Dicle Tıp Dergisi / Dicle Med J (2026) 53 (2) : 273 - 283

www.diclemedj.org

Original Article / Özgün Araştırma

Evaluation of the Role of Fluorine-18 Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in the Differential Diagnosis of Pleural Lesions

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Received: 06.10.2025; Revised: 23.03.2026; Accepted: 25.03.2026

Abstract

Objective: To retrospectively evaluate the diagnostic performance of fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) in differentiating benign versus malignant pleural thickening/effusion in patients without a known malignancy, to determine the optimal cutoff for maximum standardized uptake value (SUVmax), and to assess the added value of clinical–radiologic variables for diagnostic accuracy.

Methods: Seventy-eight patients who underwent 18F-FDG PET/CT for pleural thickening between January 2018 and October 2023 and had no diagnosis of malignancy were included. SUVmax values of pleural thickening and effusion, thickening pattern, asbestos exposure, and smoking history were analyzed retrospectively.

Results: For distinguishing benign from malignant pleural thickening based on SUVmax, sensitivity was 77.27% and specificity was 73.53%, which was statistically significant ($p < 0.05$). Among 63 patients with pleural effusion, the sensitivity and specificity of an SUVmax-based distinction were 68.8% and 55.3%, respectively, and were not statistically significant ($p > 0.05$). The optimal SUVmax cutoff was 3.58 for pleural thickening and 1.62 for effusion. FDG uptake was higher in diffuse thickening than in focal thickening (diffuse mean SUVmax 6.38 ± 4.85; focal mean SUVmax 3.95 ± 3.55). Asbestos exposure was significant only in the malignant mesothelioma group ($p < 0.05$). There was no significant association between malignancy and thickening pattern or smoking history ($p > 0.05$).

Conclusion: 18F-FDG PET/CT is valuable for the differential diagnosis of malignancy in patients with pleural thickening and/or effusion. An SUVmax cutoff of 3.58 provides diagnostic contribution for pleural thickening, whereas evaluation of effusion shows limitations. External validation in larger cohorts is required.

Keywords: Pleural Neoplasms, Pleural Effusion, Fluorodeoxyglucose F18, Positron Emission Tomography Computed Tomography, Mesothelioma, Malignant

DOI: 10.5798/dicletip.1963833

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Plevral Lezyonların Ayırıcı Tanısında 18F-Florodeoksiglukoz Pozitron Emisyon Tomografisi/Bilgisayarlı Tomografinin Rolünün Değerlendirilmesi

Öz

Amaç: Malignite tanısı bulunmayan, plevral kalınlaşması olan hastalarda Flor-18 florodeoksiglukoz pozitron emisyon tomografi/bilgisayarlı tomografi (18F-FDG PET/BT)'nin benign–malign plevral kalınlaşma/efüzyon ayrımındaki tanısal performansının retrospektif olarak değerlendirilmesi, maksimum standardize tutulum değeri (SUVmaks) için en uygun eşik değerini belirleyip klinik–radyolojik verilerle tanı doğruluğuna katkısının incelenmesi amaçlanmıştır.

Yöntemler: Ocak 2018–Ekim 2023 arasında plevral kalınlaşma nedeniyle 18F-FDG PET/BT yapılan, malignite tanısı olmayan 78 hasta dâhil edildi. Plevral kalınlaşma ve efüzyon SUVmaks değerleri, kalınlaşma paterni, asbest maruziyeti ve sigara öyküsü retrospektif olarak analiz edildi.

Bulgular: Plevral kalınlaşmaların SUVmaks değeri temelli benign–malign ayrımı açısından duyarlılığı %77,27, özgüllüğü %73,53 bulundu ve istatistiksel olarak anlamlıydı ($p<0.05$). Plevral efüzyonu olan 63 hastada SUVmaks temelli ayrımın duyarlılığı %68,8, özgüllüğü %55,3 idi ve istatistiksel olarak anlamlı değildi ($p>0.05$). Optimal SUVmaks eşik değeri plevral kalınlaşma için 3,58, efüzyon için 1,62 saptandı. FDG tutulumu diffüz kalınlaşmada fokale göre daha yüksekti (diffüz SUVmaks ortalama 6,38±4,85; fokal SUVmaks ortalama: 3,95±3,55). Asbest maruziyeti yalnızca malign mezotelyoma grubunda anlamlıydı. ($p <0.05$) Kalınlaşma paterni ve sigara ile malignite arasında anlamlı fark yoktu ($p>0.05$).

