

# Diagnostic Value of Endobronchial Ultrasonography in Sarcoidosis and Factors Associated with Diagnosis

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## ABSTRACT

**Objective:** The aim of this study was to investigate the diagnostic value of endobronchial ultrasonography (EBUS) and factors associated with diagnosis in patients with lung sarcoidosis.

**Methods:** In this prospective study, EBUS transbronchial needle aspiration (TBNA) was performed for patients with a clinical and radiological suspicion of pulmonary sarcoidosis with enlarged hilar/mediastinal lymph nodes detected on a computerized tomography scan of the chest between January 2014 and September 2015.

**Results:** During the study period, 107 patients underwent EBUS-TBNA and 1 patient underwent transesophageal endoscopic ultrasonography with fine needle aspiration (EUS-FNA). Four cases determined to be non-sarcoidosis (tuberculosis) were excluded from the study. Of the 104 cases definitively diagnosed as sarcoidosis, 28.8% were male patients and 71.2% were female, with a mean age of  $44.3 \pm 13.1$  years. A total of 92.3% of the patients (n=96) were diagnosed with EBUS-TBNA and 1% (n=1) was diagnosed based on EUS-FNA results. EBUS was nondiagnostic in 7 patients and sarcoidosis was diagnosed by mediastinoscopy in 6 patients and by right supraclavicular lymph node biopsy in 1 patient. The sensitivity of EBUS-TBNA was 92.3%, with a specificity of 100%.

**Conclusion:** EBUS-TBNA has a high sensitivity and specificity for demonstrating granulomatous inflammation in cases of suspected sarcoidosis. Given the high diagnostic rate of EBUS-TBNA, additional invasive procedures may be unnecessary.

## INTRODUCTION

Sarcoidosis is a multisystem disease with an unknown etiology. It is usually seen in young and middle-aged adults. Bilateral hilar lymphadenopathy, pulmonary infiltrations, and eye and skin lesions often occur. The diagnosis is made histopathologically with a demonstration of noncaseating epithelioid cell granuloma and the presence of clinical and radiological findings.<sup>[1]</sup> Histopathology is very important in the diagnosis. The biopsy site varies depending on the clinical presentation of the disease. In general, the most easily accessible site with the least morbidity should be preferred. Lung and mediastinal lymph node biopsies may

be performed using a fiberoptic bronchoscope with a high diagnostic value, since 95% of patients have lung involvement. The diagnostic accuracy of transbronchial lung biopsy (TBLB) is 40% to 90% when 4 to 5 biopsy specimens are obtained, depending on the experience of the bronchoscopist.<sup>[2]</sup> In cases where the bronchial mucosa appears normal and there is no endobronchial nodule or cobblestone appearance, granuloma may be seen in the histopathological examination of endobronchial biopsy material. The diagnostic value of endobronchial biopsy in sarcoidosis has been reported to be 40% to 60%.<sup>[3]</sup> Samples can be taken from intrathoracic lymph nodes with conventional transbronchial needle aspiration (TBNA).

In stage 1 or 2 sarcoidosis, the diagnostic value of the bronchoscopy increases when combined with TBLB and TBNA. Bilaçeroğlu et al.<sup>[4]</sup> found that half of stage 1 and 2 cases and 83% of stage 3 patients had mucosal abnormalities. When the mucosal biopsy was combined with TBLB, the diagnostic value of the procedure increased from 52% to 64%. In the series reported by Gupta et al.,<sup>[5]</sup> mucosal pathology was observed in one-third of the cases, and the diagnostic value of biopsy specimens retrieved from these sites was 54%, while it was 20% for those obtained from normal mucosa. Similarly, as seen in the study of Bilaçeroğlu et al.,<sup>[4]</sup> they found that the accuracy of bronchoscopic diagnosis increased from 76% to 86% when the mucosal biopsy was combined with TBLB.

The role of bronchoscopy in the diagnosis of sarcoidosis has become even more prominent in combination with endobronchial ultrasonography (EBUS), a minimally invasive method that allows real-time sampling of mediastinal and hilar lymph nodes. The objective of this research was to investigate the diagnostic value of EBUS and related factors in patients with pulmonary sarcoidosis.

