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Comparison of ^{18}F-FDG-PET/CT scans in patients diagnosed with sarcoidosis and tuberculosis

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Abstract

Positron emission tomography/computed tomography (PET/CT) is widely used to differentiate benign and malignant lesions. However, increased fluorodeoxyglucose (FDG) uptake may occur under certain benign conditions, leading to potential false positives in malignancy assessments. Tuberculosis and sarcoidosis are 2 conditions that can exhibit FDG uptake, presenting with both lymph node and extrathoracic involvement, alongside pulmonary manifestations. This study aimed to explore the utility of PET/CT in distinguishing between thoracic and extrathoracic involvement in patients with sarcoidosis and tuberculosis. A retrospective analysis was conducted on patients diagnosed with sarcoidosis or tuberculosis, either pathologically or microbiologically, who underwent ^{18}F-FDG-PET/CT as part of their diagnostic process. This study evaluated demographic data, PET/CT findings, involvement sites, and maximum standardized uptake values (SUVmax) in patients with tuberculosis and sarcoidosis. PET/CT images of 62 patients (44 with tuberculosis and 18 with sarcoidosis) were analyzed. The median patient age was 55 years. Lymph node involvement in the cervical, abdominal, retro-pancreatic, inguinal, and extrathoracic regions was significantly more prevalent in patients with sarcoidosis than in those with tuberculosis (50% vs 20.5%, $P = .0031$; 27.8% vs 4.5%, $P = .018$; 22.2% vs 0%, $P = .005$; 27.8% vs 6.8%, $P = .039$; and 66.7% vs 27.3%, $P = .009$, respectively). No statistically significant difference was found in SUV values between patients with tuberculosis and those with sarcoidosis with regard to mediastinal lymph node, extrathoracic lymph node, lung, and bone PET/CT involvement. In conclusion, ^{18}F-FDG-PET/CT imaging does not appear to be a reliable method for differentiating sarcoidosis and tuberculosis from malignant lesions, as it is not feasible to distinguish between sarcoidosis and tuberculosis solely based on ^{18}F-FDG-PET/CT SUVmax values. Nevertheless, the increased prevalence of extrathoracic lymph node involvement in sarcoidosis compared to tuberculosis may offer valuable insights for clinicians in differential diagnosis.

Abbreviations: 18F-FDG-PET = 18F-fluorodeoxyglucose positron emission tomography, COVID-19 = 2019 coronavirus disease, CT = computed tomography, EPTB = extra-pulmonary tuberculosis, SUVmax = maximum standardized uptake value, PCR = polymerase chain reaction, TB = tuberculosis.

Keywords: FDG-PET/CT, sarcoidosis, tuberculosis

1. Introduction

Since the 2000s, 18F-fluorodeoxyglucose positron emission tomography (^{18}F-FDG-PET) scans with and without computed tomography (CT) have been used with increasing frequency for various oncological indications, and today, it has gained an indispensable place in the diagnosis, staging, and follow-up of malignant diseases. FDG, an indicator of glucose metabolism, shows increased accumulation in the majority of malignant lesions; however, false-positive results can be observed in various benign lesions. Mycobacterial infections and sarcoidosis, common benign granulomatous diseases, also show PET/CT involvement.

Until the 2019 coronavirus disease (COVID-19) pandemic, tuberculosis (TB) was the leading cause of death caused by a single infectious agent. Approximately 10.6 million new TB cases and an estimated 1.3 million annual deaths caused by TB were reported worldwide by 2022; therefore, TB remains a significant global health issue.[1] Although microbiological cultures are considered the gold standard for diagnosing tuberculosis, the results may require up to 8 to 10 weeks. Imaging plays an important role in cases with negative sputum, inability to produce sputum, or suspected extrapulmonary tuberculosis (EPTB). Tuberculosis can affect any part of the body. The lymph nodes, pleura, musculoskeletal, gastrointestinal, and genitourinary systems are

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The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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commonly affected. Lymph node tuberculosis is the most common type of EPTB.[2]

Sarcoidosis, which is very similar to TB clinically, radiologically, and histopathologically, can make the differential diagnosis difficult.[3] Although pathological caseous necrosis helps us distinguish TB and sarcoidosis, sometimes necrotic tissue areas may not be stained in biopsy samples. Extrapulmonary sarcoidosis is common, occurring in 30% to 50% of patients.[4] The treatments of TB and sarcoidosis are quite different from each other, and misuse of corticosteroids in patients with TB to treat sarcoidosis may lead to the spread of the infection.[5,6] Therefore, a correct differential diagnosis of these 2 diseases is critical for patient prognosis.