Sonuç: 18F-FDG PET/BT, plevral kalınlaşmalı ve/veya efüzyonlu hastalarda malignite ayırıcı tanısında değerlidir. Plevral kalınlaşmada SUVmaks=3,58 eşiği tanısal katkı sağlar; efüzyonun değerlendirilmesinde sınırlılıklar mevcuttur. Eksternal validasyonun daha büyük kohortlarda yapılması gereklidir.

Anahtar kelimeler: Plevral neoplazmlar, Plevral efüzyon, FDG, PET/BT, Malign mezotelyoma.

INTRODUCTION

Pleural lesions are a heterogeneous clinical entity commonly encountered in practice and pose numerous diagnostic challenges, spanning a spectrum from benign inflammatory processes to malignant neoplasms[1]. Although pleural thickenings are often benign, particular caution is required in the differential diagnosis of lethal malignancies such as malignant pleural mesothelioma (MPM)[1].

Pleural effusions (PE) are characterized by fluid accumulation in the pleural space and can arise from diverse causes including malignancy, tuberculosis, and heart failure; despite extensive work-up, a considerable proportion remain of uncertain etiology[2].

Imaging modalities are fundamental tools in the evaluation of pleural disease. Chest radiography and computed tomography (CT) are widely used to detect pleural thickening and effusions; however, they are limited in distinguishing benign from malignant processes[2]. In recent years, fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) has gained prominence for characterizing pleural pathology owing to its ability to assess metabolic activity[3–5].

18F-FDG PET/CT helps noninvasively identify malignancy by detecting increased glucose metabolism in malignant cells; yet uptake may also be elevated in inflammatory conditions, which can limit specificity[3,4]. Nevertheless, studies have reported that the maximum standardized uptake value (SUVmax) measured on PET/CT—and derived scores/models—may aid in differentiating benign from malignant disease, although there is no full consensus regarding accepted cutoff values and sensitivity/specificity metrics[3,4,6,7].

The aim of this study is to evaluate the effectiveness of 18F-FDG PET/CT in differentiating benign from malignant lesions in patients with pleural thickening and/or PE who have no known history of malignancy. In addition, this study sought to determine the

optimal SUVmax cutoff and examine its concordance with histopathology[8].

METHODS

This retrospective single-center study included 78 patients who underwent ^18F-FDG PET/CT for a preliminary diagnosis of pleural thickening at the Department of Nuclear Medicine of a tertiary-care university hospital in Türkiye between January 2018 and October 2023 and had histopathologic verification after imaging.

The study protocol was approved by the Local Non-Interventional Clinical Research Ethics Committee on 18/01/2024 (decision no. 45425468-03) and was conducted in accordance with the Declaration of Helsinki. Because of the retrospective design, the requirement for individual informed consent was waived. All data were anonymized and handled in accordance with institutional policies and the Turkish Personal Data Protection Law (KVKK). Reporting followed the STROBE guidelines.

Inclusion criteria were: ^18F-FDG PET/CT performed for pleural thickening, subsequent histopathologic pleural tissue sampling, and complete clinical and pathology data. Exclusion criteria were prior chemotherapy, radiotherapy, immunotherapy, talc pleurodesis, or any pleural intervention before PET/CT; active parapneumonic/empyema effusion; and incomplete clinical or histopathologic data.

Histopathology served as the reference standard in all cases; no patient was classified solely on clinical or follow-up findings. Pleural sampling was performed by CT-guided tru-cut core needle biopsy in 59 patients, thoracoscopy in 10, thoracotomy in 4, and decortication in 5. In 12 cases with inadequate or equivocal initial sampling, repeat biopsy was performed. PET/CT readers were blinded to histopathology, and pathologists were blinded to PET/CT findings. The biopsy target corresponded to the index pleural lesion on PET/CT (highest SUVmax) with CT-guided co-localization. According to institutional practice, tissue sampling was usually performed within 2–4 weeks and no later than 6 weeks after PET/CT; patients receiving systemic therapy or pleurodesis during this interval were excluded.

