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Utility of EBUS-TBNA in Evaluating Mediastinal and Hilar Lymphadenopathy in Patients With Silica Exposure

A Retrospective Single-center Study

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Background: Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is used effectively in staging lung cancer and in the evaluation of benign causes of mediastinal and/or hilar lymphadenopathy (MHL), such as sarcoidosis. However, evidence for its utility in the diagnostic workup of silicosis is limited.

Methods: This single-center retrospective study included patients with occupational silica exposure who underwent EBUS-TBNA to evaluate MHL on computed tomography (CT). Cytology specimens were re-examined by an independent pathologist under polarized microscopy, and cytologic criteria for the diagnosis of LN silicosis were formulated from the findings. Primary outcomes were the determination of the diagnostic yield (DY) of EBUS-TBNA for LN silicosis and the assessment of its sensitivity for the diagnosis of parenchymal silicosis in patients with known chronic silicosis.

Results: Eighty-four patients with silica exposure underwent EBUS-TBNA to evaluate MHL. This population is predominantly coal miners, 77 (91%). Birefringent silica particles (BSP) were identified in 82 (97.62%), silicotic nodules (SN) in 26 (30.95%), and granulomas in 21 (25%). EBUS-TBNA demonstrated a DY of 95.2% for LN silicosis, and supported the diagnosis of parenchymal silicosis with a sensitivity of 97.6%.

Conclusion: EBUS-TBNA effectively identifies LN silicosis and confirms the diagnosis of parenchymal silicosis in the appropriate clinical-radiologic context. Granulomas can be seen in cytologic specimens of patients with silicosis. In patients with well-defined silica exposure and suspected silicosis, EBUS-TBNA does not impact the preprocedural presumed diagnosis of silicosis. Therefore, EBUS-TBNA should be reserved for cases in which alternative diagnoses are more likely.

Key Words: birefringent, diagnostic yield, EBUS-TBNA, endobronchial ultrasound, mediastinal lymphadenopathy, pneumoconiosis, silica dust, silicotic nodules

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Silicosis is an occupational lung disease caused by the inhalation of respirable crystalline silica (RCS). Workers in the coal and metal mining industries are at high risk of inhaling RCS.[1,2] The introduction of silica into modern industries, such as jewelry polishing, stone carving, dental prosthesis, and granite countertop manufacturing, can result in silicosis.[3,4] Silicosis is usually a clinical diagnosis based on a history of sufficient RCS exposure and compatible imaging features when other etiologies are less likely.[5,6] Lung biopsy is appropriate when clinical data is insufficient for a confident diagnosis. In silica-exposed individuals, chest computed tomography (CT) can reveal mediastinal and/or hilar lymphadenopathy (MHL) in isolation or in combination with parenchymal involvement. Lymph node (LN) silicosis can precede parenchymal involvement according to previous studies.[7–9] Biopsy-proven LN silicosis can confirm silicosis in patients with sufficient RCS exposure and nodular-interstitial lung involvement on CT.[10]

Over the past 20 years, endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) of LN has been proven effective in the diagnostic workup of unexplained MHL due to benign etiologies, such as sarcoidosis.[11,12] The presence of birefringent particles reliably predicted occupational dust exposure history in patients with MHL in an EBUS-TBNA cytology study.[13] The use of EBUS-TBNA in diagnosing silicosis has been previously reported,[14,15] and explored in 1 retrospective

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The approval included the Waiver of informed consent and the HIPAA Waiver. The IRB granted an amendment approval of the study protocol to allow contacting patients by telephone calls to obtain and fill out an occupational history questionnaire.

T.M.A. had full access to all data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis. T.M.A. and Y.R.S. contributed to the conception and design of the work and acquisition, analysis, and interpretation of data; drafting the manuscript and final approval of the version to be published. A.C.M. contributed to the conception and design of the work, interpretation of data, reviewing the manuscript, provided critical revision of the manuscript for important intellectual contents, and final approval of the version to be published. S.K.S. contributed to study design, acquisition of cytology data by reexamining all cytology specimens under polarized microscopy, and drafting the manuscript. M.J.A. contributed to the study design, acquisition of radiology data by reviewing chest CT scans, and reviewed the manuscript. J.L.S. contributed to data acquisition and drafting the manuscript. C.S.C. performed statistical analysis and drafted/reviewed the manuscript.