PET/CT scanning in patients with TB plays an important role in assessing disease burden, selecting the most appropriate biopsy site, evaluating the early response to treatment, and monitoring the response to treatment in extrapulmonary TB cases.[7] FDG-PET/CT can be beneficial for detecting and managing active disease, particularly in cases of fibrotic pulmonary and cardiac sarcoidosis, as well as for assessing organ-specific disease activity.[8]

This study aimed to investigate the role of PET/CT in the differential diagnosis of thoracic and extrathoracic involvement in patients with sarcoidosis and tuberculosis.

2. Materials and methods

2.1. Study design and population

In this retrospective observational study, we evaluated the medical records of patients diagnosed with tuberculosis and sarcoidosis who were monitored at our clinic between January 2020 and September 2022. This study focused on patients who underwent ^{18}F-FDG-PET/CT during diagnosis. We recorded the demographic characteristics of these patients. Presence of involvement on PET/CT, maximum standardized uptake value (SUVmax) in the affected areas, and specific organs and lymph nodes affected by the conditions.

The GE Discovery IQ Gen2 PET/CT system (3000 N Grandview Blvd, Waukesha, WI) was utilized to acquire whole-body ^{18}F-FDG-PET/CT scans. Scanning was performed following a 6-hour fasting period and 60 to 90 minutes after intravenous administration of ^{18}F-FDG (350–370 MBq). A low-dose CT scan was conducted in the supine position during normal respiration to facilitate the whole-body PET/CT imaging. All images were reconstructed with a slice thickness of 5 mm and 2.4-mm increments. The total acquisition time per patient ranged from 25 to 35 minutes. PET images were reconstructed with CT-based attenuation correction using the ordered subset expectation maximization algorithm. The maximum standardized uptake value (SUVmax) and corresponding anatomical locations of the lymph nodes and other tissues involved were recorded for all patients. The lymph node/tissue is considered to be involved by the disease if SUVmax is >2.5.

Sarcoidosis was diagnosed based on clinical presentation, demonstration of noncaseating granulomas in 1 or more tissue samples, and exclusion of other granulomatous disorders. Tuberculosis diagnosis relied on the presence of epithelioid granulomas with giant cells and central caseous necrosis observed on histopathological examination, along with a positive acid-fast bacilli staining result. Exclusion criteria included incomplete clinical data, loss to follow-up, or a final diagnosis of other conditions, such as malignancy. Patients under 18 years of age or those with known malignancies were excluded.

In the diagnosis of TB and sarcoidosis, particularly in the context of malignant diseases, other granulomatous conditions were excluded through a combination of pathological, clinical, radiological, and additional supportive tests. These included the tuberculin skin test, mycobacterium-specific polymerase chain reaction (PCR) on tissue samples, and measurement of serum angiotensin-converting enzyme levels. During the follow-up period after diagnosis, patients were monitored for the development of malignancy and their response to treatment. Only those patients who showed a positive response to treatment for sarcoidosis or tuberculosis, or who demonstrated no disease progression, were included in the study.

2.2. Statistical analysis

Statistical analysis of the data was performed using SPSS 25.0. Categorical measurements are presented as numbers and percentages, whereas continuous measurements are summarized as mean and standard deviation (or median and range where appropriate). Categorical variables were compared using the chi-squared test or Fisher exact test. Differences in SUVmax values between patients with different diseases were evaluated using the *t*-test. A value of $P < .05$ was considered statistically significant.

2.3. Ethics approval and consent to participate

The study protocol was approved by the Ethical Committee of the Cukurova University School of Medicine (126/14) and was conducted in accordance with the approved guidelines.

The Ethical Committee of Cukurova University School of Medicine waived the need for patient approval and/or informed consent due to the retrospective nature of the study.

3. Results

3.1. Patient characteristics

The FDG-PET/CT scans of 62 patients (44 with tuberculosis and 18 with sarcoidosis) were evaluated. The median age of the patients was 55 years (range, 26–73 years). Table 1 presents patient demographics, diagnostic methods, and SUVmax values for the lymph nodes and organs involved.

The distribution of lymph node and organ involvement in patients with sarcoidosis and tuberculosis, as assessed using PET/CT, is presented in Table 2. Lymph node involvement in the cervical, abdominal, retro-pancreatic, inguinal, and extrathoracic regions was significantly higher in patients with

Table 1

Clinical characteristics of patients.

