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ORIGINAL INVESTIGATION

# The Role of Endobronchial Biopsy in the Diagnosis of Pulmonary Sarcoidosis

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Abstract

**OBJECTIVES:** This study aimed to investigate the additional diagnostic value of endobronchial biopsy (EBB) in the diagnosis of pulmonary sarcoidosis.

**MATERIALS AND METHODS:** This retrospective cross-sectional study included 59 patients with a preliminary diagnosis of sarcoidosis who were admitted to the Pulmonary Diseases Outpatient Clinic of a tertiary healthcare center between January 2005 and October 2012. The socio-demographic characteristics of the patients as well as clinical and radiological findings were recorded. All patients, irrespective of the presence of an endobronchial lesion (EBL), underwent fiberoptic bronchoscopy (FOB); two to four specimens were taken using EBB from the carina of the right middle lobe in the patients with EBL.

**RESULTS:** Of the patients, 39 (66.1%) had normal bronchoscopic findings, while 5 had EBL. Diagnosis was based on EBB in 11 patients (18.6%). Six patients (15.3%) with normal bronchial mucosae were pathologically diagnosed by EBB. There was no statistically significant relationship between the diagnostic ratio of EBB and disease stage, extrapulmonary involvement, FOB findings, elevated lymphocyte rate in bronchoalveolar lavage (≥ 13%), a CD4/CD8 ratio of ≥ 3.5, and serum angiotensin-converting enzyme (ACE) level ($p > 0.05$).

**CONCLUSION:** EBB not only offers the advantage of a high diagnostic ratio in patients with mucosal abnormalities but also contributes to pathological diagnosis in patients with normal mucosa. We recommend using EBB to support diagnosis with a low complication rate for patients undergoing FOB with a preliminary diagnosis of sarcoidosis in healthcare centers, where endobronchial ultrasound (EBUS) is unavailable.

**KEYWORDS:** Diagnosis of sarcoidosis, fiberoptic bronchoscopy, endobronchial biopsy

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## INTRODUCTION

Sarcoidosis is a systemic granulomatous disease of unknown etiology that primarily affects the lungs and lymphatic system. Diagnosis is based on a compatible clinical presentation and imaging, as well as the presence of non-caseating granulomas in biopsy specimens, by excluding other causes of granulomatous diseases [1,2]. Fiberoptic bronchoscopy (FOB), which involves the acquisition of tissue specimens to eliminate other diseases, is a relatively simple procedure with a lower complication rate than other surgical procedures and is the primary diagnostic tool for sarcoidosis patients [1]. A pathological diagnosis can be achieved with the help of transbronchial lung biopsy (TBLB) and/or transbronchial needle aspiration (TBNA) of mediastinal and hilar lymph nodes. In addition, a compatible clinical presentation, imaging with lymphocytic alveolitis, and an increased ratio of CD4/CD8 lymphocytes support pulmonary sarcoidosis diagnosis in patients without a histopathological confirmation.

Today, with the introduction of real-time endobronchial ultrasound-guided TBNA (EBUS-TBNA) and transesophageal endoscopic ultrasound-guided fine needle aspiration, a higher number of patients is diagnosed with sarcoidosis [3-5]. Currently, endobronchial ultrasound (EBUS) is extensively used for mediastinal sampling; however, conventional bronchoscopic techniques are still the first choice in the diagnostic algorithm of sarcoidosis cases in many centers [1].

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The diagnostic efficiency of TBLB is particularly affected by parenchymal involvement as evidenced by radiographic studies, and patient compliance is a must for this procedure. On the other hand, TBLB may lead to serious complications including bleeding and pneumothorax. The diagnostic value of endobronchial biopsy (EBB) is high in the presence of bronchial mucosal lesions, although EBB is recommended for patients without visible mucosal lesions [6,7].

In this study, we investigated the additional diagnostic value of EBB, which is a relatively simple diagnostic procedure with a low complication rate, during FOB in the diagnosis of pulmonary sarcoidosis.

