoneal carcinomatosis.

FDG PET/CT Imaging

The patients were subjected to the F-18 FDG PET/CT necessarily due to an underlying malignancy (staging, restaging, and treatment response evaluation) or suspicion of a malignant disease. Approximately 10 mCi (370 mBq) F-18 FDG administrations via venous line with saline flush was performed after fasting for at least 4 hours. PET/CT imaging was performed by an integrated PET/CT scanner (GE Discovery PET/CT, 610, USA) by a two step procedure. Firstly a whole body CT scan without intravenous contrast administration with 130 kV, 50 mAs, a pitch of 1.5, a section thickness of 5 mm, and a field of view of 70 cm and just after the CT scan whole body PET imaging was performed with an acquisition time of 3 min per bed position in a three dimensional acquisition mode. In case of solitary pulmonary nodule evaluation late phase (approximately in 2nd hour) images including thorax were provided.

Image Analysis

The PET/CT images were evaluated by two experienced Nuclear Medicine physicians from axial, sagittal and coronal images with additional CT and fusion images. Additionally SUV_{max} levels of the lesions were determined by the workstation of GE. CT images obtained from the PET/CT scanner was analyzed by an experienced Radiology physician regarding the structure of the lesion (peripheral mass like or not) in an independent manner.

The results of PET/CT and CT were compared according to the gold standard pathology.

Statistical Analysis

The statistical analysis of the variables was performed by MedCalc v10.3.0 program. SUV_{max} cut-off levels was determined to identify malignancy by receiver operating curve (ROC) analysis and sensitivity and specificity of the tests according to this cut-off level was decided with 95% CI.

RESULTS

Among the 71 patients 21 were out of follow; 3 of them died during the follow up. Fifty patients with histopathological results were evaluated. The PET, BT and histopathological findings are summarized in Table 2.

Nine patients' pathology results were malignant mesothelioma two of which was determined by

Table 2. Crosstabulation of PET and CT versus pathology results

| | | Pathology | | Total |
|-------|------|-----------|------|-------|
| | | 0.00 | 1.00 | |
| PET | 0.00 | 10 | 10 | 20 |
| | 1.00 | 6 | 24 | 30 |
| Total | | 16 | 34 | 50 |
| | | Pathology | | Total |
| | | 0.00 | 1.00 | |
| CT | 0.00 | 12 | 19 | 31 |
| | 1.00 | 4 | 15 | 19 |
| Total | | 16 | 34 | 50 |

PET: Positron emission tomography, CT: Computed tomography.

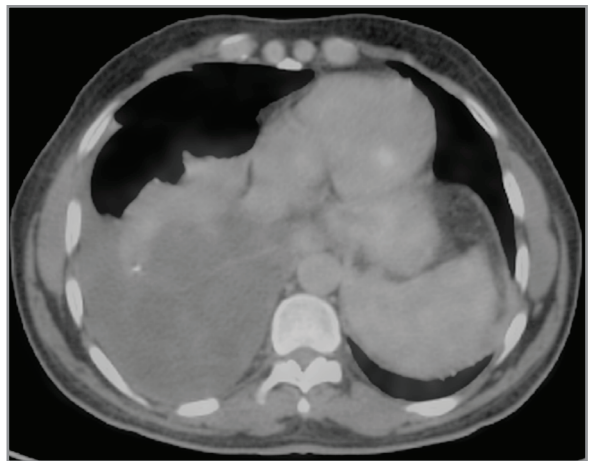


Figure 1. Transaxial fusion images from thorax region bilateral pleural plaques are observed in the base of lung with SUV_{max} level of 1.82 with additional pleural effusion which confirmed to be malignant mesothelioma pathologically.

cytology and others by blind needle or thoracoscopic biopsy. Among the patients with malignant mesothelioma diagnosis only two patients had low SUV_{max} levels (Figure 1). Fifteen patients had benign results (including tuberculosis, granulomatous inflammation, empyema, pneumonia, pleuritis). One of two patients with neuroendocrine tumors had negative PET estimation. All the remaining patients confirmed pleural invasion of another malignancy or another primary tumor (Figure 2).

The diagnostic sensitivity, specificity of CT was; 39%, 79% respectively and if the cut-off SUV_{max} level was accepted "4.8" the diagnostic sensitivity and specificity of PET was 71%, and 63% respectively (Figure 3).

The diagnostic sensitivity, specificity, accuracy, PPV and NPV of CT and PET (according to 4.8 cut-off value) are summarized in Table 3.