Characteristics	Patients
Age, yr (mean ± sd)	
Tuberculosis, n = 44	55.1 ± 11.0
Sarcoidosis, n = 18	55.7 ± 12.1
Gender (n, %)	
Tuberculosis, male, n (%)	22 (50 %)
Sarcoidosis, male, n (%)	6 (33.3 %)
Diagnostic method	
Pathological, n (%)	
Tuberculosis	38 (86.4 %)
Sarcoidosis	18 (100 %)
Microbiological, n (%)	
Tuberculosis	6 (13.6 %)
Sarcoidosis	0
SUVmax (mean ± sd)	
Mediastinal lymph node, n = 43	11.9 ± 7.7
Extrathoracic lymph node = 24	10.18 ± 6.69
Lung, n = 40	7.7 ± 5.4
Bone, n = 13	6.0 ± 3.5
Adrenal gland, n = 4	5.7 ± 3.5
Liver, n = 3	7.0 ± 2.9

Abbreviation: SUVmax = maximum standardized uptake value.

sarcoidosis than in those with tuberculosis (50% vs 20.5%, $P = .031$; 27.8% vs 4.5%, $P = .018$; 22.2% vs 0%, $P = .005$; 27.8% vs 6.8%, $P = .039$; and 66.7% vs 27.3%, $P = .009$, respectively).

There was no significant difference in SUV values between patients with tuberculosis and those with sarcoidosis for PET/CT involvement of mediastinal lymph nodes, extrathoracic lymph nodes, lungs, and bones. However, patients with tuberculosis exhibited higher SUVmax values for the extrathoracic lymph nodes, whereas those with sarcoidosis showed higher SUVmax values for mediastinal lymph nodes and bone involvement (Table 3).

The graph of the SUV max uptake values in the lymph nodes and organs of the cases is shown in Figure 1.

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Table 2

Distribution of lymph node and organ involvement on 18F-FDG-PET/CT.

	Sarcoidosis (N = 18)	Tuberculosis (N = 44)	*P*
Cervical lymph node, yes (n, %)	9 (50%)	9 (20.5%)	**.031**
Axillary lymph node, yes (n, %)	1 (5.6%)	3 (6.8%)	1.000
Abdominal lymph node, yes (n, %)	5 (27.8%)	2 (4.5%)	**.018**
Paraaortic, yes (n, %)	3 (16.7%)	1 (2.3%)	.070
Retro-pancreatic, yes (n, %)	4 (22.2%)	0	**.005**
İnguinal lymph node, yes (n, %)	5 (27.8%)	3 (6.8%)	**.039**
Mediastinal lymph node, yes (n, %)	16 (88.9%)	28 (63.6%)	.065
Extrathoracıc lymph node, yes (n, %)	12 (66.7%)	12 (27.3%)	**.009**
Lung, yes (n, %)	11 (61.1%)	28 (63.6%)	1.000
Bone, yes (n, %)	1 (5.6%)	10 (22.7%)	.152
Adrenal gland, yes (n, %)	0	4 (9.1%)	.313
Liver, yes (n, %)	2 (11.1%)	1 (2.3%)	.200

Table 3

18F-FDG-PET/CT SUVmax parameters of mediastinal lymph nodes, extrathoracic lymph nodes, lung and bone.

	Tuberculosis	Sarcoidosis	*P*
Mediastinal lymph node SUVmax	10.48 ± 7.36 (2.70–28.88) (n = 28)	14.23 ± 8.03 (3.27–31.40) (n = 16)	.127
Extrathoracıc lymph node SUVmax	10.78 ± 3.84 (5.65–16.40) (n = 12)	9.58 ± 8.84 (3.06–28.40) (n = 12)	.671
Lung SUVmax	7.31 ± 4.71 (3.03–24.95) (n = 28)	8.74 ± 7.10 (4.18–25.30) (n = 11)	.149
Bone SUVmax	5.50 ± 3.56 (2.70–15.50) (n = 11)	8.49 ± 2.28 (6.49–10.50) (n = 2)	.291

Abbreviations: SUVmax = maximum standardized uptake value.