## MATERIALS AND METHODS

### Study Population

This retrospective cross-sectional study included 59 patients with a preliminary diagnosis of sarcoidosis who were admitted to the Pulmonary Diseases Outpatient Clinic of a tertiary healthcare center between January 2005 and October 2012 (Figure 1). The study was approved by the Celal Bayar University Scientific Research Ethics Committee in Manisa (07.03.2011/0057), and a signed consent form was obtained from each patient before the procedure. None of the patients were on systemic steroid therapy or antibiotics. Patients who were previously diagnosed with sarcoidosis and received treatment or were under follow-up were excluded. Stage 0 patients were also excluded.

### Assessment

The demographic characteristics of the patients were recorded. Chest X-ray images and computed tomography (CT) scans were obtained. The presence of hilar and mediastinal lymphadenopathy and extrapulmonary lymphadenopathy (LAP) were noted. Patients with suspected extrapulmonary sarcoidosis by clinical and laboratory findings were evaluated for extrapulmonary involvement. Serum angiotensin-converting enzyme (ACE) levels, 24-h urinary $Ca^{+2}$ output, tuberculin skin test (TST), and pulmonary function test (PFT) results were also recorded. The findings of PFT used to identify obstructive and restrictive lung diseases were normal. Based on chest X-ray radiological findings, patients were staged as 0: No radiographic abnormality (adenopathy or infiltrates), I: bilateral hilar adenopathy without interstitial parenchymal infiltrates, II: bilateral hilar adenopathy with interstitial parenchymal infiltrates, III: interstitial parenchymal infiltrates without hilar adenopathy, and IV: pulmonary fibrosis [1]. Radiologic staging was performed according to chest computed tomography findings.