The mean SUV_{max} levels of the lesions with benign and malignant pathological results were significantly

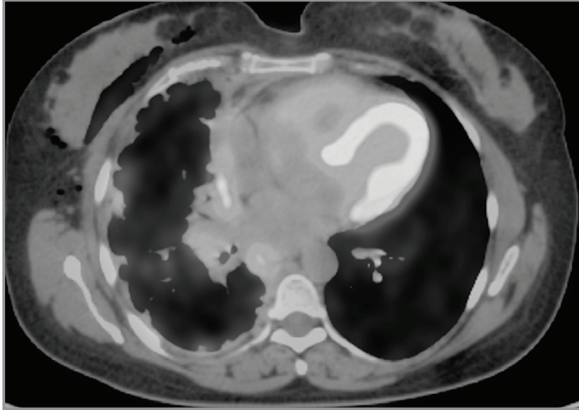


Figure 2. Transaxial fused images including thoracic region; severe pleural plaques are observed especially in paramediastinal region with high SUV_{max} levels of 9.69 which were determined as adenocarcinoma invasion in pathological analysis.

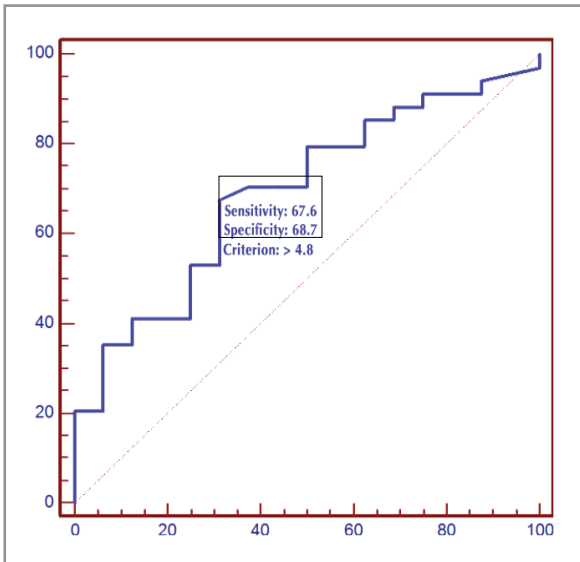


Figure 3. ROC curve of the SUV_{max} levels (y: Sensitivity, x: Specificity).

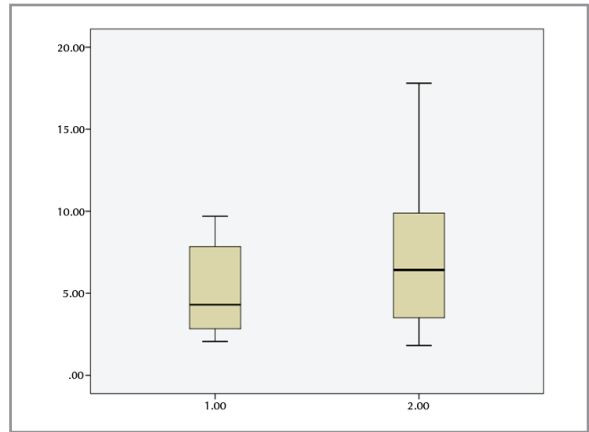


Figure 4. Graphic demonstration of the mean SUV_{max} levels of the pathologically benign and malignant lesions respectively.

different (n= 15; 5.1 ± 2.7 and n= 35; 7.1 ± 4.3 (p= 0.054) respectively) (Figure 4).

DISCUSSION

Pleural plaques need a challenging workout in order to make accurate discrimination between malignant and benign lesions. It is important to determine a cut-off value but also difficult. Since some of the malignant mesothelioma lesions may not have sufficient FDG uptake and some of the benign lesions might have significant FDG uptake and significant overlap exists between SUV_{max} levels of benign and malignant lesions. However according to our results the mean SUV_{max} levels of the benign and malignant lesions are significantly different. Additionally this study has opportunity to have pathological confirmation of pleural lesions. In this study it was not possible to provide high sensitivity or specificity levels for neither PET/CT nor CT. However it was possible to determine a cut-off level for pleural lesions to discriminate malignant and benign lesions which was “4.8”.

Kurata et al. have investigated the role of PET and osteopontin levels in asbestos related pleural disease and concluded that malignant mesothelioma has significantly higher uptake than benign asbestos related pleural disease (1). There is limited number of studies in the literature about asbestos related pleural disease in the literature (3). Kurata et al. accepted a SUV_{max}

Table 3. Criterion values and coordinates of the ROC curve

| Criterion | Sensitivity | 95% CI | Specificity | 95% CI | +LR | 95% CI | -LR | 95% CI |
|-----------|-------------|-------------|-------------|-------------|------|-----------|------|-----------|
| > 4.8 | 67.65 | 49.5 - 82.6 | 68.75 | 41.4 - 88.9 | 2.16 | 1.4 - 3.2 | 0.47 | 0.2 - 1.1 |

level of 4.1 and Orki et al. as 3.0 for determination of malignancy (1,3). However the authors stressed about the epitheloid subtype of malignant mesothelioma which is a slow growing variant of the group that has SUV_{max} levels around 2.0 (1). In this study there were two patients with similar uptake values who were decided to have malignant mesothelioma.