## MATERIAL AND METHODS

Patients who were admitted to the outpatient clinic between January 2014 and September 2015 with the clinical and radiological suspicion of sarcoidosis and who had enlarged hilar/mediastinal lymph nodes demonstrated on computerized thorax tomography (CT) were evaluated prospectively.

The diagnosis of sarcoidosis was made based on clinical and radiological findings and histopathological examination of non-necrotic granulomatous inflammation after the exclusion of mycobacterial infection and other granulomatous diseases. Patients who did not undergo EBUS and mediastinoscopy; those with diagnoses of uncontrolled angina, uncontrolled coagulopathy, bleeding diathesis or diagnoses other than sarcoidosis; and patients who had experienced myocardial infarction within the previous 6 months were excluded from the study. Anamnesis, physical examination, chest X-ray, thorax CT, electrocardiogram, pulmonary function test (PFT) and diffusing capacity of the lungs for carbon monoxide (DLCO) evaluation, and a hemogram were performed for all of the participating patients. In all cases diagnosed with sarcoidosis by EBUS or other methods, a post-diagnosis tuberculin skin test (TST), biochemical blood tests (angiotensin-converting enzyme [ACE] and serum calcium levels), measurements of 24-hour urinary calcium level, erythrocyte sedimentation rate (ESR) and C-reactive protein, a standard clinical evaluation including tests for inflammation markers, eye and cardiology examinations were performed.

All of the patients who met the inclusion criteria underwent convex probe EBUS-TBNA hilar and mediastinal lymph node sampling. Written, informed consent was obtained from all of the participants. The procedure was performed orotracheally with the patient in the supine

position under conscious sedation using an intravenous administration of midazolam and local anesthesia. A 7.5 MHz BF-UC160F convex probe bronchoscope (Olympus Corp., Tokyo, Japan) and EU C2000 processor (Olympus Corp., Tokyo, Japan) was used for EBUS procedure. The lymph nodes were defined according to the regional lymph node classification system developed by Mountain.<sup>[6]</sup> The lymph nodes numbered 2, 4, 7, 10 and 11 were systematically evaluated and the lymph node sizes were recorded. The procedure was performed using a 22-gauge NA-201SX-4022-C needle. Short axis diameter, characteristics of the margins, echogenicity, shape of the lymph nodes, lymph node station and number of passes were recorded for each lymph node detected. The EBUS-TBNA material was spread on slides and fixed with 95% alcohol, and the remainder of the material was prepared for a cell block in 95% alcohol and sent to the pathology laboratory. Material retrieved for a differential diagnosis of tuberculosis was sent to the microbiology laboratory for direct acid-fast bacilli (AFB) examination and mycobacterium culture. The diagnosis of sarcoidosis was confirmed based on a histopathological detection of granuloma, epithelioid histiocytes, multinucleated giant cells, the absence of direct AFB, lack of growth in mycobacterial culture, and exclusion of other granulomatous diseases. Mediastinoscopy and other invasive procedures for definitive diagnosis were recommended in patients for whom a histopathological diagnosis could not be made with EBUS-TBNA. The diagnostic value, sensitivity, specificity, and negative and positive predictive values of EBUS were calculated.

