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ORIGINAL PAPER

Cytopathological diagnoses obtained in endobronchial ultrasound-guided transbronchial needle aspiration – a single-center one-year analysis

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ABSTRACT

Introduction and aim. Endobronchial ultrasound-guided fine needle aspiration (EBUS-FNA) is a widely adopted technique that replaces mediastinoscopy for the diagnosis of mediastinal lesions, significantly improving patient safety. This study assesses its diagnostic effectiveness and compares procedural quality with the existing literature, in order to identify characteristics of the patient population referred to the center.

Material and methods. During a year-long retrospective analysis, data from 312 EBUS-FNA procedures were collected, resulting in a final study group of 274 patients. For patients initially without a definitive diagnosis, reinterventions were conducted, typically with additional EBUS or tissue biopsy, followed by precise statistical analyses and calculations.

Results. The sensitivity of the EBUS examination to detect sarcoidosis, non-small cell lung cancer, small cell lung cancer, and lymphoproliferative disorders was determined to be 87.36%, 87.23%, 91.30% and 20%, respectively, based on false negative findings. Among patients who received a final diagnosis (n=237), a significant majority, i.e. 206 individuals or 86.92%, obtained it based on the first intervention.

Conclusion. EBUS-TBNA is an effective method to diagnose the cause of mediastinal lymphadenopathy, allowing for a definitive diagnosis in a significant majority of patients in the first intervention and showing high sensitivity in detecting metastatic malignant lymph node involvement and sarcoidosis.

Keywords. EBUS, lymphadenopathy, sarcoidosis

Introduction

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is an effective and recognized bronchoscopic technique for the diagnosis of mediastinal lesions. Since its widespread adoption, it has replaced mediastinoscopy as a diagnostic tool for mediastinal lymphadenopathy, mediastinal tumors, and pulmonary hilum lesions, significantly improving patient safety and showing to be more effective tool.[1-4] The obtained material often reveals malignant primary or metastatic tumor cells, epithelioid cell granulomas consistent with tuberculosis or sarcoidosis diagnosis, as well as cells present in silicotic and reactive nodes. In this study, our objective was to analyze the results from our center to determine diagnostic effectiveness, comparing the quality of our procedures with those reported in publications. Furthermore, based on a one-year patient sample, we sought to identify the specific characteristics of the patient population referred to our center.

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Aim

In particular, to our knowledge, this is the first study to evaluate the diagnostic performance of EBUS-TBNA in our region, providing novel insights into the characteristics and diagnostic outcomes of this specific population. Our findings contribute valuable regional data that can improve a better understanding of EBUS-TBNA between diverse patient groups.

Material and methods

This study was approved by the Bioethics Committee of the University of Rzeszów (KB 08/2025).

In a retrospective analysis covering a 12-month period (from June 2021 to June 2022), we collected data on patients referred to our clinic for EBUS-TBNA due to mediastinal lymphadenopathy or hilar tumors. Data were obtained from the hospital computer system, anonymized, and compiled in a spreadsheet. During this period, 312 EBUS-TBNA examinations were performed in our clinic. We excluded 38 records related to a second or subsequent diagnostic intervention, resulting in a final study group consisting of 274 patients undergoing their initial EBUS examination.