Unfortunately the number of patients with malignant pleural disease is increasing in recent years because of the workers who are exposed to the asbestos related products (4). Additionally there are specific regions in which their soils include asbestos and people built their houses with this material as in our country. These reasons may be related to the relative higher SUV_{max} levels in our study.

Diffuse pleural disease consists of the diffuse involvement of visceral pleura rather than parietal pleura; with significant definition on CT scan (4,5). In this study the mass like lesion in CT component of PET/CT; which was a non contrast and low dose CT study; was accepted as positive for malignancy in pleural plaques however the diagnostic accuracy of CT alone was not sufficient. Comparative studies with contrast enhanced normal dose CT imaging may be planned in the future. MR has higher sensitivity and specificity in the discrimination of benign and malignant pleural disease; 98-100% and 92-93% respectively (6). In a recent study comparing the results of FDG PET/CT and dynamic contrast enhanced MRI in the evaluation of malignant pleural mesothelioma have showed that prognostic information regarding overall survival might be predicted by SUV_{max} levels while MRI washout curve shape is related with overall survival as well (7). Another prospective study with the patients with diagnosis of unresectable malignant pleural mesothelioma showed that SUV_{max} is correlated with progression free and overall survival and chemotherapy response potential (8). The results of the study about the response evaluation of pleural mesothelioma to chemotherapy treatment have demonstrated that SUV_{max} might point out the responders (9).

Previous reports have shown a diagnostic sensitivity of 60-100%, specificity of 78-100% and accuracy of 91-98% (10,11). In a previous study in case of SUV_{max} level of 2.0 accepted as a cut-off level the sensitivity of FDG PET was 91% and specificity was 100% (12). However the SUV_{max} cut-off level of 2.5 was significantly not specific in this study. This differ-

ence may be consequences of significant number of false positive cases in our country due to benign diseases contribute to high SUV_{max} levels especially granulomatous diseases like Tuberculosis. Thus it is difficult to determine a certain cut-off level for SUV_{max} in especially countries with high number of false positive cases. However in case of presence of malignant mesothelioma it is possible to accurately stage the disease especially by showing extrathoracic involvement and provide prognostic information (13,14). Additionally in a previous study in patients with mesothelioma it has been suggested that FDG uptake in pretreatment scan was a significant predictor of survival (15).

The pleural effusion may be observed in most of the patients with mesothelioma in the disease course and may be important to discriminate malignant from benign pleural disease (16,17). In one of two patients with low uptake malignant mesothelioma in this study there was additional pleural effusion as well. In case of additional pleural effusion adjacent to the suspicious pleural lesion the careful interpretation may be necessary regardless of the uptake of the lesion. Additionally miliary diffuse disease have been reported as case reports in the literature in mesothelioma and lymphangitic disease distribution may be observed in advanced stages of the disease (17-19).

There is limited number of studies investigating the benign and malignant plaque discrimination capacity of FDG PET/CT (16). Elboga et al. investigated the malignancy potential of pleural plaques and found that PET is useful modality in discrimination of malignant and benign plaques and delayed imaging may determine benign disease by showing decreased uptake in late phase (20). There are some large series with significant number of patients in past however those studies include PET only estimation however it is important to determine recent PET/CT scanners' results. As an example talc pleurodesis is another important reason of false positive FDG uptake in pleural plaques that can be discriminated by means of correlation with CT appearance (21,22). Additionally this study has superiority of having CT scan comparison with estimation of a different observer and advantage of the same time study for PET/CT and CT.

Another important finding of this study is the high ratio of malignant disease involvement of pleura. This

may be a consequence of the population involved (including patients with different primary tumors) rather than patients who have only suspicious pleural plaques.

Limitations of this study are its retrospective structure and lack of intravenous contrast administered diagnostic CT scan results.

PET/CT might have high enough diagnostic accuracy in comparison with CT in discrimination of benign and malignant pleural plaques with careful evaluation regarding false positive causes and SUV_{max} cut-off level of "4.8".

CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: ZPK, PÖK, YB

Analysis/Interpretation: All of authors.

Data Acquisition: All of authors.

Writing: ZPK, PÖK

Critical Revision: ZPK, PÖK

Final Approval: All of authors.

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