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ORIGINAL ARTICLE

The Diagnostic Role of PET/CT in Patients with Malignant Pleural Effusion

Malign Plevral Efüzyonu Olan Hastalarda PET / BT'nin Tanıdaki Rolü

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ABSTRACT

Background: Malignant pleural effusion (MPE) is defined as the presence of malignant cells in pleural effusion (PE) or biopsy specimens and occurs in 15% of all cancer patients. The most common cause is lung cancer in men and breast cancer in women. The reason for hospital admission is usually shortness of breath. The main goal of treatment is to relieve symptoms and prevent recurrence. PET/CT is an imaging system that combines the metabolic properties of PET with the morphologic properties of computed tomography. The patient can be managed more rapidly if malignant effusion can be detected on PET/CT. In this study, we aimed to predict the diagnostic impact of metabolic uptake of fluid in patients with malignant pleural effusion.
Methods: In our study, we aimed to find the contribution of PET/CT to the diagnosis of malignant pleural effusion by examining patients between 18 and 90 years of age who had malignancy as a result of pleural cytology and who underwent PET/CT with a primary diagnosis of malignancy. 26 patients were evaluated. The values analyzed were; the presence of PE FDG uptake, the presence of single or double uptake in PE, the presence of multiple pulmonary nodules, the presence of pleural thickness (PT) increase, PT diameter, the presence of FDG uptake in PT, primary pathology being lung or other organ, PE Standardized Uptake Value (SUV) max, PE SUVmax/ Med SUVmax, PE SUVmax/ Liver SUVmax, PE SUVmax/ primary tumor SUVmax, primary tumor SUV values.
Results: 6 of 26 patients had bilateral effusions and 12 patients had FDG uptake. 5 patients had pleural thickening and 4 of them had pleural uptake. In the ROC analysis, PE SUVmax, PE SUV / Med SUV, PE SUV / Liver SUV, and PE SUV / Primary tumor SUV values were found to be significant in terms of predicting PE FDG uptake, while PT diameter was not significant.
Conclusions: Patients with MPE have a short life expectancy. Diagnosis and treatment management of patients should be performed effectively and rapidly. PET/CT can be used as a noninvasive diagnostic method for this purpose. Therefore, if further studies are performed, PET/CT in the diagnosis of MPE will contribute to patient management.

Keywords: malignant pleural effusion, PET/CT, 18F-fluorodeoxyglucose, cancer, pleural metastasis

ÖZ

Giriş: Malign plevral efüzyon (MPE) , plevral efüzyon (PE) veya biyopsi örneklerinde malign hücrelerin varlığı olarak tanımlanır ve tüm kanser hastalarının %15' inde görülür. Erkeklerde en sık sebep akciğer kanseri iken kadınlarda meme kanseridir. Hastaneye başvuru sebebi genelde nefes darlığıdır. Tedavide ana hedef semptomları ortadan kaldırmak ve tekrarlamasını önlemektir. PET/BT, PET' in metabolik özellikleri bilgisayarlı tomografinin morfolojik özelliklerini birleştiren görüntüleme sistemidir. PET/BT' de malign efüzyon tespit edilebilirse hastanın yönetimi daha hızlı yapılabilir. Biz bu çalışmada malign plevral efüzyon olan hastalarda sıvının metabolik tutulumunun tanıdaki etkisini öngörmeyi amaçladık.
Materyal-Metod: Çalışmamızda plevral sitoloji sonucu malignitesi olup primer malignite tanısı olan PET/BT çekilmiş 18-90 yaş aralığında hastaları inceleyerek malign plevral efüzyon için PET/BT'nin tanıya katkısını bulmayı amaçladık. 26 hastayı değerlendirmeye aldık. Analize tabi tutulan değerler; PE FDG tutulumu varlığı, PE'de tek ya da çift taraflı tutulum olması, çoklu pulmoner nodül varlığı, plevral kalınlık (PK) artışı varlığı, PK çapı, PK'da FDG tutulumu varlığı, primer patolojinin akciğer veya diğer organ olması, PE Standardized Uptake Value (SUV) max, PE SUVmax/ Mediastinal (med) SUVmax, PE SUVmax/ Karaciğer SUVmax, PE SUVmax/ primer tümör SUVmax, primer tümör SUV değerleridir.
Bulgular: 26 hastanın 6'sında efüzyon çift taraflıydı ve 12 hastanın efüzyonunda FDG tutulumu vardı. 5 hastada plevral kalınlaşma vardı bunların 4'ünde plevra tutulumu mevcuttu. Yapılan ROC analizinde PE FDG tutulumunu tahmin bakımından; PE SUVmax, PE SUV / Med SUV, PE SUV / Karaciğer SUV, PE SUV / Primer tümör SUV değerlerinin anlamlı olduğu, PK çapının anlamlı olmadığı görülmüştür.
Sonuç: MPE hastalarında kısa bir yaşam süresi söz konusudur. Hastaların tanı ve tedavi yönetiminin etkin ve hızlı bir şekilde yapılması gerekmektedir. PET/BT bu amaçla noninvaziv bir tanı yöntemi olarak kullanılabilir. Bu nedenle ileri çalışmaların yapılması halinde malign plevral efüzyon tanısında PET/BT' nin hasta yönetimine katkısı olacaktır.