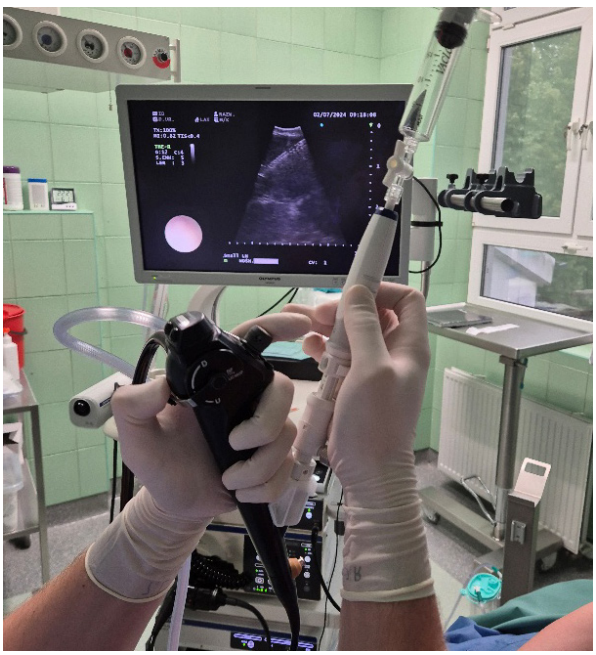

Fig. 1. The EBUS examination is performed using an OLYMPUS fiberoscope model. BF-UC190F and OLYMPUS single use 22 gauge aspiration needle, on the screen behind the endoscopist you can see the needle passing through station 7 mediastinal lymph node

Patients in our center receive local anesthesia with lidocaine solutions, followed by general anesthesia, usually with fentanyl and propofol. EBUS examination is performed using an OLYMPUS fiberoscope model: BF-UC190F and OLYMPUS 22 gauge single use aspiration needle (Fig. 1.). During a single examination, material is aspirated multiple times from available nodal or tumor lesions (Fig. 2), usually 3-5 times, depending on technical conditions, the amount of aspirated material, and the examination's purpose.

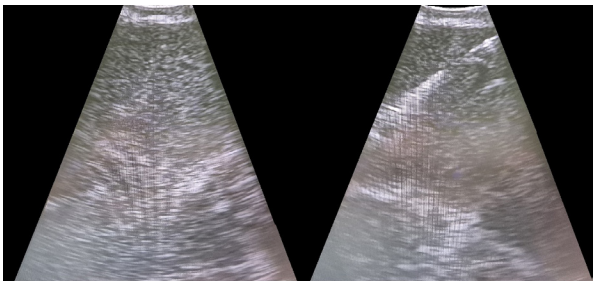

Fig. 2. Ultrasound image of the enlarged mediastinal lymph node found during examination (on the left) and the needle that passed through the lesion during biopsy (on the right)

The pathology department receives 10% buffered formalin, slides with smears fixed with CytoFix, and EBUS needle bronchial washings from the EBUS needle preserved with 96% ethanol. The cytological examination results based on this material were recorded in the spreadsheet. All material collected during this examination and considered by this study was acquired by needle aspiration. We refrained from performing an endobronchial forceps biopsy, bronchoalveolar lavage, or brush bronchial biopsy. Below are example micrographs of histopathological specimens, including those conventionally stained with hematoxylin and eosin, as well as samples stained during immunohistochemical analyses specific to the given diagnosis.

Lung adenocarcinoma: sheets of atypical cells, some with micropapillae, with marked nuclear pleomorphism; typical lung immunoprofile positive for TTF-1 and negative for p40 (Fig. 3).

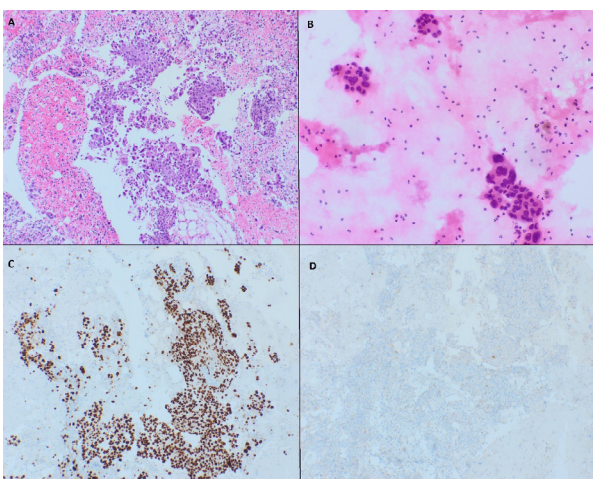

Fig. 3. Lung adenocarcinoma A: hematoxylin and eosin (H&E), 200×, B: H&E, 400×, C: TTF1, 100×, D: p40, 100×

Lung squamous cell carcinoma: multilayered sheets of cells with well-defined cell borders and intercellular bridges, some of them with keratinizing cells with a pyknotic nucleus (Fig. 4).