Pleural effusion was present in 63 of 78 patients, and cytopathologic examination was performed where appropriate. Primary analyses focused on pleural thickening, whereas effusion-related findings were analyzed as a subgroup.

Imaging protocol

All ^18F-FDG PET/CT studies were performed on an integrated PET/CT system (Siemens Biograph 6 LSO, Erlangen, Germany). Patients fasted for at least 4–6 hours, and those with serum glucose <150 mg/dL received intravenous ^18F-FDG 440–625 MBq (~12–17 mCi; preferably ~3–5 MBq/kg). Imaging was acquired 60 ± 10 minutes after injection. A scout topogram and non-contrast low-dose CT from the vertex to mid-thigh were followed by PET over the same range. CT was used for attenuation correction and anatomical co-registration.

PET data were reconstructed iteratively (OSEM, 3 iterations × 21 subsets; matrix 256×256; voxel size ~3–4 mm; TOF/PSF enabled) with 23% bed overlap and 2 minutes per bed. Multiplanar images were reviewed in axial, coronal, and sagittal planes. Quality control and scanner-dose calibration were performed according to manufacturer recommendations and maintained in EARL-compliant fashion.

Data collection and image analysis

Demographic and clinical variables, including age, sex, smoking history, asbestos exposure, pleural effusion, pleural thickening pattern, PET/CT and CT findings, and histopathologic diagnosis, were collected using a standardized form from institutional archives and the electronic medical record. Clinical variables

were obtained from the note closest to the PET/CT date, preferably within ±30 days.

On CT, pleural effusion was defined as free or loculated fluid with a maximum axial thickness ≥10 mm or as explicitly reported as effusion. Pleural thickening was classified as focal (limited segmental or nodular/plaque-like involvement) or diffuse (involvement of ≥1/3 of the hemithoracic pleural surface).

SUVmax was measured using 3D VOIs placed over pleural lesions. VOIs were manually defined as spherical (1–3 cm^3) and positioned with CT co-registration to separate pleura from adjacent lung parenchyma; calcified plaques, bone, injection tract, and artifact-prone areas were excluded. Background SUVmax values were recorded from small spherical VOIs placed in the ascending aorta and right hepatic lobe. In patients with pleural effusion, a large freehand VOI was drawn within the fluid to measure effusion SUVmax while excluding pleural surface or wall thickening. Potential underestimation due to partial-volume effects was considered for lesions with a thickness <8–10 mm.

Cutoff selection

Although the Youden-optimal cutoff in ROC analysis was 3.75, SUVmax 3.58 yielded a similar sensitivity-specificity balance and provided a slight advantage for the study's clinical priority of higher sensitivity. Therefore, the primary decision threshold was prespecified as SUVmax ≥3.58. This value corresponds to the midpoint of the institutional threshold band (~3.5–3.8) used to support biopsy decisions and was considered a practical threshold that may reduce the impact of measurement uncertainty and inter-scanner variability.

Statistical analysis

Continuous variables were expressed as mean ± SD or median (IQR), and categorical variables as counts and percentages. Normality was assessed with the Shapiro–Wilk test. Group comparisons were performed using the independent-samples t test or Mann–Whitney U test for two groups, and one-way ANOVA or Kruskal–Wallis test for three groups, with Dunn–Bonferroni post hoc testing where appropriate. Categorical variables were compared using the χ^2 or Fisher's exact test. A two-tailed $p<0.05$ was considered statistically significant.

Diagnostic performance of SUVmax was assessed by ROC analysis using histopathology as the reference standard. AUCs with 95% confidence intervals (DeLong method), the Youden-optimal cutoff, and prespecified threshold metrics, including sensitivity, specificity, PPV, NPV, accuracy, and confusion-matrix counts, were reported. Independent predictors of malignant histopathology were evaluated by binary logistic regression including SUVmax (continuous), thickening pattern (focal vs diffuse), and pleural effusion (yes vs no), and results were expressed as odds ratios with 95% confidence intervals. Model fit and discrimination were assessed using the Hosmer–Lemeshow test, Nagelkerke R^2, and AUC. Analyses were performed as complete-case analyses using IBM SPSS Statistics version 26 and R version 4.2 (pROC package).