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study of a small sample size (N = 11).[16] The aim of this study is to assess the diagnostic yield (DY) of EBUS-TBNA for LN silicosis and to assess its utility in the diagnosis of parenchymal silicosis in 84 patients with silica exposure and MHL. In this study, we define LN silicosis according to specific EBUS-TBNA cytologic criteria within a proposed diagnostic confidence classification.

MATERIALS AND METHODS

We conducted a single-center retrospective observational study. We reviewed records of bronchoscopy procedures performed at the Endoscopy Unit of Cabell Huntington Hospital from March 1, 2017 to February 29, 2024. The Institutional Review Board of Marshall University's Office of Research Integrity provided the ethical approval (IRB #2145496). The study included patients with occupational silica dust exposure who underwent EBUS-TBNA to evaluate MHL. Inclusion and exclusion criteria are illustrated in Supplementary Figure S1, Supplementary Digital Content 4, http://links.lww.com/LBR/A351.

Pre-EBUS/Follow-up Chest CT

MHL was defined by the presence of enlarged LN on CT (> 10 mm diameter in short axis). On the basis of the radiologist's re-analysis of pre-EBUS CT scans, findings were categorized as isolated MHL, adenopathy with typical chronic silicosis, or adenopathy with atypical features of chronic silicosis. Typical and atypical features of chronic silicosis were determined based on available literature,[17] as listed in Supplementary Table S1, Supplementary Digital Content 1, http://links.lww.com/LBR/A348. Available follow-up chest CT scans were also reviewed.

Bronchoscopy Procedures

All EBUS-TBNA procedures were performed using a Convex-Probe EBUS bronchoscope (CP-EBUS, BF-UC180F, Olympus, Japan) and flexible 19-G EBUS-TBNA needles (VIZISHOT FLEX 19-G and VIZISHOT 2 FLEX 19-G, Olympus). A transesophageal approach using the CP-EBUS scope (EUS-B-FNA) was performed to biopsy LNs that could not be biopsied from the airways. Cytotechnologists provided rapid-on-site evaluation to assess sample adequacy. The proceduralist's documentation in electronic records provided LN sampling difficulty data.

Data Sources and Study Outcomes

Cytology specimens, including slides made from monolayer preparations, formalin-fixed paraffin-embedded cell blocks, and smears made during EBUS-TBNA procedures, were retrieved from pathology archives. An independent board-certified anatomic pathologist with 18 years of experience and interest in pulmonary pathology used polarized light microscopy (PLM) to re-examine all specimens. Pre-EBUS chest CT scans, positron emission tomography (PET/CT), and follow-up chest CT scans were re-analyzed by a board-certified general radiologist with 15 years of experience. Detailed occupational history (occupations, job tasks, and duration) and additional clinical follow-up information were collected from all patients by telephone calls. All other data were extracted from electronic records.

Primary outcomes were the determination of DY of EBUS-TBNA for LN silicosis and the assessment of its sensitivity for a diagnosis of parenchymal silicosis in a subgroup of patients with clinically proven chronic silicosis.

TABLE 1. Population Demographics and Occupational Exposure Characteristics (N = 84)

Variables	n (%)	Mean ± SE
Age		61.2 ± 1.14
Male sex	84 (100)	
Race		
White	82 (97.62)	—
African American	2 (2.38)	—
Smoking history		
Yes	53 (63.1)	—
No	31 (36.9)	—
History of prior malignancy		
Yes	9 (10.71)	—
No	75 (89.29)	—
Presenting symptoms		
Asymptomatic	11 (13.09)	—
Dyspnea	68 (80.95)	—
Chest pain	4 (4.76)	—
Chronic cough	37 (44.05)	—
Hemoptysis	2 (2.38)	—
Weight loss	7 (8.33)	—
History of coal mining		
No	7 (8.33)	—
Yes	77 (91.67)	—
Silica dust exposure source		
Coal mining	60 (71.43)	—
Coal mining+other occupation exposures	17 (20.24)	—
Occupational exposures other than coal mining	7 (8.33)	—
Occupational exposures other than coal mining		
Steelwork	6 (7.14)	—
Construction	11 (13.09)	—
Rock hauling	3 (3.57)	—
Stone cutting	4 (4.76)	—
Coal mining type		
Underground	51 (60.71)	—
Surface	8 (9.52)	—
Both	18 (21.42)	—
Main coal mining task* description		
Drilling	23 (27.38)	—
Mining/cutting machine operator	5 (5.95)	—
Roof bolting/mining construction	13 (15.47)	—
Maintenance technician/mechanics,	12 (14.28)	—
Conveyor belt operator/shoveler	13 (15.47)	—
Electrician	2 (2.38)	—
Mining surveyors	1 (1.19)	—
Manager/supervisor	1 (1.19)	—
Heavy/loading machine operator	5 (5.95)	—
Coal processing	2 (2.38)	—
Active exposure at the time of bronchoscopy		
No	73 (86.9)	—
Yes	11 (13.09)	—
Silica dust exposure duration (y)		24.37 ± 0.94
Latency period† (y)		38.82 ± 1.06
Time since last exposure‡ (y)		16.71 ± 0.99