## RESULTS

During the study period, EBUS-TBNA was performed in 107 cases, and transesophageal endoscopic ultrasound with fine needle aspiration (EUS-FNA) was performed for 1 patient. As a result of the tests, 4 patients who received a non-sarcoidosis (tuberculosis) diagnosis were excluded from the study. Three of the 4 cases were diagnosed as tuberculosis based on a finding of granulomatous inflammation without necrosis using EBUS-TBNA and as a result of the regression of adenopathies with tuberculosis treatment, and the fourth patient was diagnosed based on AFB culture positivity of lymph node aspirate. The remaining 104 patients were diagnosed as sarcoidosis and these patients were included in the study. The diagnosis of sarcoidosis was established in 97 patients (93.3%) with EBUS-TBNA/EUS-FNA. In the remaining 7 patients, sarcoidosis was diagnosed in 6 cases using mediastinoscopy and in 1 patient with a right supraclavicular lymph node biopsy. EBUS-TBNA successfully diagnosed 1 patient as stage 0, 82 (97.6%) of the 84 patients ultimately diagnosed as stage 1, and 13 (68.4%) of 19 stage 2 cases. The stage of the disease did not significantly change the rate of effective diagnosis with EBUS ( $p>0.05$ ). In all, 28.8% ( $n=30$ ) of the patients were male and 71.2% ( $n=74$ ) were female. The mean age was  $44.3\pm 13.1$  years (min-max: 20–76 years). There was no significant statistical relationship between age and

**Table 1.** Distribution of extrapulmonary comorbidities

Involvement	n	%
Erythema nodosum	22	21.2
Hepatomegaly	8	7.7
Skin (excluding erythema nodosum)	5	4.8
Uveitis	5	4.8
Splenomegaly	4	3.8
Peripheral lymph node	2	1.9
Parotitis	1	1
Facial paralysis	1	1

gender and the diagnostic efficiency of EBUS ( $p>0.05$ ).

Eleven (10.5%) patients were asymptomatic. Among the symptomatic patients, the most common symptom was cough, followed by shortness of breath (46.2%,  $n=48$ ), fatigue (29.8%,  $n=31$ ), and joint pain (26.9%,  $n=28$ ). There was no statistically significant difference between the symptoms or duration of symptoms and the diagnostic efficiency of EBUS ( $p>0.05$ ). Extrapulmonary involvement was found in 46.1% ( $n=48$ ) of the patients. Erythema nodosum (21.1%,  $n=22$ ) was the most common indication of extrapulmonary involvement (Table 1). No statistically significant difference was observed between extrapulmonary involvement and the diagnostic efficiency of EBUS ( $p>0.05$ ).

TST results were negative in 98% and ACE levels were elevated in 39.4% of the patients. The mean ACE level was  $57.9\pm 42.5$  U/L (min-max: 10–191 U/L). The blood calcium level was high in 3.8% ( $n=4$ ) of the cases and the mean value was  $9.6\pm 0.9$  mg/dL (min-max: 6.02–11.8 mg/dL). The 24-hour urinary calcium level was high in 11.5% ( $n=12$ ) and the mean measurement was  $185.6\pm 131.7$  mg/24 hours (min-max: 3.8–714 mg/24 hours). An increased ESR was detected in 57.7% ( $n=60$ ) cases, and the mean ESR was  $35.9\pm 28.6$  mm/hour (min-max: 4–104 mm/hour). A positive correlation was found between the ACE level and the diagnostic efficiency of EBUS ( $p=0.013$ ).

**Table 3.** Distribution of lymph nodes sampled using EBUS-TBNA

Localization	n	%
Subcarinal-7	98	40
Right lower paratracheal-4R	68	28
Left interlobar-11L	50	21
Right interlobar-11R	19	8
Left lower paratracheal-4L	6	3
Total	241	100

EBUS-TBNA: Endobronchial ultrasonography-transbronchial needle aspiration.

PFT results indicated that there was respiratory dysfunction in 22.2% of the patients, categorized as restrictive (12.5%,  $n=13$ ), obstructive (7.7%,  $n=8$ ), or a mixed pattern (2%,  $n=2$ ). When analyzed by stage, respiratory dysfunction was present in 20.3% ( $n=17$ ) of stage 1 and 31.6% ( $n=6$ ) of stage 2 cases. DLCO testing revealed diffusion disorder in 20.2% ( $n=21$ ) of the patients, with a mean DLCO value of  $91\pm 23.8$  (min-max: 18–181). DLCO/alveolar volume measure was normal or high in 85.6% of the patients ( $n=89$ ) and low in 14.4% ( $n=15$ ). The mean DLCO/alveolar volume value was  $96\pm 21.5$  (min-max: 22–170) (Table 2). There was no statistically significant relationship between PFT and DLCO and the diagnostic efficiency of EBUS ( $p>0.05$ ).