Anahtar kelimeler: malign plevral efüzyon, PET/BT, 18F-florodeoksiglukoz, kanser, plevral metastaz

Introduction

In healthy individuals, there is 0.1-0.3 ml/kg fluid between the visceral and parietal pleura surrounding the lungs. Abnormal accumulation of this fluid, which allows the pleural leaves to move freely during respiration, can be defined as pleural effusion (PE) (1). Congestive heart failure, pulmonary embolism, pulmonary hypertension, gastrointestinal system diseases, liver diseases, renal diseases, infection, rheumatologic diseases, use of certain drugs such as amiodarone, methotrexate, different benign pathologies as well as malignancy may lead to this condition. This wide spectrum can make diagnosis and effective treatment difficult. Considering that pleural effusions have high mortality and morbidity, noninvasive methods and rapid diagnostic methods gain more importance in terms of the prognosis of the disease, especially in patients with malignant disease

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(2).

MPE is defined as the presence of malignant cells in pleural fluid or pleural biopsy specimens and occurs in 15% of all cancer patients. The most common causes include malignancies such as lung cancer, breast cancer, malignant lymphoma, ovarian cancer, and gastrointestinal cancers (3). Malignant tumors invade the pleura directly or indirectly and cause pleural effusion. It is thought that malignancy-related pleural effusions develop due to increased fluid passage into the pleural cavity and/or impaired lymphatic drainage (4). Malignant effusions have a higher recurrence rate, duration of hospitalization, and financial and emotional burden on the physician, patient, and hospital compared to other benign effusions. Therefore, early and effective diagnosis becomes more important.

Diagnostic methods in MPE include invasive procedures such as thoracentesis, pleural biopsy, thoracoscopy, and thoracotomy as well as radiologic imaging. These methods include chest radiography, computed tomography (CT), thoracic ultrasonography, thoracic magnetic resonance imaging, and positron emission tomography. Fluorine-18-fluorodeoxyglucose (18F FDG) positron emission tomography/computed tomography (PET/CT) is an integrated imaging modality that combines the metabolic properties of PET with the morphologic properties of CT and provides significant guidance (5).

If malignant effusion can be detected on PET/CT, patients can be managed more quickly and easily. The role of PET/CT in the diagnosis of MPE has not yet been fully elucidated due to significant heterogeneity and discrepancies between existing studies. In this study, we aimed to predict MPE in patients with pleural effusion based on metabolic uptake of the fluid using PET/CT.