*The only or the longest-held job duty in the coal mining industry.
†The time period between the beginning of silica dust exposure and the bronchoscopy referral for diagnostic evaluation of abnormal chest imaging.
‡The time period between cessation of silica dust exposure and the bronchoscopy referral.

The DY was determined by the indexed bronchoscopic cytology results using the ATS/ACCP research statement (strict definition),[18] as displayed in Supplementary Figure S2, Supplementary Digital Content 5, http://links.lww.com/LBR/A352. The secondary outcome was to determine if

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TABLE 2. Pre-EBUS Chest CT and PET/CT Imaging Characteristics (N = 84)

Variables	n (%)	Mean ± SE
Isolated MHL	16 (19.04)	—
Typical chronic silicosis+MHL	42 (50)	—
Atypical chronic silicosis+MHL	26 (30.96)	—
LN calcification on CT*	34 (40.48)	—
PMF or clustered conglomerate nodules (complicated silicosis/CWP)	14 (16.67)	—
Pre-EBUS PET/CT available	66 (78.57)	—
Extrathoracic LN enlargement on PET/CT	10 (11.9)	—
Short axis diameter of the largest intrathoracic LN (mm)		17.55 ± 0.51
SUV_{max} for MHL on PET/CT (g/mL)		7.31 ± 0.35

*On pre-EBUS chest CT scans review, variable degrees of LN calcifications were noted (an eggshell calcification pattern was present in only 2 patients).

CT indicates computed tomography; CWP, coal worker pneumoconiosis; LN, lymph node; MHL, mediastinal and/or hilar lymphadenopathy; PET, positron emission tomography; PMF, progressive massive fibrosis; SUV_{max}, maximum standardized uptake value.

EBUS-TBNA provided alternative diagnoses when silicosis was clinically suspected.

Clinical-cytologic Criteria for LN Silicosis

The study assessed the following cytology findings: (1) birefringent silica particles (BSP) under PLM, (2) silicotic nodules (SN), (3) anthracotic pigment, (4) dust-laden macrophages, (5) granuloma, and (6) malignancy. These findings were qualitatively assessed without grading or quantification.

In the clinical-radiologic context, LN silicosis is defined by the presence of BSP with or without SN or dust-laden macrophages in specimens and the absence of cytologic evidence of malignant or specific benign LN disease that could account for the LN enlargement. Existing literature defines LN silicosis by the presence of both SN and BSP.[8,9] This study categorized the diagnostic confidence of an LN silicosis diagnosis made by EBUS-TBNA based on the presence or absence of certain cytologic findings as follows: (1) definitive LN silicosis is when both BSP and SN are identified with or without granulomas; (2) probable LN silicosis is when BSP are identified without SN or granulomas; and (3) possible LN silicosis is when BSP are identified without SN in the presence of granulomas.

Statistical Analyses

All statistical analyses were conducted using Python, utilizing the SciPy, StatsModels, and NumPy libraries. Descriptive statistics, including means and SE, were computed. For continuous variables, the SE was computed to estimate the variability of the sample mean. All statistical outputs were reviewed for accuracy and consistency.

RESULTS

All 84 patients (100%) were male, 82 (97.2%) were white, and 53 (63%) had either active or prior smoking history. The mean age was 61.2 ± 1.14 years. Table 1 summarizes study population demographics and occupational exposure characteristics. The main source of silica dust exposure was coal mining (N = 77, 91.6%), predominantly underground (N = 69, 82.1%). Drilling was the most frequently cited job task (N = 23, 27.38%). Mean silica dust exposure duration was 24.37 ± 0.94 years, and mean time since last exposure was 16.71 ± 0.99 years. Pulmonary function tests were available for only 52 patients (Supplementary Table S2, Supplementary Digital Content 2, http://links.lww.com/LBR/A349).