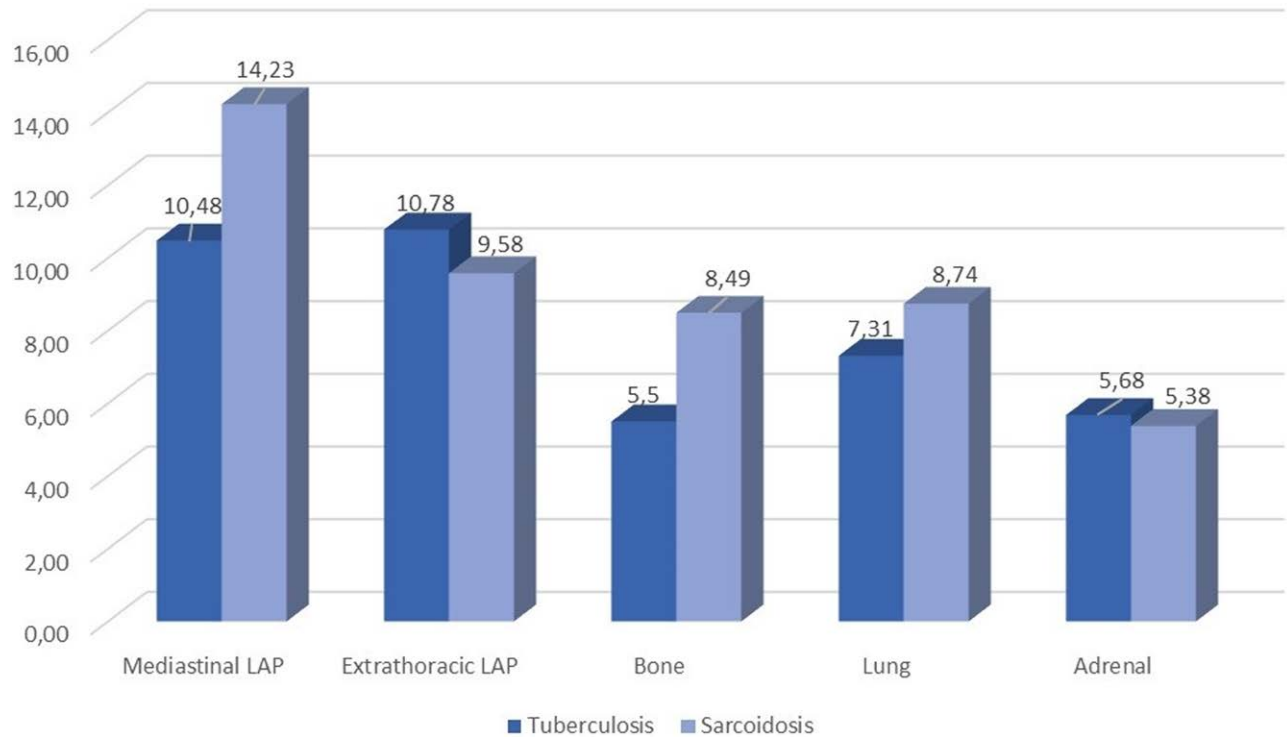


Figure 1. The graph of the SUVmax uptake values in the lymph nodes and organs of the cases. Abbreviation: SUVmax = maximum standardized uptake value.

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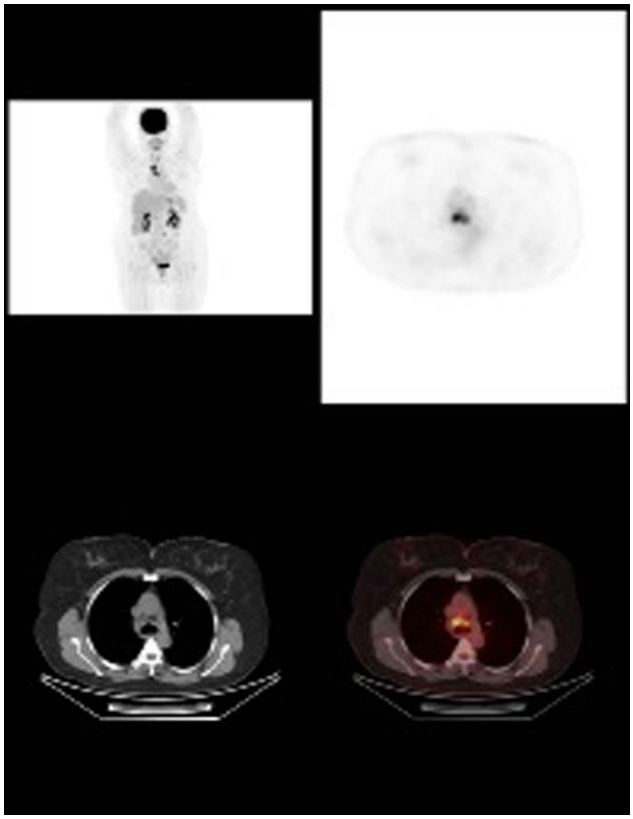


Figure 2. Axial and coronal ^{18}F-FDG-PET/CT images of a 54-yr-old woman diagnosed with tuberculosis, show hypermetabolic lesions in the left cervical, mediastinal, right upper and lower paratracheal, subcarinal, and left lower paratracheal lymph nodes. Abbreviations: FDG = fluorodeoxyglucose, PET/CT = positron emission tomography/computed tomography.