Material was obtained with EBUS from a total of 241 lymph nodes from 103 patients. When the lymph nodes were evaluated according to their location, 98 (40%) of the 241 were subcarinal, 68 (28%) were in the right lower paratracheal region, 50 (21%) in the left interlobar region, 19 (8%) in the right interlobar, and 6 (3%) in the left lower paratracheal region (Table 3). The diagnostic efficiency of EBUS for paratracheal lymph nodes was found to be statistically significant ( $p=0.013$ ). The shape, echogenicity, and characteristics of the margins of lymph nodes were also evaluated using EBUS. The nodes were round in shape in 54% ( $n=130$ ), multiple conglomerate configurations in

**Table 2.** Patient pulmonary function test and diffusing capacity of the lungs for carbon monoxide (single breath) results according to stage

	Stage 0 (n=1)	Stage 1 (n=84)	Stage 2 (n=19)	Total (n=104)
	n (%)	n (%)	n (%)	n (%)
<b>Pulmonary function test</b>				
Normal	1 (1)	67 (79.8)	13 (68.4)	81 (77.8)
Obstruction	–	6 (7.1)	2 (10.5)	8 (7.7)
Restriction	–	10 (11.9)	3 (15.7)	13 (12.5)
Mixed	–	1 (1.2)	1 (5.4)	2 (2)
<b>Diffusing capacity of the lungs for carbon monoxide (single breath)</b>				
Decreased	1 (1)	13 (15.4)	7 (36.8)	21 (20.2)
Normal	–	67 (79.8)	11 (57.9)	78 (75)
Increased	–	4 (4.8)	1 (5.3)	5 (4.8)

40% (n=97), hypoechoic in 46.4% (n=112), heterogeneous in 27.3% (n=66), isoechoic in 23.2% (n=56), prominent margins in 95.4% (n=230), and indistinct margins in 4.6% (n=11) of the cases (Table 4). No statistically significant correlation was found between the size, shape, echogenicity, or marginal features of lymph nodes and the diagnostic efficiency of EBUS ( $p>0.05$ ).

A total of 241 lymph nodes in 103 patients were sampled using EBUS. The mean number of lymph nodes per patient was 2.33. A total of 632 aspiration biopsies were performed from 241 lymph nodes. The mean number of aspirations performed per lymph node was 2.62, and 6.13 aspirations per patient (Table 5). The diagnostic efficiency of

EBUS significantly increased from 1 to 2 passes ( $p=0.004$ ) and from 2 to 3 passes per lymph node ( $p=0.004$ ). The increase in the number of sampled lymph node stations did not result in a significant increase in the diagnostic efficiency of EBUS ( $p>0.05$ ).

The cytological evaluation of the EBUS lymph node samples revealed granulomatous disease localized in right lower paratracheal lymph nodes in 73.6% (n=50), left lower paratracheal lymph nodes in 83.3% (n=5), subcarinal lymph nodes in 62.2% (n=61), right interlobar lymph nodes in 52.7% (10), and left interlobar lymph nodes in 56% (28) of the cases (Table 6). The use of a common cell block for lymph node samples with negative smear results

**Table 4.** Distribution of morphological characteristics of lymph nodes sampled using EBUS-TBNA by location

	4R	4L	7	IIR	IIL
	n (%)	n (%)	n (%)	n (%)	n (%)
<b>Shape</b>					
Round	41 (63.1)	3 (50)	39 (39.8)	9 (47.4)	38 (76)
Multiple conglomerate	23 (35.4)	3 (50)	58 (59.2)	4 (21.1)	9 (18)
Oval	1 (1.5)	–	1 (1)	6 (31.5)	3 (6)
<b>Echogenicity</b>					
Hypoechoic	41 (63.1)	3 (50)	31 (31.6)	12 (63.2)	25 (50)
Heterogeneous	9 (13.8)	1 (16.7)	45 (45.9)	–	11 (22)
Isoechoic	14 (21.6)	2 (33.3)	21 (21.4)	7 (36.8)	12 (24)
Hyperechoic	1 (1.5)	–	1 (1)	–	2 (4)
<b>Margins</b>					
Indeterminate	2 (2.9)	–	6 (6.2)	1 (5.3)	2 (4)
Prominent	66 (97.1)	6 (100)	92 (93.8)	18 (94.7)	48 (96)

EBUS-TBNA: Endobronchial ultrasonography-transbronchial needle aspiration.