TABLE 3. EBUS Bronchoscopy-related Data (N = 84)

Variables	n (%)
EBUS-TBNA biopsy indications*	
To exclude malignancy	58 (69.04)
To confirm silicosis or to evaluate for competing benign diagnoses†	29 (34.52)
Lung cancer staging	2 (2.38)
ILD evaluation	4 (4.76)
Refusal of watchful waiting	5 (5.95)
Clinical factors that influenced EBUS-TBNA biopsy decisions	
PET avidity of intrathoracic LN	55 (65.47)
History of malignancy (recent/remote)	7 (8.33)
Interval increase in LN size on CT	7 (8.33)
Suspicious parenchymal lesions on CT (size/interval growth/laterality/PET avidity)	17 (20.24)
Weight loss	7 (8.33)
Hemoptysis	2 (2.38)
Lobar/segmental atelectasis on CT‡	3 (3.57)
Extrathoracic adenopathy on PET/CT§	8 (9.52)
Atypical features of parenchymal silicosis on CT	19 (22.61)
No. LN stations sampled per procedure (mean)	2.29
Location of LNs sampled	
2L	1 (1.19)
4L	16 (19.04)
10L	3 (3.57)
11L	22 (26.19)
4R	48 (57.14)
7	60 (71.42)
8	6 (7.14)
10R	1 (1.19)
11R (superior/inferior)	52 (61.9)
LN sample adequacy (≥1 LN station)	
Adequate	82 (97.61)
Inadequate	2 (2.38)
EBUS-related significant bleeding‖	4 (4.76)
Difficulty in LN sampling (≥1 LN station)	15 (17.85)

*The indications for EBUS bronchoscopy were based on the preprocedural interventional pulmonology clinic documentation and the records of the referring outside general pulmonologists. The EBUS-TBNA indications listed are not mutually exclusive.

†Other competing benign etiologies include sarcoidosis and infections.

‡Chest CT evidence of lobar/segmental atelectasis raised the possibility of endobronchial pathology and the need for bronchoscopy.

§The presence of extrathoracic adenopathy (unusual for silicosis) on PET/CT raised concerns for sarcoidosis and lymphoma, which prompted performing EBUS-TBNA.

‖EBUS-related significant bleeding was defined as documented blood loss of ≥30 mL, hypoxia, brisk bleeding with frequent removal of large clots, or premature interruption of planned procedures due to a heightened rebleeding risk.

CT indicates computed tomography; EBUS-TBNA, endobronchial ultrasound-guided transbronchial needle aspiration; ILD, interstitial lung disease; LN, lymph node; PET, positron emission tomography.

Pre-EBUS CT findings are summarized in Table 2. All 84 patients (100%) had enlarged mediastinal and/or hilar LN. The mean short axis of the largest LN was 17.55 ± 0.51 mm. Parenchyma involvement was noted in 68 patients, 42 (50%) with typical nodular silicosis and 26 (30.9%) with atypical imaging features. MHL without parenchymal involvement was noted in 16 (19.04%). The mean maximum standardized uptake (SUV_{max}) for PET-avid LNs was 7.31 ± 0.35 g/mL.

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Bronchoscopy-related data are outlined in Table 3. The most common indication for EBUS-TBNA was to exclude malignancy (N = 58, 69.04%), followed by confirming silicosis or evaluating for other benign pathology (N = 29, 34.52%). The most frequently cited factors in EBUS-TBNA biopsy decisions included LN PET avidity (N = 55, 65.47%) and atypical imaging parenchymal features of silicosis (N = 19, 22.61%). Bronchoalveolar lavage fluid was obtained from 46 patients (54.76%), and all mycobacterial/fungal cultures were negative. Concurrent transbronchial biopsies for suspicious parenchymal lesions were performed in 14 patients (16.67%), and all were negative for malignancy.