RESULTS

Seventy-eight patients with pleural thickening were included. Demographic characteristics, 18F-FDG PET/CT findings, and histopathologic results are summarized in Table I. Twenty-one (26.9%) were female and 57 (73.1%) male; the mean age was 63.6 ± 10.8 years. Asbestos exposure was present in 45/78 patients (57.7%), and smoking in 51/78 (65.4%). Histopathology showed malignant pleural mesothelioma (MPM) in 25 (32.1%), benign pleural thickening (BPT) in 34 (43.6%), and pleural metastasis in 19 (24.4%). MPM subtypes were epithelioid (n = 19), biphasic (n

= 3), and sarcomatoid (n = 3). In the BPT group, granulomatous infection was observed in 2 patients. Pleural effusion was present in 63/78 patients (80.8%).

Table I: Baseline clinical and imaging characteristics of the study population

Variable	Value
Total number of patients	78
Age, years, mean ± Standard deviation	63.6 ± 10.8
Female sex, n (%)	21 (26.9)
Male sex, n (%)	57 (73.1)
Diffuse pleural thickening, n (%)	38 (48.7)
Focal pleural thickening, n (%)	40 (51.3)
Benign pleural thickening, n (%)	34 (43.6)
Malignant pleural mesothelioma, n (%)	25 (32.1)
Pleural metastasis, n (%)	19 (24.4)
Pleural effusion present, n (%)	63 (80.8)
Benign pleural effusion, n (%)†	47 (74.6)
Malignant pleural effusion, n (%)†	16 (25.4)
Asbestos exposure, n (%)	45 (57.7)
Smoking history, n (%)	51 (65.4)

† Calculated within the pleural effusion subgroup (n=63).

When 18F-FDG PET/CT findings were compared with histopathology, pleural thickening areas were morphologically classified as diffuse (n = 38) and focal (n = 40). In the patient-based primary analysis, ROC analysis of SUVmax at the index lesion demonstrated significant discriminative ability (AUC = 0.785, 95% confidence interval [CI]: 0.683–0.886; p < 0.001). As shown in Table II, using an SUVmax cutoff of 3.58 for malignancy yielded a sensitivity of 77.27%, specificity of 73.53%, positive predictive value (PPV) of 79.07%, negative predictive value (NPV) of 71.43%, and accuracy of 75.64%; the confusion-matrix counts were true positive (TP) = 34, false positive (FP) = 9, true negative (TN) = 25, and false negative (FN) = 10 (total n = 78). At the commonly used SUVmax = 2.5 threshold in the literature, sensitivity increased to 86.4% while specificity decreased to 44.1% (p = 0.002), indicating that lower cutoffs increase sensitivity at the expense of specificity.

Table II. Diagnostic performance of pleural thickening SUVmax for differentiating benign and malignant pleural histopathology at different thresholds

Threshold	Sensitivity	Specificity	PPV	NPV	Accuracy	TP/FP/TN/FN	Youden index
SUVmax ≥2.50	86.4%	44.1%	66.7%	71.4%	67.9%	38 / 19 / 15 / 6	0.305
SUVmax ≥3.58	77.27%	73.53%	79.07%	71.43%	75.64%	34 / 9 / 25 / 10	0.508
SUVmax ≥3.75	72.7%	76.5%	80.0%	68.4%	74.4%	32 / 8 / 26 / 12	0.492

ROC analysis showed an AUC of 0.785 (95% CI 0.683–0.886, p<0.001). The threshold of 3.58 was used as the primary clinical cutoff because it provided a balanced diagnostic profile with slightly higher sensitivity than the Youden-optimal threshold.