Materials And Methods

After the approval of the local ethics committee dated 18.11.2022 and numbered 323, the data, PET/CT images, and pathology parameters of 26 patients in the digital archive of our hospital were retrospectively analyzed. Patients between the ages of 18-90 years with effusion and malignancy who could be evaluated in our study and who underwent PET-CT were included. Patients younger than 18 years and older than 90 years with no pleural cytology results and patients with benign cytology results were excluded from the study. Values subjected to analysis were the presence of PE FDG uptake, the presence of single or double uptake in PE, presence of multiple pulmonary nodules, presence of pleural thickness (PT) increase, PT diameter, presence of FDG uptake in PT, primary pathology being lung or other organ, PE Standardized Uptake Value (SUV) max, PE SUVmax/ Med SUVmax, PE SUVmax/ Liver SUVmax, PE SUVmax/ primary tumor SUVmax, primary tumor SUV values.

18F FDG PET/CT images were acquired with a Philips GEMINI TF PET/CT scanner with TOF imaging (Philips Medical Systems, Cleveland, Ohio, USA) and a 64-slice CT scanner. 18F FDG uptake in pleural effusion was evaluated. SUVmax was calculated if uptake was present. Mediastinum (aortic arch), liver, and primary tumor basal FDG uptake values were recorded as SUVmax. A quantitative value was then obtained by dividing the pleural fluid FDG uptake rate by the mediastinum, liver, and primary tumor uptake rates, respectively. In patients with pleural effusion, we drew a region of interest (ROI) of 1 cm3 and looked for FDG uptake in this area. While doing this, we ensured no hypermetabolic lesion or pleural focus in the neighborhood. We also tried to get maximum ROI in patients with effusion smaller than 1 cm3.

Statistical analyses were performed using the IBM SPSS Statistics 25 software program. Compliance of the parameters with normal distribution was evaluated by Kolmogorov-Smirnov test. One Way Anova test was used to compare quantitative data for normally distributed parameters and Mann-Whitney U-test was used to compare non-normally distributed parameters. The chi-square test was used to compare quantitative data. $P < 0.05$ was accepted to indicate statistical significance.

Reslts

Sixteen of our patients were female and ten were male. Approximately 46% of our patients had 18F-FDG uptake in PE (Figure 1,2) and 77% had unilateral effusion. When we examined the pleura, approximately 20% of the patients had increased PT, while 15% had 18F-FDG uptake in PT. The diagnosis of 5 patients was made by thoracoscopy, the others were confirmed by cytologic examination of thoracentesis fluid. The primary malignancy diagnoses of the patients were as follows: 9 lung adenocarcinoma, 2 mesothelioma, 2 small cell lung cancer, 2 breast cancer, 1 bladder cancer, 1 malignant mesenchymal tumor, 2 plasma cell myeloma, 2 lymphoma, 1 renal cell cancer, 2 ovarian cancer, 1 colon adenocarcinoma, 1 mixed

müllerian tumor. PE SUVmax, PE SUVmax/ Med SUV, PE SUVmax/ Liver SUVmax, and PE SUVmax/ primary tumor SUVmax values were correlated with each other as expected. No correlation was observed between PT diameter and SUVmax values (p>0.05).