Diagnostic Yield

EBUS-TBNA cytology re-analysis identified BSP in 82 patients (97.62%), SN in 26 (30.95%), granuloma in 21 (25%), dust-laden macrophages in 78 (92.85%), and anthracotic pigments in 77 (91.67%). The only identified neoplastic disease was chronic lymphocytic leukemia in 1 (1.19%) patient. Figure 1 depicts cytology findings evaluated in this study. The DY of EBUS-TBNA (Fig. 2) for LN silicosis was 95.2%. The 80 patients with LN silicosis were categorized according to the aforementioned proposed criteria: 25 (29.8%) with definitive, 38 (45.2%) with probable, and 17 (20.2%) with possible LN silicosis. In 42 patients (Fig. 3) known to have chronic silicosis, EBUS-TBNA of LN supported the diagnosis of parenchymal silicosis in 41 patients with a sensitivity of 97.6%. In 26 patients with atypical parenchymal features on CT, EBUS-TBNA established the diagnosis of silicosis in 25 (96.1%). Among 16 patients with MHL without parenchymal involvement, EBUS-TBNA established the diagnosis of LN silicosis in 14 (87.5%). Of 21 patients with granuloma, 20 (95%) had nonnecrotizing granuloma. In patients with cytologic evidence of granuloma, all bronchoalveolar lavage mycobacterial/fungal cultures and special cytology staining for organisms on EBUS-TBNA specimens (Supplementary Table S3, Supplementary Digital Content 3, http://links.lww.com/LBR/A350) were negative.

Follow-up Data

Follow-up imaging was available only for 60 patients (71.4%). MHL was stable in 55 patients (91.67%), decreasing in size in 3 patients (5%), and progressing in 2 patients (3.33%). Of the 49 patients (81.67%) who had nodular-interstitial parenchymal disease on chest CT, 19 (38.78%) had radiologic progressive disease, 2 (4.08%) had interval radiologic improvement, and 28 (57.14%) remained stable. The mean radiology follow-up time was 34.32 ± 2.7 months. All 84 patients (100%) in the study were alive at the time of the study review. Clinical follow-up was available for 80 patients (95.2%), with a mean clinical follow-up time of 43.67 ± 2.9 months. Of the 16 patients (20%) who had repeat EBUS-TBNA or lung biopsies during follow-up, 2 were diagnosed with lung cancer. None of the patients had cancer involving the LN during follow-up.

DISCUSSION

When occupational history and MHL on chest CT suggest possible LN silicosis, EBUS-TBNA has a DY of 95.2%. In the context of well-defined occupational exposures to RCS and parenchymal involvement on chest imaging (nodular-interstitial pattern), biopsy-proven LN silicosis can confirm a diagnosis of parenchymal silicosis without additional lung biopsy. Therefore, for a subgroup of patients in our study with clinically diagnosed chronic silicosis, based on occupational exposures and typical parenchymal findings on CT, EBUS-TBNA supported a parenchymal silicosis diagnosis with a sensitivity of 97.6%.

Study results for the DY of EBUS-TBNA for silicosis confirm previous results reported by Shitrit et al,[16] who