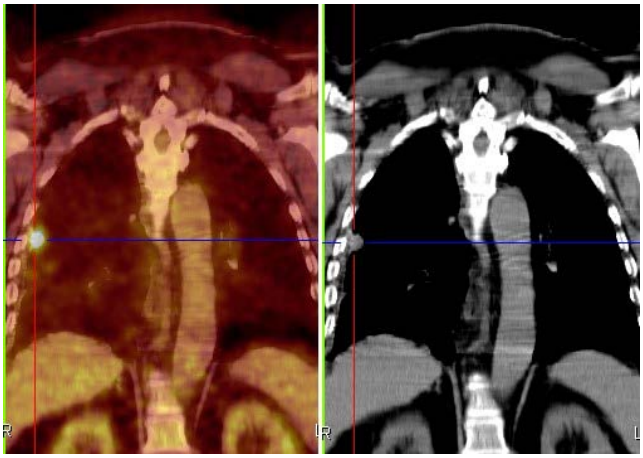

Figure I. Example of pleural metastasis from lung adenocarcinoma: Coronal fused 18F-FDG PET/CT and CT images of a 74-year-old male smoker with pleural thickening whose histopathology revealed metastatic lung adenocarcinoma. A focal area of pleural thickening along the costal pleura of the right hemithorax shows an SUVmax of 9.97.

Pleural effusion subgroup analysis in which cytopathology data were evaluated together with SUVmax showed that among the 63 of 78 patients with PE, cytopathology reported 16 malignant pleural effusions (MPE) and 47 benign pleural effusions (BPE). ROC analysis of effusion SUVmax for BPE versus MPE discrimination yielded AUC=0.615 (95% confidence interval [CI] 0.462–0.768; p=0.172) and did not demonstrate statistically significant discrimination. Using the SUVmax cutoff of 1.62, FDG positive cases (SUVmax ≥1.62) were n=32 (11 MPE, 21 BPE) and FDG negative cases (SUVmax <1.62) were n=31 (5 MPE, 26 BPE); the confusion matrix was TP=11, FP=21, TN=26, FN=5 (n=63). Accordingly, sensitivity was 68.8% (11/16), specificity 55.3% (26/47), PPV 34.4%, NPV 83.9%, and accuracy 58.7%. Detailed subgroup metrics are presented in Table IV. These findings indicate that effusion SUVmax alone has limited discriminatory value as a univariable marker for clinical decision making, since the CI includes 0.50 and p=0.172, and suggest that assessments are better performed together with pleural thickening SUVmax and CT morphology. An example PET/CT study from a patient whose histopathology and cytopathology were reported as BPT and BPE respectively is shown in Figure II.

Table IV: Diagnostic performance of effusion SUVmax in the pleural effusion subgroup

Variable	Value
Total patients with pleural effusion	63
Benign pleural effusion (BPE), n	47
Malignant pleural effusion (MPE), n	16
FDG-positive effusion (SUVmax ≥1.62), n	32
True positive (MPE), n	11
False positive (BPE), n	21
FDG-negative effusion (SUVmax <1.62), n	31
True negative (BPE), n	26
False negative (MPE), n	5
Sensitivity	68.8%
Specificity	55.3%
PPV	34.4%
NPV	83.9%
Accuracy	58.7%
AUC	0.615
95% CI	0.462–0.768
p value	0.172

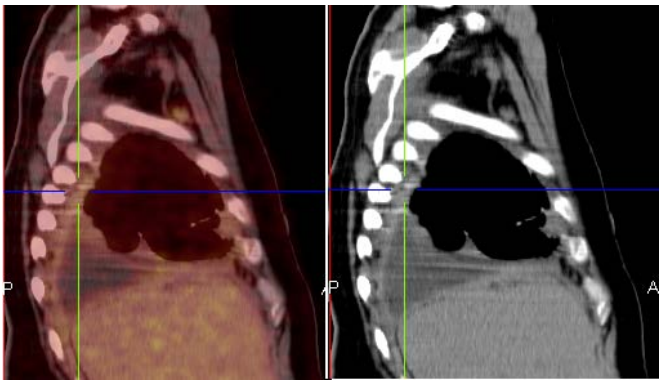

Figure II. Case example showing BPT and BPE cytopathology results. Sagittal fused 18F-FDG PET/CT and CT images of a 48-year-old male smoker without asbestos exposure who has diffuse pattern pleural thickening and PE. Pleural thickening SUVmax 1.74

and pleural fluid SUVmax 1.11. Pathology results were BPT and BPE.