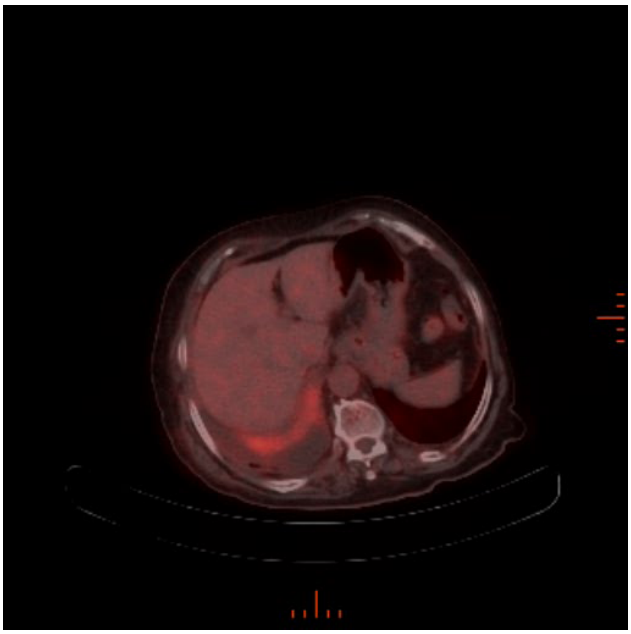

Figure 1. ROC analysis graph

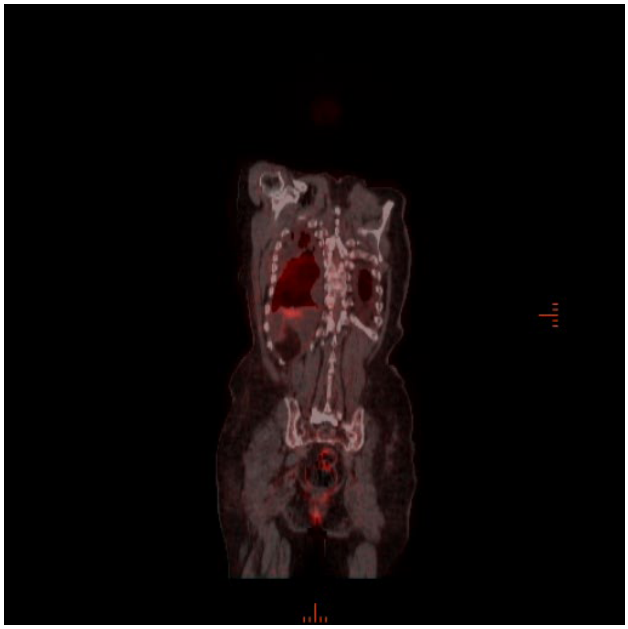

Figure 2. Axial cross-sectional PET/CT image of a patient with high SUV uptake in pleural effusion.

The presence of PE FDG uptake was correlated with higher SUVmax values (PE SUVmax, PE SUVmax/ Med SUV, PE SUVmax/ Liver SUVmax, PE SUVmax/ primary tumor SUVmax) (p<0.001). On the other hand, the presence of PE FDG uptake was not associated with PT diameter and primary tumor SUVmax (p>0.05). Single or double uptake in PE was not associated with SUVmax values and PT diameter (p>0.05). There was no correlation between the presence of PT enhancement and SUVmax values (p>0.05). The presence of FDG uptake in PT was associated with increased PT diameter (p<0.001).

There was no correlation between the primary pathology being lung or other organs and the parameters considered in our study (p>0.05). There was no correlation between the presence of multiple pulmonary nodules and the parameters considered in our study (p>0.05).

In terms of the association with the presence of PE FDG uptake, it was evaluated according to the presence of single-double nodules, the presence of increased PT, the presence of FDG uptake in PT, the presence of multiple pulmonary nodules and whether the primary pathology was lung or not, and it was found that there was no association with these parameters.

In the ROC analysis, PE SUVmax, PE SUVmax / Med SUV, PE SUVmax / Liver SUVmax, and PE SUVmax / Primary tumor SUVmax values were found to be significant in terms of predicting PE FDG uptake, while PT diameter was not significant (Table 1) (Figure 3).

Table 1. Prediction of PE FDG uptake in ROC analysis.

Parameter	Significance Level	Area Under Curve (AUC)	Cut-off Value
PE SUVmax	p<0,001	0,976	1,50
PE SUV / Med_SUV	p<0,001	0,911	0,94
PE SUV / Liver_SUV	p<0,001	0,935	0,77
PE SUV / Primer_Tm_SUV	p<0,001	0,881	0,23
PT diameter	p>0,1	-	-

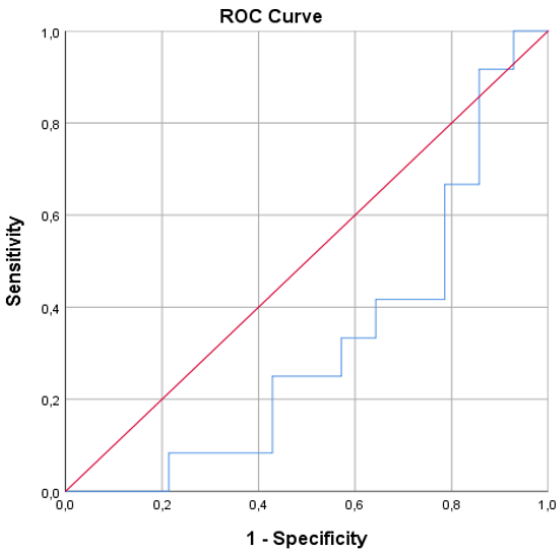

Figure 3. Coronal cross-sectional PET/CT image of a patient with high SUV uptake in pleural effusion