**Table 5.** Dimensions of lymph nodes measured with EBUS and mean ( $\pm$ SD) number of passes performed

Lymph node	Size	Diameter	Number of passes
	Mean $\pm$ SD	Minimum-Maximum	Mean $\pm$ SD
Subcarinal-7	2.06 $\pm$ 0.93 cm	1–4 cm	2.88 $\pm$ 0.59
Right lower paratracheal-4R	1.98 $\pm$ 0.89 cm	1–5 cm	1.75 $\pm$ 1.4
Left lower paratracheal-4L	2.16 $\pm$ 1.60 cm	1–5 cm	1.83 $\pm$ 0.75
Right interlobar-IIR	1.58 $\pm$ 0.47 cm	1–2.5 cm	2.11 $\pm$ 0.45
Left interlobar-IIL	1.63 $\pm$ 0.5 cm	0.5–3 cm	2.47 $\pm$ 0.61

EBUS: Endobronchial ultrasonography; SD: Standard deviation.

**Table 6.** Smear results by location of lymph nodes sampled using EBUS-TBNA

	4R	4L	7	IIR	IIL
	n (%)	n (%)	n (%)	n (%)	n (%)
Granulomatous disease	50 (73.6)	5 (83.3)	61 (62.2)	10 (52.7)	28 (56)
Lymphocytes	9 (13.2)	1 (16.7)	26 (26.5)	7 (36.8)	9 (18)
Inadequate material	9 (13.2)	–	11 (11.3)	2 (10.5)	13 (26)

EBUS-TBNA: Endobronchial ultrasonography-transbronchial needle aspiration.

**Table 7.** Results of 10 studies where EBUS was performed with the initial diagnosis of sarcoidosis

Author	Type of study	Number of patients	Stage	Median (range) size of lymph nodes (mm)	Number of lymph nodes	EBUS diagnostic sensitivity %
Garwood <sup>[7]</sup>	Prospective	50	0–4	4–40 (16)	82	85
Plit <sup>[8]</sup>	Retrospective	40	1.2	8–36 (16)	61	84
Wong <sup>[9]</sup>	Prospective	65	1.2	7–37 (20.5)	77	87.5
Tremblay <sup>[10]</sup>	Prospective	24	1.2	16.5	4 (Mean)	83.3
Oki <sup>[11]</sup>	Prospective	62	1.2	10–33 (16.2)	123	94
Nakajima <sup>[12]</sup>	Retrospective	38	1.2	7.3–30	51	91.4
Sun <sup>[13]</sup>	Prospective	120	1.2	6–32 (16)	284	93.6
Çağlayan <sup>[14]</sup>	Prospective	72	1.2	19.6	121	79.5
Gupta <sup>[15]</sup>	Prospective	62	1.2	–	–	74.5
Navani <sup>[16]</sup>	Prospective	40	1.2	10–45 (24)	71	85

EBUS: Endobronchial ultrasonography.

was found to be statistically significant in the identification of granulomatous inflammation ( $p < 0.001$ ).