In the cohort, pleural thickening was morphologically classified as diffuse (n=38) and focal (n=40). Patterns did not differ significantly between BPT and malignant pleural thickening (p=0.346). When SUVmax levels were examined by pattern, diffuse thickening had a median of 5.14 (IQR 1.37–23.27) and a mean of 6.38±4.85, whereas focal thickening had a median of 3.27 (IQR 1.12–21.48) and a mean of 3.95±3.55. These findings indicate that SUVmax is higher in the diffuse pattern, yet the distribution of patterns alone is not sufficient to determine the benign–malignant distinction.

Asbestos exposure was present in 45 of 78 patients (57.7%). In the overall benign versus malignant comparison by pleural histopathology, no association was found between asbestos history and malignancy (χ^2=0.003, p=0.957). The numeric distribution for asbestos absent/present was benign 15/19 and malignant 18/26. The odds ratio for malignancy with asbestos present versus absent was 1.14 (95% confidence interval CI 0.46–2.82, non-significant). In subgroup analyses, asbestos exposure clustered strongly in favor of MPM. For MPM versus pleural metastasis χ^2=12.57, p<0.001, Fisher p=0.00017, distribution MPM 21/4 and metastasis 5/14 for asbestos present/absent. For MPM versus benign χ^2=4.01, p=0.045, Fisher p=0.027, distribution MPM 21/4 and benign 19/15. These findings suggest that asbestos history is not discriminatory for overall malignancy risk, but at the subtype level it provides a clue increasing the likelihood of MPM.

Table III: Comparison of PET/CT and exposure variables according to pleural histopathology

Variable	BPT (n=34)	MPM (n=25)	Pleural metastasis (n=19)	p value
Pleural thickening SUVmax, median (IQR)	2.83 (1.74-3.77)	4.79 (3.60–6.82)	5.73 (3.07–10.19)	<0.001*
Pleural thickening SUVmax, mean ± SD	3.1 ± 1.8	5.6 ± 3.1	8.0 ± 6.7	<0.001*
Asbestos exposure present, n (%)	19 (55.9)	21 (84.0)	5 (26.3)	—
Asbestos exposure absent, n (%)	15 (44.1)	4 (16.0)	14 (73.7)	—

** Overall comparison for SUVmax across the three histopathologic groups.*

Pairwise comparisons: BPT vs MPM for SUVmax, p<0.001; MPM vs pleural metastasis for SUVmax, p=0.620; BPT vs MPM for asbestos exposure, p=0.045; MPM vs pleural metastasis for asbestos exposure, p<0.001.

In the overall benign-versus-malignant comparison, asbestos exposure was not associated with malignancy (p=0.957), but it was significantly more frequent in the MPM subgroup.

Smoking was present in 51 of 78 patients (65.4%) and was not significantly associated with benign versus malignant pleural histopathology (χ^2=0.37, p=0.542; Fisher's exact p=0.475). Smoking no/yes was distributed as 17/27 in the malignant group and 10/24 in the benign group. The odds ratio for malignancy was 0.66 (95% CI 0.25–1.72), with a small effect size (φ/Cramer's V=0.069). Accordingly, smoking history did not appear to be an independent marker in this cohort.

Multivariable logistic regression results are presented in Table V. Pleural thickening SUVmax remained an independent predictor of malignant pleural histopathology (OR=1.549, 95% CI 1.168–2.055, p=0.002), whereas diffuse uptake pattern was not independently associated with malignancy (OR=0.975, 95% CI 0.320–2.974, p=0.965). The presence of pleural effusion showed a borderline association with malignancy (OR=3.948, 95% CI 0.951–16.391, p=0.059). Model calibration was acceptable (Hosmer–Lemeshow p=0.343), with Nagelkerke R^2=0.351 and an overall classification accuracy of 78.2%. In ROC analysis, SUVmax yielded an AUC of 0.785 (95%

CI 0.683–0.886, p<0.001). Although the Youden-optimal cutoff was 3.75 (sensitivity 72.7%, specificity 76.5%), the performance at 3.58 was very similar and offered a slight advantage in sensitivity; values between 3.5 and 3.8 differed by only a few percentage points.