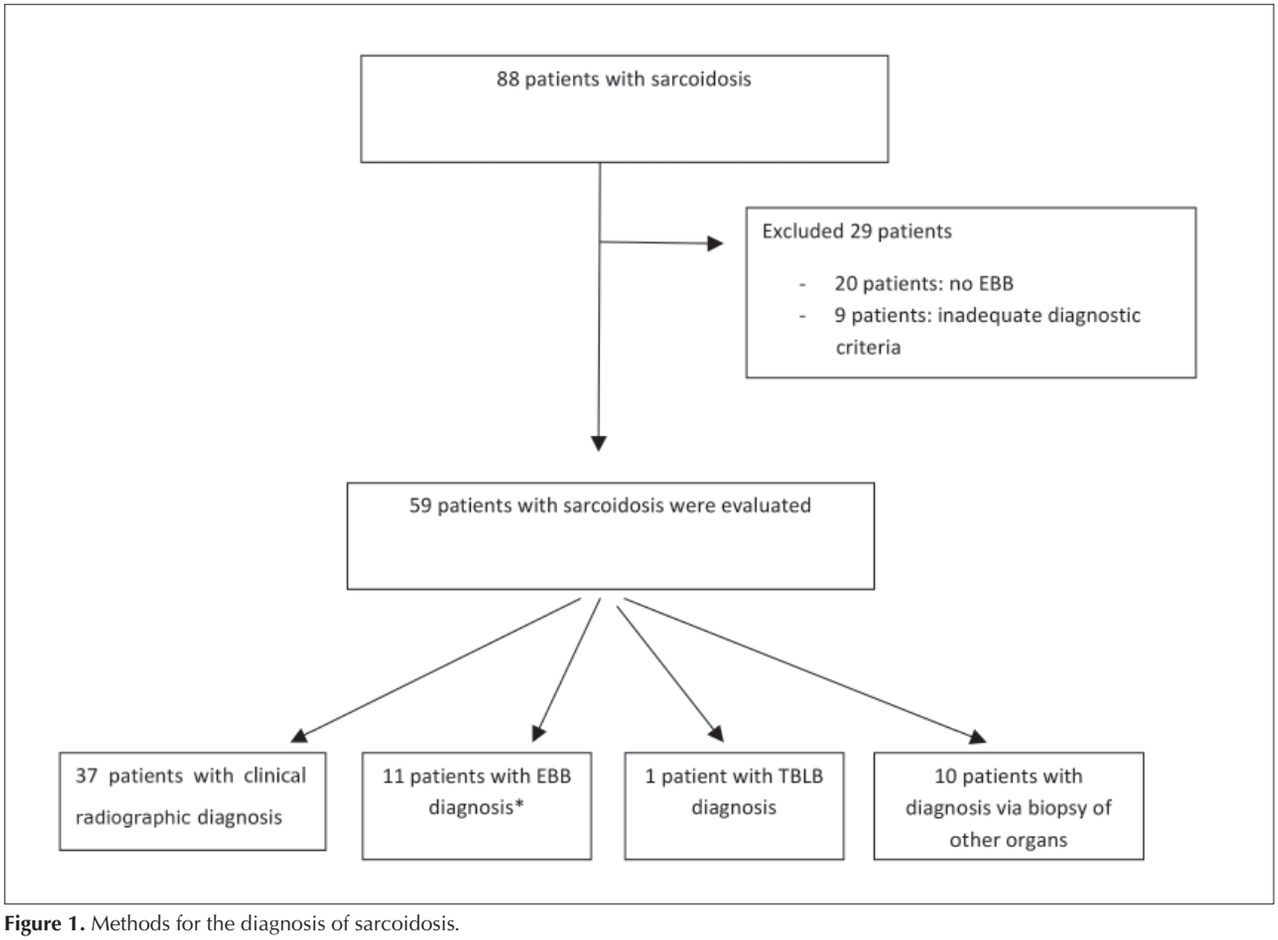


**Figure 1.** Methods for the diagnosis of sarcoidosis.
*The pathologic diagnosis was done with both EBB and TBLB in one patient.
EBB: endobronchial biopsy; TBLB: transbronchial lung biopsy.

**Bronchoscopy**

Fiberoptic bronchoscopy was performed under local anesthesia with midazolam and lidocaine. Bronchoalveolar lavage (BAL) was performed in the right middle lobe using 20 cc portions of sterile saline with a total amount of 120 cc. Patients with left lung involvement underwent BAL through the left lingula. TBNA was performed with a 22-gauge needle in patients with mediastinal and hilar LAP, when present in the CT scan. Afterwards, transbronchial lung biopsies were performed in parenchymal involvement areas. Two to four EBB specimens were taken from the abnormal mucosae; if abnormal bronchoscopic findings were not present, two to four additional EBB specimens were taken from the main carina and right middle-lower lobe carinas. FOB findings were classified as a: normal, b: blunt carina, c: extrinsic compression, d: endobronchial lesion, e: submucosal involvement, and f: hypervascularity. TBLB and TBNA could not be performed in all patients due to high complication rates, patient unwillingness, incompliance or procedure-related hypoxia. CD4/CD8 ratio was not studied in a group of patients due to the unavailability of laboratory facilities.

**Diagnostic Criteria**

The pathological diagnostic criterion was the presence of non-caseating epitheloid cell granulomas in biopsy specimens taken during FOB. In patients with clinical and imaging findings compatible with sarcoidosis without non-caseating epitheloid cell granulomas, positive diagnostic criteria were as follows: a: bilateral hilar LAP, b: elevated serum ACE and 24-hour urinary $Ca^{+2}$ output, c: negative tuberculin skin test (TST), d: lymphocytic alveolitis or increased CD4/CD8 lymphocytes. These patients were included in the group in which diagnoses were based on clinical and radiological data.

The histopathological examination of bronchoscopic specimens eliminated the presence of tuberculosis in these patients by microbiological inspection.