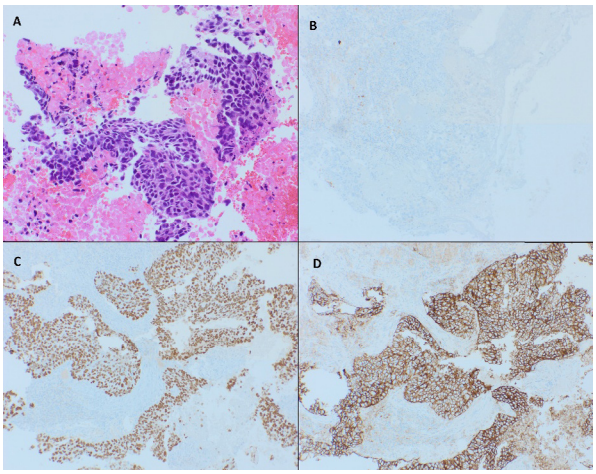

Fig. 4. Squamous cell carcinoma A: H&E, 200×, B: TTF1, 200×, C: p40, 200×, D: PD-L1, 200×

Small cell lung cancer: small cells with scant cytoplasm, with nuclear molding, and dark, hyperchromatic nuclei without nucleoli; positive for TTF-1 and the neuroendocrine marker synaptophysin (Fig. 5).

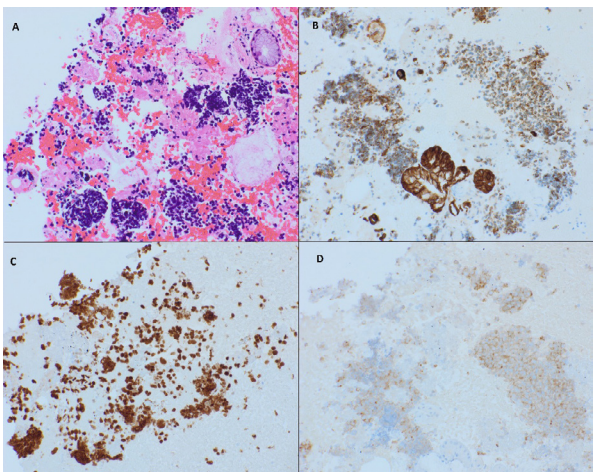

Fig. 5. Small cell lung cancer A: H&E, 200×, B: pancytokeratin, 200×, C: TTF1, 200×, D: synaptophysin, 200×

Metastatic prostatic adenocarcinoma: cellular cribriform aggregates of small, uniform cells with well-defined centrally located nucleoli and generally positive NKX 3.1 and PSA (Fig. 6).

Sarcoidosis: non-crotizing granulomas composed of epithelioid histiocytes, giant multinuclear cells, and small amounts of lymphocytes in the background (Fig. 7).

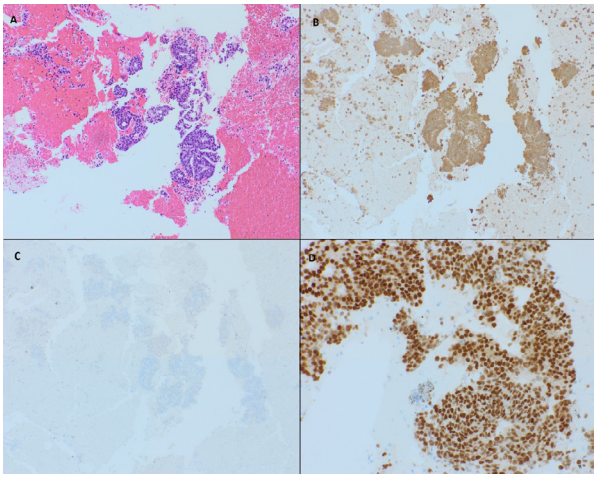

Fig. 6. Metastatic prostatic adenocarcinoma A: H&E, 100×, B: PSA, 100×, C: TTF1, 100×, D: NKX3.1, 200×