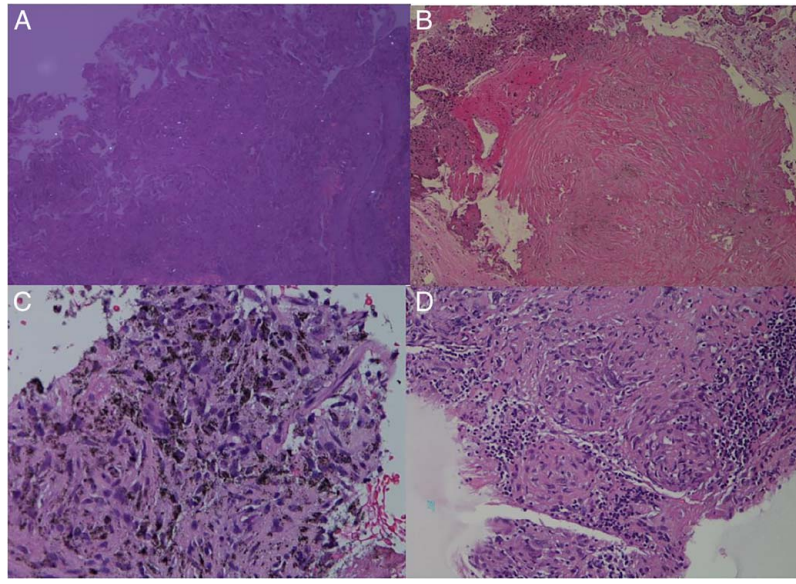

FIGURE 1. EBUS-TBNA cytology findings of a hilar LN. (A) Polarized light microscopy reveals numerous weakly birefringent crystals (H&E; original magnification, x100). (B) Silicotic nodule characterized by a circumscribed nodule with whorled hyalinized collagen (H&E; original magnification, x100). (C) Photomicrograph showing histiocytes with dark pigment (H&E; original magnification, x200). (D) Nonnecrotizing granuloma with epithelioid histiocytes (H&E; original magnification, x200). EBUS-TBNA indicates endobronchial ultrasound-guided transbronchial needle aspiration; H&E, hematoxylin and eosin; LN, lymph node.

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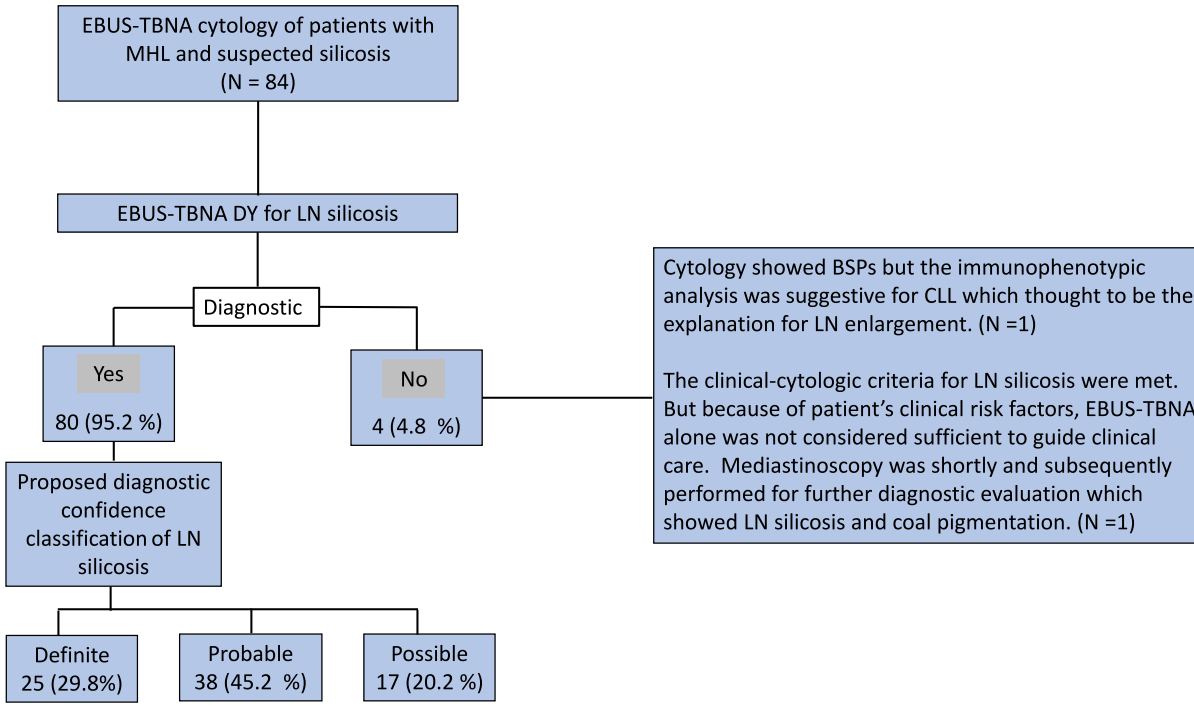

FIGURE 2. EBUS-TBNA diagnostic yield and diagnostic confidence classification for lymph node silicosis. Data are presented as the number of patients (%) unless otherwise indicated. BSP indicates birefringent silica particles; CLL, chronic lymphocytic leukemia; DY, diagnostic yield; EBUS-TBNA, endobronchial ultrasound-guided transbronchial needle aspiration; LN, lymph node; MHL, mediastinal and/or hilar lymphadenopathy.

found in a small retrospective study (N = 11) of workers cutting high-silica content artificial stones and having MHL with parenchymal involvement that EBUS-TBNA was 100% diagnostic for silicosis based mainly on the identification of BSP in LN aspirates. In contrast to Shitrit and colleagues' study, our population was relatively larger (N = 84), and predominantly coal miners with exposure to both coal and silica dusts. SNs were identified in 30% of our cohort. For the first time, this study proves the feasibility of identifying SNs in EBUS-TBNA specimens, as shown in Figure 1, not only in larger biopsies obtained using mediastinoscopy or surgical lung biopsies.