**Statistical Analysis**

Statistical analyses were performed with Statistical Package for the Social Sciences 15.0 (SPSS, Inc., Chicago, USA). Descriptive data were expressed as median with range or mean with standard deviation, according to the distribution of the parameters. Disease stage, extrapulmonary involvement, FOB findings, BAL lymphocyte predominance, CD4/CD8 ratio of ≥ 3.5 and blood ACE levels were compared with EBB. The chi-square test was used and p values < 0.05 were considered to be statistically significant.

**RESULTS**

Fifty-nine patients who were diagnosed with sarcoidosis were evaluated between January 2005 and October 2012. Forty-eight patients (81.4%) were females and 11 (18.6%) were males. The mean age was 45.9 ± 11.2 (range 24 to 66) years. Forty-four patients (74.6%) were housewives. Clinical characteristics of the patients are shown in Table 1.

**Table 1.** Clinical characteristics of the patients

| | | n (%) |
|---|---|---|
| TST | Not yet | 11 (18.6) |
| | Anergic | 37 (61.7) |
| | to 10 mm | 4 (6.8) |
| | 11 to 15 mm | 1 (1.7) |
| | > 15 mm | 6 (10.2) |
| Pulmonary function test | Not yet | 19 (32.2) |
| | Normal | 30 (50.8) |
| | Obstructive disorder | 4 (6.8) |
| | Restrictive disorder | 6 (10.2) |
| Disease stage | I | 18 (30.5) |
| | II | 38 (64.4) |
| | III | 2 (3.4) |
| | IV | 1 (1.7) |
| Others organ involvement | No involvement | 33 (55.9) |
| | Erythema nodosum | 20 (33.9) |
| | Uveitis | 4 (6.8) |
| | Other | 2 (3.4) |
| Serum ACE level | Not yet | 18 (30.5) |
| | Normal | 13 (22.0) |
| | Abnormal | 28 (47.5) |
| 24-h urinary Ca+2 | Not yet | 43 (72.9) |
| | Normal | 14 (23.7) |
| | Abnormal | 2 (3.4) |
| Diagnostic methods | Clinico-radiographic | 37 (62.7) |
| | EBB | 11 (18.6) |
| | TBLB | 1 (1.7) |
| | Other organ biopsy | 10 (16.9) |

TST: tuberculin skin test; ACE: angiotensin-converting enzyme; EBB: endobronchial biopsy; TBLB: transbronchial lung biopsy.

All patients underwent FOB. Thirty-nine (66.1%) had normal bronchoscopic findings, while EBL was observed in 5 patients. These five patients were all in stage II. BAL was performed in all 59 patients. CD4/CD8 ratio was studied in 44 patients. Ten patients underwent TBLB, while 46 underwent TBNA. EBB was performed in all 59 patients. The bronchoscopic findings of the patients are presented in Table 2. No complications related to the diagnostic procedures were observed.

Twenty-two patients (37.2%) were diagnosed with sarcoidosis according to the pathological examination. The diagnosis was based on EBB (non-caseating granulomatous inflammation) in 11 patients (18.6%), including EBB plus TBLB in one patient (1.6%), TBLB

**Table 2.** Bronchoscopic findings of the patients

| | | n (%) |
|---|---|---|
| FOB findings (n= 59) | No abnormality | 39 (66.1) |
| | Blunt main carina | 6 (10.2) |
| | Extrinsic compression | 7 (11.9) |
| | Endobronchial lesion | 5 (8.5) |
| | Submucosal involvement | 1 (1.7) |
| | Hypervascularity | 1 (1.7) |
| Findings supporting sarcoidosis in BAL (lymphocytic alveolitis or increased CD4/CD8 lymphocytes) (n= 59) | Yes | 48 (81.4) |
| | No | 11 (18.6) |
| Diagnosis with EBB* (n= 59) | Normal bronchial mucosa | 33 (55.9) |
| | Non-caseating granulomatous inflammation | 11 (18.6) |
| | Inflammatory alterations | 15 (25.4) |
| Diagnosis with TBLB *(n= 10) | Yes | 2 (20) |
| | No | 8 (80) |
| CD4/CD8 ratio (n= 44) | ≥ 3.5 | 37 (84.1) |
| | < 3.5 | 7 (15.9) |
| Lymphocyte rate (n= 59) | ≥ 13 | 37 (62.7) |
| | < 13 | 22 (37.3) |