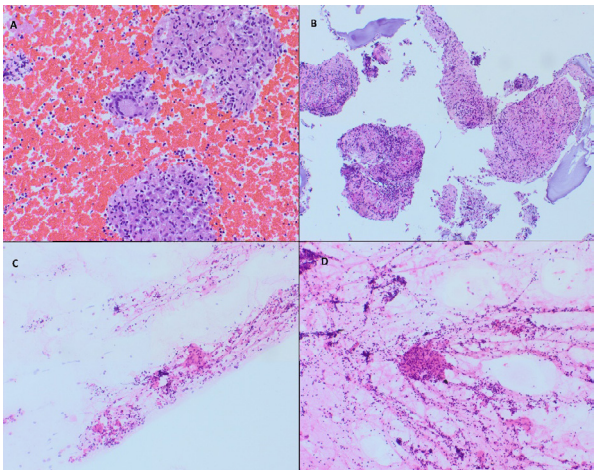

Fig. 7. Sarcoidosis A: H&E, 200×, B: H&E, 100×, C: H&E, 40×, D: H&E, 100×

Pneumoconiotic lymph nodes: three-dimensional clusters of lymph node tissue with deposits of dark, coal pigment (Fig. 8).

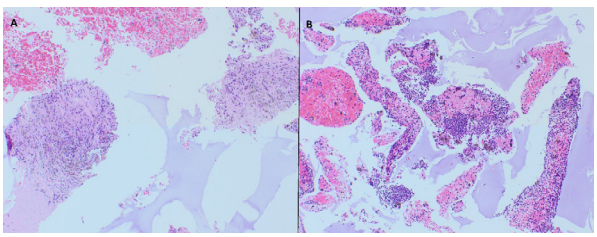

Fig. 8. Pneumoconiotic lymph nodes A, B: H&E, 100×

For patients without a definitive diagnosis (initially negative group), a reintervention is usually performed, either with another EBUS examination or, in justified cases, tissue biopsy for histopathological material. Typically, a tissue biopsy is taken from the lung parenchyma, lymph node biopsy in the neck and supraclavicular region, or mediastinoscopy.

For these patients (initially negative group), the hospital's computer system was searched for cytological and histopathological results of subsequent interventions or entry into outpatient clinics with respect to their further treatment. Based on these constructed assumptions, further subgroup divisions and calculations were performed. All calculations were carried out with precision to two decimal places.

Results

The study group consisted of 181 males and 93 females. Based on the material obtained in the initial EBUS examination, diagnoses were established: non-small cell lung cancer (n=82), small cell lung cancer (n=21), lymphoproliferative disorders (n=1), sarcoidosis (n=76). A total of 180 received a definitive diagnosis (initially positive group). The material from the remaining 94 patients contained fragments of lymph nodes: normal, reactive or silicotic, occasional epithelioid granulomas, inflammatory cells, and other findings considered benign or not sufficiently expressed to provide a definitive diagnosis (initially negative group). In every examination, the pathologist has found lymph node tissue or tumor tissue, therefore, there were no cases of nondiagnostic material. Table 1 presents the detailed distribution of diagnoses in the study group.

Table 1. Detailed distribution of diagnoses in the study group (n=274) after the initial procedure

Diagnoses	n
Sarcoidosis	76
Adenocarcinoma	33
Squamous-cell carcinoma	24
NSCLC NOS	23
Large cell carcinoma	2
Small cell carcinoma	21
Neoplastic lymphatic growth	1
Normal or non-specific lymph nodes	94

Patients with normal or nonspecific findings were offered diagnostic reinterventions, often preceded by additional imaging studies. In 6 patients, complete regression of the lesions was observed on chest CT images, and further interventions were abandoned. Despite the proposal, 37 patients did not present for reintervention or follow-up visits, leading to the exclusion of these records from further analysis. Among the remaining 51 patients, ongoing evaluation revealed: persistent absence of definitive disease (n=20), disease progression (false negative results group, n=31). The results of secondary interventions/evaluations in the initially negative group are presented in Table 2.