## DISCUSSION

The diagnosis of sarcoidosis uses a histopathological demonstration of epithelioid cell noncaseating granulomas together with clinical and radiological findings and the exclusion of other similar diseases.<sup>[1]</sup> In 95% of patients, diagnosis is established by pulmonary physicians due to intrathoracic involvement. Pulmonary physicians often use bronchoscopic techniques, such as endobronchial mucosa biopsy, TBLB, and TBNA for diagnosis because of their high diagnostic efficiency. The role of bronchoscopy in the diagnosis of sarcoidosis with EBUS, which is a minimally invasive method that allows real-time sampling of mediastinal and hilar lymph nodes, has become more prominent. In our study, 103 patients with mediastinal and/or hilar lymphadenopathy and a pre-diagnosis of sarcoidosis were diagnosed with EBUS-TBNA and 1 patient underwent EUS-FNA. The sensitivity of EBUS-TBNA in this study was determined to be 92.3%, the specificity 100%, and the positive predictive value 100%. The diagnostic value of EBUS-TBNA was 100% (1/1) in stage 0 cases, 97.6% (82/84) in stage 1 cases, and 68.4% (13/19) in stage 2 cases.

In the literature, the reported diagnostic value of EBUS-TBNA in sarcoidosis has ranged between 74.5% and 94% (Table 7).<sup>[7–16]</sup> Garwood et al.<sup>[7]</sup> performed EBUS in 50 patients with the initial diagnosis of sarcoidosis, and a diagnosis of 41 (85%) patients could be made using EBUS-TBNA. The success was greater in detecting stage 1 patients (94%) relative to stage 2 patients (80%).<sup>[7]</sup> Similarly, in our study, the rate of diagnosis was greater in stage 1 patients relative to stage 2 patients (97.6% vs 68.4%), without any statistically significant intergroup difference ( $p > 0.05$ ). Wong et al.<sup>[9]</sup> performed EBUS-TBNA in 65 patients, and 56 patients were diagnosed with sarcoidosis; the diagnostic accuracy of EBUS-TBNA was 87.5%. Tremblay et al.<sup>[10]</sup> examined the diagnostic efficiency of TBNA

with a 19-gauge needle in 50 patients with suspected sarcoidosis and performed EBUS-TBNA in 24 and TBNA in 26. The diagnostic sensitivity of EBUS-TBNA was determined to be 83.3%, and the sensitivity of TBNA alone was 60.9%. Oki et al.<sup>[11]</sup> reported that the use of TBLB after EBUS-TBNA in 62 patients suspected to have sarcoidosis resulted in a finding of epithelioid cell granuloma without caseating necrosis in 51 (94%) patients. EBUS-TBNA diagnosed sarcoidosis in 37 (97%) of 38 stage 1 patients and 14 (88%) of 16 stage 2 patients. The sensitivity and specificity of EBUS-TBNA was 94% and 100%, respectively. TBLB diagnosed sarcoidosis in 19 (37%) of 52 patients. Nakajima et al.<sup>[12]</sup> consecutively performed bronchoalveolar lavage, TBLB, and EBUS-TBNA in 38 patients during the same session. Fourteen patients (40%) were diagnosed with TBLB and 32 patients with EBUS-TBNA, with a sensitivity of 91.4%. In a study of 120 patients conducted by Sun et al.<sup>[13]</sup> granulomatous inflammation was detected in 104 (93.6%) of 111 patients diagnosed with sarcoidosis using EBUS-TBNA a diagnostic sensitivity of 93.6%, specificity of 100%, and positive and negative predictive values of 100% and 94.3%, respectively, were calculated for EBUS-TBNA.

Çağlayan et al.<sup>[14]</sup> studied 72 patients who underwent EBUS-TBNA and arrived at the diagnosis of sarcoidosis in 35 patients and tuberculosis in 16; the sensitivity of EBUS-TBNA was calculated as 79.5% (74.1% for stage 1 and 92.3% for stage 2). Gupta et al.<sup>[15]</sup> randomized 130 patients into EBUS-TBNA ( $n=68$ ) and conventional TBNA ( $n=62$ ) groups, and all of the patients underwent endobronchial mucosa biopsy and TBLB. Granulomatous inflammation was demonstrated in 30 patients who underwent TBNA, and the rate of diagnosis was estimated as 48.4%. EBUS-TBNA revealed granulomatous inflammation in 41 patients, and the rate of diagnosis was 74.5%. When EBUS-TBNA was combined with endobronchial mucosa biopsy and TBLB, the rate of diagnosis was 92.7%. Navani et al.<sup>[16]</sup> performed EBUS-TBNA followed by TBLB and endobronchial mucosa biopsy in 40 suspected sarcoidosis patients. The sensitivity of EBUS-TBNA was found to be