* The pathologic diagnosis was done with both EBB and TBLB in one patient. FOB: fiberoptic bronchoscopy; BAL: bronchoalveolar lavage; EBB: endobronchial biopsy; TBLB: transbronchial lung biopsy.

alone in one patient (1.6%), and pathological specimens from other organs in 10 patients (16.9%). In the remaining 37 patients (62.75%), the diagnosis was based on clinical and radiological findings (Figure 1).

Among the 39 patients with normal bronchoscopic findings, 6 patients (15.3%) had a pathological diagnosis by EBB. The diagnosis was based on EBB in 5 of 20 patients (25%) with abnormal bronchoscopic findings (endobronchial lesion in 3 and mucosal abnormality in 2). However, normal or abnormal bronchoscopic findings did not affect the diagnostic accuracy of EBB (p= 0.369). There was no statistically significant relationship between the diagnostic accuracy of EBB and disease stage, extrapulmonary involvement, FOB findings, lymphocytic alveoli in BAL (≥ 13%), CD4/CD8 ratio of ≥ 3.5, and serum ACE level (p> 0.05). The characteristics of the patients who were diagnosed by EBB are shown in Table 3. There was no statistically significant difference in pulmonary function tests between patients with normal or abnormal bronchoscopic findings (p= 0.166).

The cell distribution of BAL revealed lymphocyte percentages greater than 13 in nine patients (81.8%). Nine patients (100%) in whom CD4/CD8 was studied had a ratio of ≥ 3.5, whereas seven of nine patients (77.7%) in whom serum ACE level was measured had increased levels (Table 3).

Pathological examination of the EBB specimens showed inflammation in 15 patients (25.4%). Nine of these patients (60.0%) were in stage II. Inflammatory alterations in EBB specimens were not associated with disease stage, extrapulmonary involvement, FOB findings, CD4/CD8 ratio of ≥ 3.5, and serum ACE level (p> 0.05).

No statistically significant relationship was observed between disease stage and extrapulmonary involvement, FOB findings, non-caseating granulomatous inflammation in EBB specimens, elevated lymphocyte percentage in BAL (≥ 13%), CD4/CD8 ratio of ≥ 3.5, and serum ACE level (p> 0.05).

**Table 3.** Characteristics of patients who were diagnosed by EBB*

| Disease stage | Other organ involvement | FOB findings | Lymphocyte rate (%) | CD4/CD8 ratio | ACE level | PFT |
|---|---|---|---|---|---|---|
| II | No | EBL | ≥ 13 | 11.00 | Abnormal | Restriction |
| II | No | EBL | < 13% | - | - | Normal |
| I | No | No abnormality | ≥ 13 | 6.00 | Normal | - |
| II | No | Extrinsic compression | ≥ 13 | 17.8 | - | Obstruction |
| II | No | No abnormality | ≥ 13 | 4.00 | Abnormal | Normal |
| I | No | No abnormality | ≥ 13 | - | Abnormal | - |
| II | No | Blunt carina | ≥ 13 | 12.30 | Abnormal | Normal |
| II | Uveitis | EBL | < 13 | 4.00 | Normal | Normal |
| II | Uveitis | No abnormality | ≥ 13 | - | Abnormal | Restriction |
| II | Erythema nodosum | No abnormality | ≥ 13 | 4.49 | Abnormal | Obstruction |
| II | Erythema nodosum | No abnormality | ≥ 13 | 22.00 | Abnormal | Normal |

* p> 0.05, Pearson chi-square. EBB: endobronchial biopsy; FOB: fiberoptic bronchoscopy; ACE: angiotensin-converting enzyme; PFT: pulmonary function test; EBL: endobronchial lesion.