Table V: Multivariable logistic regression analysis for predictors of malignant pleural histopathology

Variable	OR	95% CI	p value
Pleural thickening SUVmax	1.549	1.168–2.055	0.002
Diffuse uptake pattern	0.975	0.320–2.974	0.965
Presence of pleural effusion	3.948	0.951-16.391	0.059

Model performance: Hosmer–Lemeshow test p=0.343; Nagelkerke R^2=0.351; overall classification accuracy=78.2%.

DISCUSSION

In this study, consistent with the literature, 18F-FDG PET/CT was useful for differentiating benign from malignant pleural thickening, with an SUVmax cutoff of 3.58 for the benign–malignant distinction.

PET/CT complements anatomic imaging with metabolic information and contributes to the differentiation of BPT from MPT, including MPM, solitary fibrous tumors, lipomatous tumors, and pleural metastases[9]. Because pleural thickening and effusion may be seen in both benign conditions, such as asbestos-related disease, inflammation, infection, and tuberculosis, and in malignant processes, CT alone has limited discriminatory value[10]. This has increased the role of metabolic imaging in pleural disease evaluation.

Regarding SUVmax thresholds, Orki et al.[9] reported sensitivity of 100% and specificity of 94.8% using a threshold of 3.0 in 83 patients with suspected malignant pleural lesions. In this cohort, the 3.58 cutoff yielded 77% sensitivity and 74% specificity, suggesting that population characteristics and methodology influence threshold selection. At the widely used threshold of 2.5, sensitivity remained high but specificity decreased markedly. Similarly, Ceylan et al.[11] used SUVmax >2.5 as positive in 30 patients with pleural thickening and/or effusion and reported sensitivity of 81.8% and specificity of 54.5% in the pleural thickening subgroup. In our study, the 2.5 cutoff yielded sensitivity of 86.4% and specificity of 44.1%, indicating that lower thresholds increase false positives, likely because reactive or granulomatous processes can also raise FDG uptake.

Kaplan et al.[12] also found significantly higher FDG uptake in MPT than in BPT, in line with our findings. Likewise, Bénard et al.[13] reported higher SUVmax values in malignant than benign pleural lesions in patients with suspected MPM. The relatively high SUVmax in the benign group may be explained by chronic active inflammation and granulomatous inflammation in several BPT cases. False-positive FDG uptake has also been described in pleurodesis, inflammatory pleuritis, benign asbestos plaques, and tuberculous pleuritis[14], although none of these patients had talc pleurodesis.

False-negative PET findings should also be considered. Lococo et al.[15] reported PET negativity in 11.6% of MPM patients and found associations with older age and early stage; they also noted lower FDG uptake in epithelioid tumors than in biphasic or sarcomatoid subtypes. In this series, 10 malignant cases had SUVmax <3.58, including five MPMs and five metastases. The predominance of epithelioid histology among MPM cases, together with small lesion size and partial-volume effects, may explain these false-negative results [15].

SUVmax was higher in diffuse pleural thickening in our cohort. This may reflect the more frequent diffuse presentation of MPM and extensive metastatic pleural involvement, as well as underestimation of uptake in thin focal plaques due to partial-volume effects. Prior inflammation may also have contributed to diffuse hypermetabolism. In contrast, Elkholy et

al.[16] reported higher SUVmax in focal pleural thickening in a breast cancer population, which may reflect differences in patient selection and tumor spectrum.

We found no significant difference in mean SUVmax between MPM and pleural metastasis, indicating that FDG uptake can be high in both and that SUVmax alone is insufficient for their differentiation. Elkholy et al.[16] reported high diagnostic performance in metastatic pleural disease in breast cancer patients, but our cohort differed in that patients were evaluated without a known primary malignancy, which may explain the lack of statistical separation.