85% (89% in stage 1 and 78% in stage 2). Plit et al.<sup>[8]</sup> found that among 40 patients with suspected sarcoidosis EBUS-TBNA established the diagnosis in 84% (n=31/37), TBLB in 78% (n=29/37), and endobronchial mucosa biopsy in 27% (n=10/37). EBUS-TBNA established the diagnosis in 80% of stage 1 and 86% of stage 2 patients.

In our study, a total of 241 lymph nodes were sampled using EBUS. The most frequently sampled lymph nodes were subcarinal lymph nodes (n=98, 40%) with a median diameter of 20.6 mm, followed by right lower paratracheal lymph nodes (n=68, 28%) with a median diameter of 19.8 mm. Similarly, the most frequently cited samples in the literature are subcarinal and right lower paratracheal lymph nodes.<sup>[8,9,11,12]</sup> Wong et al.<sup>[9]</sup> used EBUS to measure 67 mediastinal and 10 hilar lymph node samples and reported a median diameter of 20.5 mm. The most frequently sampled among the 77 lymph nodes were subcarinal lymph nodes (n=29, 38%) with a median diameter of 22.4 mm, followed by right lower paratracheal lymph nodes (n=16, 21%) with a median diameter of 15.8 mm. Oki et al.<sup>[11]</sup> sampled 123 lymph nodes with EBUS-TBNA and found a mean diameter of 16.2 mm. The most often sampled were right lower paratracheal and subcarinal lymph nodes. A total of 409 lymph nodes were sampled in a study conducted by Ozgul et al.,<sup>[17]</sup> including 158 subcarinal and 84 right lower paratracheal lymph nodes with a median diameter varying between 5 and 70 mm. Thirty (7.3%) lymph nodes had a short axis of less than 1 cm, while 379 (92.7%) lymph nodes above 1 cm were found.<sup>[17]</sup> In our study, subcarinal and paratracheal lymph nodes were most frequently sampled and the diagnostic accuracy of paratracheal lymph nodes was statistically significant (p=0.013). There was no statistically significant relationship between lymph node size and the diagnostic efficiency of EBUS (p>0.05). The use of a common cell block to show granulomatous inflammation in smear- negative lymph node samples was statistically significant (p<0.001).

In the present study, a total of 632 aspirations were performed from 241 lymph nodes in 130 patients using EBUS-TBNA. The mean number of lymph nodes per patient was 2.33, the number of aspirations per lymph node was 2.62, and the number of aspirations per patient was 6.13. Wong et al.<sup>[9]</sup> reported 1.2 lymph nodes sampled per patient. Garwood et al.<sup>[7]</sup> noted that the rate of diagnosis per lymph node exceeded 80% after 5 passes; however, it did not increase further after 7 passes. Sun et al.<sup>[13]</sup> found that the diagnostic efficiency of EBUS-TBNA was related to the stage of the disease, but the number of sampled lymph node stations was found to be unrelated to the number of passes per patient. The length of the short axis of the node, more than 1 pass per lymph node, and the stage of the disease were determined to be independent risk factors associated with positive pathology. Diagnostic efficiency plateaued at 3 aspirations per lymph node and decreased after 5 aspirations. Çağlayan et al.<sup>[14]</sup> studied 208 passes performed on 121 lymph nodes of 72 patients. The median number of passes per patient was

2.88, and the median pass count per lymph node was 1.71. The sensitivity was 72.7% when sampling was performed only from a single lymph node station and increased to 85.3% in samplings made from multiple lymph node stations. When only a single pass per patient was performed, the sensitivity was 50%, but when more than one pass was performed, the sensitivity increased to 83%. In our study, as the number of passes per lymph node increased, the diagnostic efficiency of EBUS showed a statistically significant increase (p=0.002). However, the increase in the number of lymph nodes in the sample did not increase the diagnostic efficiency of EBUS (p>0.05).