**DISCUSSION**

The diagnostic ratio of EBB has been reported in a wide range for patients with sarcoidosis [3,4,6-9]. This study aimed to investigate the additional diagnostic value of EBB in the diagnosis of pulmonary sarcoidosis. We found the diagnostic accuracy of this technique to be 18.6%. Kiter et al. [8] reported a 50% diagnostic accuracy for EBB, which was considered to be related to the multicenter and retrospective nature of their study. Also, Navani et al. [4], Bjemer et al. [6] and Kieszko et al. [9] diagnosed 11%, 45%, and 40% of their study patients by EBB, respectively [4,6,9]. In another study, in which the majority of patients (64.7%) were Afro-American, Shorr et al. [7] reported that the diagnostic ratio of EBB was 61.8% with an additional diagnostic value of 20.6%. In a multicenter study by Tournoy et al. involving 137 patients with a preliminary diagnosis of sarcoidosis, [3] a total of 121 patients underwent FOB, and a definitive diagnosis was achieved in 42% of these patients. The authors reported that the diagnostic ratios of TBLB, EBB, and TBNA were 54%, 20%, and 31%, respectively.

Although normal bronchial mucosa can be seen in sarcoidosis patients, airway abnormalities have been reported in up to 60% of patients [10]. These abnormalities include mucosal hyperemia or edema, bronchial distortion, bronchial constriction, and granulomas and ulcerations [10]. Shorr et al. [7] found normal airways in 29.4% of patients, while Kiter et al. [8] reported that 37.1% of patients had no airway abnormality, as confirmed by FOB.

In our study, we found normal bronchial mucosa in 39 patients (66.1%). However, we observed abnormal mucosal findings in 33.9% of patients. There was no statistically significant relationship between positive EBB results and normal or abnormal airway anatomy. On the other hand, Shorr et al. [7] observed a significant correlation between positive EBB results and normal or abnormal airway anatomy (p= 0.014). The authors also reported positive EBB results in 75% of patients with abnormal airway anatomy. However, they did not differentiate endobronchial lesions and granulomas. These results can be greatly attributed to the race of the subjects.

Ishii et al. [11] performed TBLB, BAL, and EBB in 18 Japanese patients who were primarily suspected to have sarcoidosis with bronchoscopic normal mucosa findings. The diagnostic ratios of TBLB and EBB were 61.1% (n=11) and 5.5% (n=1), respectively. The authors observed pulmonary involvement in all patients, as confirmed by CT and BAL; however, none of the patients had FOB-related complications. Extrapulmonary involvement was also seen in five patients. The authors concluded that EBB in combination with TBLB did not improve the diagnostic ratio in sarcoidosis patients with normal bronchial mucosae. Pulmonary sarcoidosis with endobronchial involvement was attributed to the race of the subjects. In another study, Shorr et al. [7] reported that the diagnostic ratio of EBB was 30% in patients with normal bronchial mucosae and higher in patients with abnormal bronchial mucosae. In addition, Torrington et al. [12] reported a 2.2 fold higher ratio for the diagnosis of sarcoidosis in Afro-Americans using EBB. Burke et al. [13] reported that a higher diagnostic ratio of EBB was associated with increased granuloma density of bronchial and lung tissues in this patient population. In our study, we achieved a pathological diagnosis of sarcoidosis in 15.3% of patients (n=6/39) with normal bronchial mucosae as assessed by FOB, based on the EBB specimens and the presence of non-caseating granulomas. Differences in the diagnostic ratios of EBB across these studies may be explained by the sample sizes and by the races of the participants.

In our study, pathological examination of the EBB specimens showed inflammatory alterations in 25.4% of patients (n= 15). Despite the lack of non-caseating granulomas, this finding supports the presence of inflammation in sarcoidosis patients. However, this finding alone does not allow us to achieve a pathological diagnosis. In addition, biopsy specimens were likely to be taken in the adjacent sites of granuloma in these patients.