3.2. Representative cases

Figure 2 presents a portion of the ^{18}F-FDG-PET/CT scan of a 54-year-old woman, which reveals hypermetabolic lesions in the left cervical, mediastinal, right upper and lower paratracheal, subcarinal, and left lower paratracheal lymph nodes. The lymph node exhibiting the highest glucose metabolism was located in the right upper paratracheal region, measuring 19 × 17 mm with a SUVmax of 16.68. Pathological examination of lymph node biopsies from stations 4R and 7 revealed caseous necrotizing granulomas, and tissue samples tested positive for Mycobacterium tuberculosis by PCR. The patient was subsequently diagnosed with TB and initiated on appropriate treatment.

Figure 3 displays the ^{18}F-FDG-PET/CT scan of a 56-year-old male patient. The scan shows hypermetabolic involvement in the bilateral supraclavicular, right axillary, paraaortic, paratracheal, subcarinal, and bilateral hilar lymph nodes, with the largest lesion measuring 26 × 23 mm and a SUVmax of 10.18. Additionally, there is intraabdominal and peripancreatic involvement, with the largest lesion approximately 14 × 14 mm in size and an SUVmax value of 12.33. A right inguinal lesion, measuring 16 × 13 mm, shows a SUVmax value of 9.84. Sarcoidosis was diagnosed following a biopsy of the lymph node at station 7, which revealed non-necrotizing granulomatous inflammation.

4. Discussion

To the best of our knowledge, this is the first study evaluating and comparing SUVmax values in patients with TB and sarcoidosis. In some situations, it may be difficult to differentiate TB and sarcoidosis by clinical, laboratory, imaging, and pathological findings. Therefore, we need some additional modalities.

In our study, lymph node involvement in the cervical, abdominal, retro-pancreatic, inguinal and extrathoracic regions was significantly more prevalent in patients with sarcoidosis than in