The cytologic criteria in our study to define silicosis in LN relied on limited data,[14–16] and required that the clinical-radiologic context be considered when interpreting EBUS-TBNA findings. EBUS-TBNA silicosis-related cytologic criteria relied on the presence of BSP under PLM to be considered diagnostic for silicosis, in the absence of malignancy or another specific benign LN disease to explain LN enlargement. Current pathology literature requires the presence of both SN and BSP for histopathologic diagnosis of LN silicosis.[8,9,19] SNs are the histopathologic hallmarks of chronic silicosis in both lung parenchyma and LNs; however, SNs are not always present.[4] Earliest histologic changes in silicosis are characterized by stellate aggregates of loose reticulin fibers and dust-laden macrophages, which eventually form SNs.[20] Recent data showed a dose-response relationship between a cumulative RCS of more than 25 to 30 years and the detection of SNs in mediastinal LNs, indicating that the absence of SNs does not preclude silica exposure or undetected silicosis.[21] Therefore, we did not consider SNs mandatory cytologic evidence of silicosis. However, their presence increases the diagnostic confidence for silicosis. Therefore, the identification of SNs and other cytology findings informed a diagnostic confidence classification for EBUS-TBNA results: definitive, probable, or possible silicosis.

In patients with known chronic silicosis who received bronchoscopy to exclude malignancy, EBUS-TBNA found 1 malignancy, a case of chronic lymphocytic leukemia thought to explain LN enlargement. Similarly, in patients with suspected silicosis based on atypical imaging for whom EBUS-TBNA was utilized to confirm silicosis or to evaluate for other pathology, EBUS-TBNA did not provide an alternative diagnosis to silicosis. Thus, in the setting of well-defined RCS exposure, EBUS-TBNA does not alter the preprocedural presumed silicosis diagnosis. EBUS-TBNA is effective for the diagnosis and confirmation of silicosis. However, it should be reserved for cases of diagnostic uncertainty, such as when exposure history is cryptic or alternative diagnoses are highly suspected.

Increased LN/parenchymal lesion PET avidity influenced biopsy decisions in 55 cases (65.47%) in our cohort. Interestingly, in the 82 cases (97.61%) for which EBUS-TBNA yielded adequate samples, no malignancy or infections were identified. This supports data that showed FDG-PET/CT offers limited utility in diagnosing malignancy in coal worker pneumoconiosis and chronic silicosis due to the high false positive rate.[22,23] When FDG-PET avidity is used to discriminate progressive massive fibrosis from lung cancer, using an SUV_{max} cut-off of 7.4 in combination with other CT parameters (short-axis/long-axis diameters, Hounsfield units of lung masses on PET/CT) can improve diagnostic performance.[24] Our study showed that enlarged LNs in silicosis may remain metabolically active (mean SUV_{max} of 7.31 g/mL) for many years after the

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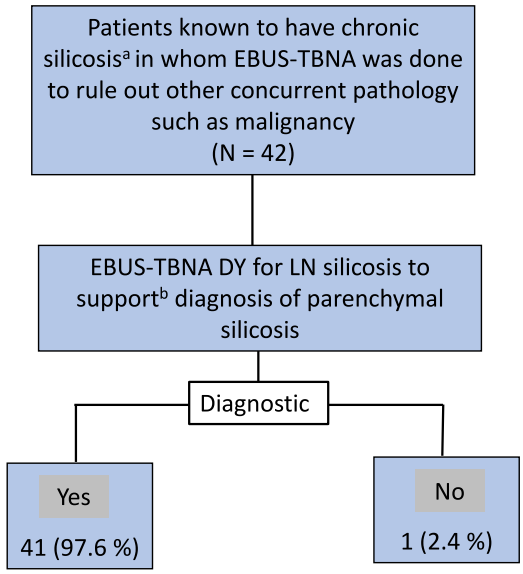