The CD4/CD8 ratio was ≥ 3.5 in all patients who were diagnosed through EBB, while 81.8% of patients had lymphocyte rates of ≥ 13% in BAL and 77.7% of patients had elevated serum ACE levels. These results thus suggest that laboratory test results are supportive for sarcoidosis; however, EBB is useful in the diagnosis of patients with normal bronchial mucosae.

Pulmonary sarcoidosis may be accompanied by obstructive or restrictive lung diseases in a varying range. Granulomatous lesions and bronchial constriction by lymph nodal compression may lead to obstructive lung disease, whereas pulmonary parenchymal disease may result in restrictive lung disease [10]. In our study, 10% of patients (n= 40) had obstructive lung disease, while 15% (n= 40) had restrictive lung disease, as assessed by PFT. There was no relationship between radiological staging and PFT variables. No significant difference in PFT variables was observed among patients with normal or abnormal bronchoscopic findings. A Case Control Etiologic Study of Sarcoidosis (ACCESS) trial demonstrated that 14% of patients had obstructive lung disease, while 30% had restrictive disease patterns [14]. Kieszko et al. [9] found abnormal PFT results in more than half of the patients with EBB positivity. Bjemer et al. [6] reported that the inflammatory activity ratio was higher in European patients with sarcoidosis and that bronchial involvement may worsen the clinical course of the disease, leading to an increased incidence of pulmonary dysfunction. Consistent with these findings, 4 of 11 patients (36.3%) diagnosed with EBB had abnormal PFT results in our study.

No significant relationship between disease stage and positive EBB results was observed. However, the diagnostic ratio of EBB was higher (23.6%) among patients with stage II disease. Additionally, majority of the patients (81.8%)

who underwent EBB were in stage 2 (n=9). The diagnostic ratio of EBB was lower (11.1%) in patients with stage 1 disease. In another study, Navani et al. [4] found stage II sarcoidosis in three of nine patients (33%). However, none of the patients (n= 18) with stage I were diagnosed using EBB. Only three patients (n= 27) with stage Iand stage II disease were diagnosed using EBB. The authors suggested that TBLB and EBB are used as an initial procedure in the diagnosis of pulmonary sarcoidosis. Similarly, studies that were conducted in Turkey reported the diagnostic ratios of EBB to be 45%, 50%, and 68% in patients with stage I, stage II, and stage III disease, respectively, indicating no additional diagnostic value when used in combination with TBLB [8].

The major limitation of the study was the lack of a comparative analysis between EBB and another bronchoscopic diagnostic technique, including TBLB. In addition, TBLB could not be performed in all patients for several reasons, including incompatible imaging findings, lack of cooperation, patient's unwillingness, and procedure-related complications such as bleeding and pneumothorax. Another limitation was the absence of a pathological diagnosis, although we performed TBNA in 46 patients. The diagnosis rate was 23.9% (11 of 46 patients) for patients who were undiagnosed by TBNA but who underwent EBB. This may be explained by inadequate specimen collection and the absence of a cytologist in our center.

In conclusion, despite the introduction of novel bronchoscopic techniques, standard FOB is the primary diagnostic tool for sarcoidosis patients. EBB not only offers the advantages of a high diagnostic ratio in patients with mucosal abnormalities but also contributes to pathological diagnosis in patients with normal bronchial mucosae. Our study results also suggest that EBB improves the diagnostic ratio in sarcoidosis, even in the presence of normal bronchial mucosae. We thus recommend that for patients without evidence of parenchymal findings who do not accept TBLB and who are undiagnosed by TBNA, EBB may be used to support the diagnosis, with a low complication rate, for patients undergoing FOB with a preliminary diagnosis of sarcoidosis in healthcare centers where EBUS is not available.

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**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Ministry of Health Clinical Research Ethics Committee in Manisa.