Discussion

In cancer patients, the diagnosis of MPE indicates advanced disease and poor prognosis. It changes and complicates the treatment approach. In patients with PE with primary malignancy, rapid characterization by PET/CT without invasive procedures may facilitate patient management. Many studies have shown the usefulness of PET/CT in the differential diagnosis of pleural diseases in patients with cancer (6). However, there is still no consensus on this issue. PET/CT is an effective method for the detection of cancerous cells with high glucose uptake. The sensitivity and specificity of MPE detection with this method vary between 89-100% and 67-94%, respectively (7, 8). Our study shows similar results to other studies.

Simsek et al. (9) evaluated the efficacy of PET/CT in the evaluation of PE using 23 parameters. According to their results, none of these parameters provided sufficient clinical benefit when used alone. Therefore, they created a combined approach. These parameters are; 1) Diffuse-nodular/nodular pleural thickening, 2) Post-obstructive atelectasis, 3) nodule/mass in the lung with SUVmax > 2.5, and 4) multiple pulmonary nodules. The accuracy rate was approximately 90% and the positive predictive value (PPV) was 100%. In their study, the cut-off value for PE SUVmax was >1.3, while in our study it was 1.50. The cut-off value of PE SUVmax/Liver SUVmax was 0.65 whereas it was 0.77 in our study (9).

On the other hand, various parameters have been examined in many studies. The size, location, side of effusion, lymph node involvement, and metastasis status of PT are some of these parameters (10-12). Nakajima et al. reported 100% sensitivity, 56% PPV, and 69% accuracy for PE with SUVmax > 1.39 and found that SUV uptake was higher in MPE compared to benign effusions (6, 13). Sun et al. (14) suggested pleural glucose metabolism and PT to differentiate MPE from benign effusion. Zhang et al. (15) determined false negativity on PET/CT imaging in 18 patients with MPE. Most of these patients did not have an underlying atelectasis, consolidation, and inflammation. In another study, 27 patients with MPE and 6 patients with benign effusion were analyzed. Among these, PET/CT gave false positive results in one patient with tuberculous pleurisy (16).

SUVmax is a PET/CT parameter used to detect malignancy, predict prognosis, and evaluate invasion and metastasis. Li et al. found significant differences in this value in differentiating MPE and benign effusion but did not consider them as independent factors in predicting MPE. However, they determined SUVmax > 2.5 as a predictive factor and revealed that PE SUVmax value is an important parameter in defining MPE (5). Porcel et al. (17) performed a meta-analysis study to evaluate the effectiveness of PET/CT in the diagnosis of MPE. In this analysis, they examined 407 patients with MPE and 232 patients with benign effusion. They found a sensitivity of 83.3% and specificity of 92.2%. In a different study, PET/CT was found to be effective in excluding MPE from tuberculous pleurisy and other benign effusions (12).

The limitations of this study are the retrospective analysis of the data, the single-center nature of the study, and the limited number of patients. Some of the parameters we studied were found to be significant in the characterization of PE and the diagnosis of MPE, and we think that they will facilitate diagnosis and treatment in the future.

In conclusion, PET/CT is an effective and non-invasive method for the differential diagnosis of MPE in patients with PE in other radiologic imaging studies. Increased pleural FDG uptake and pleural thickening indicate pleural metastases. Such studies may increase patient comfort by reducing unnecessary invasive procedures in the diagnosis of MPE and may also lead to the decision of pleurodesis by making an accurate diagnosis. Therefore, if multicenter, prospective studies with a larger number of patients are conducted, the efficacy of PET/CT in the diagnosis of MPE will be clarified more clearly and will contribute to patient management.

Declarations

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This study was approved by the local ethics committee (Dated: 18.11.2022; Approval Number: 323)

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