FIGURE 3. EBUS-TBNA diagnostic yield and performance to support parenchymal silicosis diagnosis. Data are presented as number of patients (%) unless otherwise indicated. [a]Clinical diagnosis of silicosis relied on a history of well-defined silica dust exposure and typical parenchymal changes and adenopathy on chest CT. [b]In the appropriate clinical-radiologic context, biopsy-proven LN silicosis can support the diagnosis of parenchymal silicosis without additional lung biopsy. CT, computed tomography; DY, diagnostic yield; EBUS-TBNA, endobronchial ultrasound-guided transbronchial needle aspiration; LN, lymph node.

exposure (mean time since last exposure was 16.7 y). Therefore, for patients with suspected silicosis, the diagnostic workup should warrant EBUS-TBNA based on clinical and imaging findings and not mainly increased PET avidity.

Silicosis With Granulomatous Disease

While beryllium and talc (hydrated magnesium silicates) are well-recognized causes of pulmonary granuloma,[25] exposure to RCS is not. However, recent multiple case reports note patients with RCS exposure and biopsy-proven silicosis who also had sarcoid-like granulomas containing BSP under PLM.[14,26,27] Multiple epidemiological studies showed a strong association between RCS exposure and increased risk of sarcoidosis, indicating that silica exposure might be a trigger for sarcoidosis.[28–36] However, causality is not yet proven. In this study, granulomas appeared in the cytology specimens of 25% (21/84) of patients with known/suspected silicosis, the highest rate yet reported in the literature. This suggests that PLM should be performed whenever granulomas are identified, especially if well-recognized causes of granuloma are not highly suspected or when occupational exposures are cryptic. The diagnostic criteria for sarcoidosis adopted by the American Thoracic Society in 2020,[37] require the exclusion of alternative causes of granuloma, such as metal (inorganic) dust exposure and pneumoconiosis. The presence of granuloma can confound a diagnosis of silicosis because silicosis and sarcoidosis share a number of radiologic features, which can be a diagnostic challenge if exposure history is unclear. In our cohort, chronic beryllium disease is unlikely but cannot be completely excluded. Granulomatous (tuberculosis/fungal) infections are less likely because available stains and cultures were negative.

This retrospective study has several strengths. All pivotal data, including occupational exposures and chest CT/cytology findings, were uniformly re-examined, re-analyzed, and collected at the time of the study review from a relatively large sample, which generated useful clinical evidence. The study generated (imaging/clinical/follow-up) data, which showed the impact of EBUS-TBNA on clinical care. EBUS-TBNA can guide workplace-related secondary preventive strategies by identifying early stages of silicosis (LN-only silicosis without parenchymal involvement). LN-only silicosis can precede parenchymal silicosis according to large autopsy studies; however, temporal sequence could not be confirmed.[8,9] LN fibrosis impairs the elimination of silica dust from the lung, increasing the lung dust burden, which likely contributes to the development of parenchymal silicosis.[9] Therefore, patients with LN-only silicosis are at a much higher risk of developing parenchymal silicosis, a devastating and often progressive disease with no effective treatment.

Our findings have several limitations. One experienced interventional pulmonologist performed 97% of all EBUS-TBNA procedures, possibly limiting the results' generalizability. The cytology review was performed by 1 pathologist, which precluded assessment of interobserver agreement for silicosis-related cytopathological findings. Only 19-G EBUS needles were used in this study; therefore, the effect of different needle sizes on the DY was not assessed. The majority of patients were exposed to both RCS and coal dusts, which creates the diagnostic possibility of mixed dust pneumoconiosis, not only chronic silicosis. However, coal dust exposure is unlikely to have significantly affected study results since coal worker pneumoconiosis and chronic silicosis have somewhat similar radiologic features and share some pathologic characteristics.[17] Recent data show that exposure to RCS appears causal in the surge of severe pneumoconiosis among coal miners.[38]

CONCLUSIONS

EBUS-TBNA can effectively diagnose LN and parenchymal silicosis in the appropriate clinical-radiologic context. In patients with suspected silicosis and well-defined silica dust exposure, EBUS-TBNA does not change the preprocedural presumed diagnosis of silicosis. Therefore, a high degree of suspicion for alternative diagnoses is required before considering EBUS-TBNA. Prospective research is needed to validate the silicosis-related cytologic criteria used in this study, especially to assess interobserver agreement among pathologists. Prospective longitudinal studies are also needed to understand more clearly the disease process in patients with silicosis and coexisting granulomatous disease.

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