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - T.G., P.Ç., A.Ö.A.; Design - T.G., P.Ç., A.Ö.A.; Supervision - P.Ç., A.Ş.C., Y.H.; Resources - T.G., A.Ö.A., Y.H., A.I.; Materials - A.I., T.G., Y.H.; Data Collection and/or Processing - T.G., Y.H., A.I.; Analysis and/or Interpretation - T.G., P.Ç., A.I.; Literature Search - T.G., P.Ç., A.Ö.A.; Writing Manuscript - T.G., P.Ç., A.Ö.A.; Critical Review - A.Ş.C., A.Y., P.Ç.; Other - A.Y., A.Ş.C., P.Ç.

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## REFERENCES

1. Hunninghake GW, Costabel U, Ando M, et al. ATS/ERS/WASOG statement on sarcoidosis. American Thoracic Society/European Respiratory Society/World Association of Sarcoidosis and other Granulomatous Disorders. Sarcoidosis Vasc Diffuse Lung Dis 1999;16:149-73.
2. Baughman RP, Culver DA, Judson MA. A concise review of pulmonary sarcoidosis. Am J Respir and Crit Care Med 2011;183:573-81. **[CrossRef]**
3. Tournoy KG, Bolly A, Aerts JG, et al. The value of endoscopic ultrasound after bronchoscopy to diagnose thoracic sarcoidosis. Eur Respir J 2010;35:1329-35. **[CrossRef]**
4. Navani N, Booth HL, Kocjan G, et al. Combination of endobronchial ultrasound-guided transbronchial needle aspiration with standard bronchoscopic techniques for the diagnosis of stage I and stage II pulmonary sarcoidosis. Respirology 2011;16:467-72. **[CrossRef]**
5. Herth FJ, Schuler H, Gompelmann D, et al. Endobronchial ultrasound-guided lymph node biopsy with transbronchial needle forceps: a pilot study. Eur Respir J 2012;39:373-7. **[CrossRef]**
6. Bjermer L, Thunell M, Rosenhall L, Stjernberg N. Endobronchial biopsy positive sarcoidosis: relation to bronchoalveolar lavage and course of disease. Respir Med 1991;85:229-34. **[CrossRef]**
7. Shorr AF, Torrington KG, Hnatiuk OW. Endobronchial biopsy for sarcoidosis: a prospective study. Chest 2001;120:109-14. **[CrossRef]**
8. Kıter G, Musellim B, Cetinkaya E, et al. Clinical presentations and diagnostic work-up in sarcoidosis: a series of Turkish cases (clinics and diagnosis of sarcoidosis). Tuberk Toraks 2011;59:248-58. **[CrossRef]**
9. Kieszko R, Krawczyk P, Michnar M, et al. The yield of endobronchial biopsy in pulmonary sarcoidosis: connection between spirometric impairment and lymphocyte subpopulations in bronchoalveolar lavage fluid. Respiration 2004;71:72-6. **[CrossRef]**
10. Polychronopoulos VS, Prakash UB. Airway involvement in sarcoidosis. Chest 2009;136:1371-80. **[CrossRef]**
11. Ishii H, Otani S, Iwata A, et al. Limited role of auxiliary endobronchial biopsy in the diagnosis of Japanese patients with sarcoidosis. Tohoku J Exp Med 2011;223:119-23. **[CrossRef]**
12. Torrington KG, Shorr AF, Parker JW. Endobronchial disease and racial differences in sarcoidosis. Chest 1997;111:619-22. **[CrossRef]**
13. Burke RR, Stone CH, Havstad S, Rbybicki BA. Racial differences in sarcoidosis granuloma density. Lung 2009;187:1-7. **[CrossRef]**
14. Baughman RP, Teirstein AS, Judson MA, et al. Clinical characteristics of patients in a case control study of sarcoidosis. Am J Respir Crit Care Med 2001; 164: 1885-9. **[CrossRef]**