Sarcoidosis can be seen in both sexes, and in all races and age groups. In our country, the average patient age was 44 years in a study performed by a study group of the Tuberculosis and Thorax Association.<sup>[18]</sup> Two-thirds of their study group was female, and the onset of sarcoidosis in women was found to be 10 years earlier than men. Similarly, in our study, 71.2% of our patients were female with an average age of 44.3 years. The symptom distribution of our patients was compared with the study of TTD Sarcoidosis Study Group. In our study, the mean ACE level was 57.9±42.5 U/L (min-max: 10-191 U/L). A positive correlation was found between the ACE value and the diagnostic efficiency of EBUS (p=0.013). The sensitivity of ACE measurement is low, however, so it is not diagnostic. The sensitivity and specificity rates have been reported as was 57% and 90%, respectively.<sup>[2]</sup>

In conclusion, EBUS-TBNA has high sensitivity and specificity in demonstrating granulomatous inflammation in patients with suspected sarcoidosis, and this diagnostic capability can make other invasive procedures unnecessary.

#### Ethics Committee Approval

Approved by the local ethics committee.

#### Informed Consent

Prospective study.

#### Peer-review

Internally peer-reviewed.

#### Conflict of Interest

None declared.

#### Authorship Contributions

Concept: B.N.Ç., S.Ş.C.; Design: B.S., Ö.Ç.; Data collection &/or processing: F.K.; Analysis and/or interpretation: B.Ç., S.Ş.C.; Literature search: Ö.Ç., F.K.; Writing: Ö.Ç., S.Ş.C.; Critical review: B.Ç., B.S.

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## Sarkoidozda Endobronşiyal Ultrasonografinin Tanı Değeri ve Tanıyla İlişkili Faktörler

**Amaç:** Çalışmamızda akciğer sarkoidozu olan olgularda endobronşiyal ultrasonografinin (EBUS) tanı değerini ve tanıyla ilişkili faktörleri araştırmayı amaçladık.

**Gereç ve Yöntem:** İleriye yönelik olarak planlanan bu çalışmada, Ocak 2014 ile Eylül 2015 tarihleri arasında polikliniğimize başvuran, klinik ve radyolojik olarak akciğer sarkoidozu düşünülen, toraks bilgisayarlı tomografisinde (BT) büyümüş hiler/mediastinal lenf bezi saptanarak EBUS transbronşiyal iğne aspirasyonu (TBİA) yapılan olguları inceledik.

**Bulgular:** Çalışma periyodu içerisinde 107 hastaya EBUS-TBİA, bir hastaya endoskopik ultrason eşliğinde transözofajial iğne aspirasyonu (EUS-TÖİA) yapıldı. Sarkoidoz dışı tanı (tüberküloz) alan dört hasta çalışmadan çıkarıldı. Sarkoidoz tanısı alan 104 hastanın %28.8'ini erkek, %71.2'sini kadın hastalar oluşturmaktaydı. Yaş ortalaması 44.3±13.1 yıl saptandı. Yüz dört hastanın 96'sına (%92.3) EBUS-TBİA, bir hastaya (%1) EUS-TÖİA ile sarkoidoz tanısı kondu. Tanı elde edilemeyen yedi hastanın altısına mediastinoskopi bir hastaya sağ supraklavikular lenf nodu biyopsisi ile sarkoidoz tanısı kondu. EBUS-TBİA'nın sensitivitesi %92.3 spesifitesi %100 bulundu.

**Sonuç:** Sarkoidoz şüphesi olan hastalarda granümatöz enflamasyonu göstermede EBUS-TBİA yüksek sensitivite ve spesifiteye sahip olup, yüksek tanı oranı ile ileri invaziv işlemleri gereksiz kıldığı sonucuna varılmıştır.

**Anahtar Sözcükler:** Endobronşiyal ultrasonografi; sarkoidoz; tanı değeri.