Pleural effusion occurs in many thoracic and systemic diseases, and distinguishing BPE from MPE is clinically important[17]. Previous studies have reported high diagnostic performance for PET in selected cancer populations using mainly visual assessment or higher-prevalence malignant cohorts[17–19]. In this study, however, an effusion SUVmax cutoff of 1.62 yielded an AUC of 0.615 (p=0.172), with sensitivity of 68.8%, specificity of 55.3%, PPV of 34.4%, and NPV of 83.9, indicating limited discriminatory ability. This may be expected in a cohort without known malignancy and with the inherently low counting statistics of pleural fluid measurements. Indeed, both benign and malignant effusions were observed across low and high effusion SUVmax values, underscoring the need for multimodal interpretation rather than reliance on effusion SUVmax alone.

Environmental asbestos exposure remains an important issue in Türkiye, particularly in regions where white soil use is common, and data from Eskişehir and surrounding areas support this association with MPM[20]. The demographic characteristics of our MPM subgroup were consistent with national data reported by Metintaş et al.[20]. In our study, asbestos exposure differed significantly between MPM and benign cases, supporting the regional relevance of this risk factor.

By contrast, the literature does not show a clear association between smoking and MPM risk[21,22], and smoking history was likewise not associated with benign versus malignant pleural pathology in this series. Nevertheless, because smoking is associated with malignancies such as lung and breast cancer[23,24], it may still indirectly influence the etiology of pleural metastases and should be interpreted in the broader clinical context.

From a clinical perspective, an optimized threshold such as SUVmax 3.58 contributes meaningfully to the BPT–MPT distinction but should not be considered decisive in isolation. PET/CT findings should be interpreted together with CT morphology, clinical context, and ultimately histopathology. Because effusion SUVmax has limited diagnostic value, visual assessment of effusion in combination with the SUVmax of pleural thickening may be more informative. In addition, false negativity in epithelioid MPM and early-stage disease should be kept in mind, and pretest probability should be individualized, especially in regions with substantial asbestos exposure.

This study has several limitations. Its retrospective, single-center design may introduce selection bias and center-specific practice effects. Although all cases had histopathologic confirmation, sampling methods were heterogeneous, and repeat biopsy was required in some patients. The interval between PET/CT and biopsy may also have affected metabolic activity in individual cases. SUVmax-based analyses are susceptible to noise and partial-volume effects, especially in lesions thinner than 8–10 mm, and effusion measurements are additionally limited by low count density. Because our cohort consisted of patients presenting with pleural thickening and no known malignancy, the findings may not be directly generalizable to active cancer populations or treated patients. External validation was not performed, interreader

reproducibility was assessed only in a limited subgroup, and contrast-enhanced CT or additional quantitative PET parameters such as metabolic tumor volume and total lesion glycolysis were not evaluated.

CONCLUSION

This study shows that 18F-FDG PET/CT provides high diagnostic accuracy for differentiating benign from malignant pleural thickenings in patients without a known history of malignancy. The identified SUVmax cutoff of 3.58 emerged as a meaningful boundary in favor of malignancy.

Although the diagnostic contribution of SUVmax was limited in the presence of pleural effusion, evaluating metabolic imaging together with morphologic data contributes substantially to the differential diagnosis. In addition, the significant association between asbestos exposure and the MPM group highlights the need to consider environmental risk factors.

18F-FDG PET/CT can be used as a guiding and complementary method in evaluating pleural lesions for malignancy. When interpreted together with clinical, radiologic, and histopathologic data, it enhances diagnostic accuracy. Larger, multicenter, prospective studies are needed to advance knowledge in this area.

Presentation: The presentation was included as a poster at the 37th National Nuclear Medicine Congress, held from April 9-13, 2025 in Belek/Antalya.

Acknowledgments

This study used archive data obtained from the nuclear medicine department of a tertiary-care university hospital in Türkiye. No additional acknowledgments are declared.

Ethics Committee Approval: Ethics approval for this study was obtained from the Eskişehir Osmangazi University Non-Interventional Clinical Research Ethics Committee with the decision dated 18.01.2024 and numbered 45425468-03. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Conflict of Interest: The author(s) declare that there is no financial conflict of interest related to this article.

Financial Disclosure: The authors have stated that no financial support was provided for this study.

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