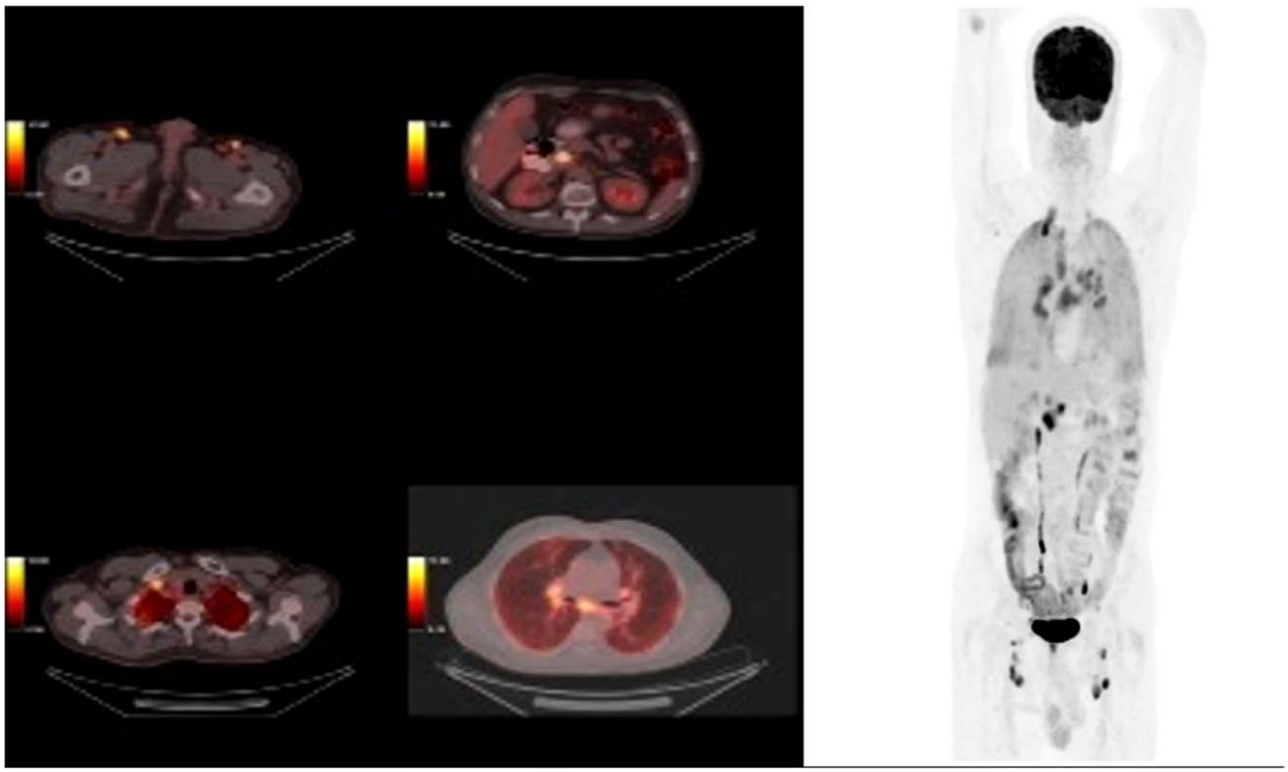


Figure 3. Axial and coronal ^{18}F-FDG-PET/CT images of 56-year-old male sarcoidosis patient. The scan shows hypermetabolic involvement in the bilateral supraclavicular, right axillary, paraaortic, paratracheal, subcarinal, hilar, intraabdominal and peripancreac lymph nodes. Abbreviations: FDG = fluorodeoxyglucose, PET/CT = positron emission tomography/computed tomography.

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those with TB. An analysis of SUVmax values for lymph node involvement indicated that although the mean SUVmax values were elevated in both patient groups, the differences were not statistically significant. These findings suggest that PET/CT SUVmax values may not be effective in differentiating sarcoidosis from TB or in distinguishing these conditions from malignancy solely based on SUVmax values. Nonetheless, the increased incidence of extrathoracic lymph node involvement observed in sarcoidosis could serve as a valuable diagnostic marker.

FDG-PET/CT allows whole-body mapping of the active inflammatory sites in sarcoidosis and tuberculosis. In the study by Chen et al, which compared ^{18}F-FDG-PET/CT findings between patients with sarcoidosis and those with lung cancer, the SUVmax values in sarcoidosis patients were significantly higher than those in lung cancer patients (13.38 ± 7.68 vs 9.19 ± 5.00 [$P < .001$]).[9]

In a study conducted by Sathekge et al, which compared tuberculomas and malignant lung lesions, the median SUVmax values for malignant lesions and tuberculomas were reported as 6.7 and 7.6, respectively.[10] Additionally, in a case series examining 9 out of ten tuberculomas, the mean SUVmax value was found to be 4.2 ± 2.2.[11] Consistent with the literature, our study found the SUVmax for lung lesions in tuberculosis patients to be 7.31 ± 4.71. Lefebvre et al reported that the mean SUVmax value for 18 patients with lymph node tuberculosis was 8.7 ± 5.0. In our study, the SUVmax values for mediastinal and extrathoracic lymph nodes were determined to be 10.48 ± 7.36 and 10.78 ± 3.84, respectively.[12]

Chen et al found that patients with sarcoidosis had a significantly higher proportion of extrapulmonary lymph node involvement than patients with lung cancer (64.7% vs 29.8%, $P < .001$). The study suggested that an SUVmax >13.86, combined with a short axis measurement exceeding 11.5 mm, could serve as an independent predictor for assessing extrapulmonary lymph node involvement.[9]

This study had several limitations. First, this was a retrospective, single-center investigation. Additionally, FDG-PET imaging is costly and may not be accessible to all patients with sarcoidosis and tuberculosis owing to reimbursement constraints. Despite these limitations, our study provides an important examination of the utility of PET/CT for differentiating between these 2 conditions.

In conclusion, consistent with the existing literature, ^{18}F-FDG-PET/CT imaging does not appear to be a reliable modality for differentiating sarcoidosis and tuberculosis from malignant lesions.[7–11] Our study corroborates that distinguishing sarcoidosis from tuberculosis based on ^{18}F-FDG-PET/CT SUVmax alone is not feasible. However, we believe that the increased prevalence of extrathoracic lymph node involvement in sarcoidosis as compared to tuberculosis may offer valuable insights for clinicians in differential diagnosis.

Author contributions

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Writing – original draft: Pelin Pınar Deniz, Pelin Duru Çetinkaya.
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