Based on the results of false negative findings, the sensitivity of the examination to detect sarcoidosis, non-small cell lung cancer small cell lung cancer and lymphoproliferative disorders can be determined, respectively, at levels of 87.36%, 87.23%, 91.30%, and 20%. Table 3 presents a compilation of the final diagnoses in the study group, taking into account the results of the initial EBUS examination and follow-up.

Table 2. Secondary intervention / evaluation results in the initially negative group (n=94)

Secondary interventions/evaluations	n
Other benign lesions (verified negative)	20
Sarcoidosis	11
Adenocarcinoma	3
Squamous-cell carcinoma	3
NSCLC NOS	6
Small cell carcinoma	2
Hodgkin Lymphoma	3
Other lymphatic growth	1
Tuberculosis	2
Radiological regression	6
Lost to follow-up	37

Table 3. Final diagnoses in the study group, considering the results of the initial EBUS examination and the follow-up data

Diagnosis		n	Percentage
Patients with definite diagnosis		237	100%
Non-small cell carcinoma (total)		94	39.66%
	Not otherwise specified	29	12.24%
	Adenocarcinoma	36	15.19%
	Squamous-cell carcinoma	27	11.39%
	Large cell carcinoma	2	0.84%
Small cell carcinoma		23	9.70%
Neoplastic lymphatic growth (total)		5	2.11%
	Hodgkin lymphoma	3	1.27%
	Other lymphatic growth	2	0.84%
Benign lesions (total)		115	48.52%
	Sacroidosis	87	36.71%
	Tuberculosis	2	0.84%
	Other benign lesions	20	10.97%

Based on this, it can be stated that among patients who received a final diagnosis (n=237), a significant majority, that is, 206 individuals or 86.92%, obtained it based on the first intervention.

Discussion

The EBUS-TBNA procedure is widely recognized and used globally in numerous centers as a diagnostic tool for mediastinal disorders, primarily for the diagnosis of mediastinal lymphadenopathy. Its widespread adoption has almost replaced mediastinoscopy, which, although still useful and necessary in many cases, is not performed as frequently. The shift from a surgical procedure burdened with, especially in inexperienced hands,

a relatively high risk of bleeding complications to a minimal-risk bronchoscopic procedure was an obvious step in the entire field of cancer diagnostics.

Over the years, EBUS has been thoroughly examined and has shown high sensitivity and specificity. In the 2014 ESTS guidelines, the reported sensitivity of EBUS-TBNA in lung cancer staging ranges from 87% to 93%, with nearly 100% specificity.[5] Furthermore, Crombag et al. demonstrated a sensitivity of 82% in diagnosing sarcoidosis.[6] The good safety profile and low learning curve for EBUS-TBNA training have encouraged many physicians to implement this method in their centers. However, it is crucial for the endoscopists performing the procedure to verify its effectiveness over the years. In centers where young physicians are trained, this is particularly important, as the excellent test parameters reported in clinical studies are achieved by experienced bronchoscopists. For this reason, we conducted an analysis in our center, where resident physicians are also trained to perform EBUS-TBNA. We can consider the results obtained satisfactory, with an average sensitivity of 89% to detect lung cancer metastases and 87% to detect sarcoidosis, supporting the continuation of our current examination and training doctrine. In a similar study, Murthi et al. aimed to evaluate the effectiveness of EBUS-TBNA in the hospital, staffed by pulmonologists with and without formal interventional lung training. EBUS-TBNA for all pathologies had a precision of 81.2% (CI 95% 73.8–87.4) and a sensitivity of 55.1% (CI 95% 41.5-67.3).[7]

One issue we need to address in this discussion is the low sensitivity to detect lymphomas (20%). Almost all patients required histopathological material for diagnosis, which is noteworthy. Erer OF et al. reported in their study that none of the cases of Hodgkin lymphoma was diagnosed using EBUS-TBNA, but there are also studies where sensitivity can reach close to 91%.[8-9] The wide range of reported results may be due to the needle sizes used, the availability of flow cytometry, and criteria for diagnosis. In many pathology departments, it is accepted that the diagnosis of lymphomas can only be based on the architectural assessment of the node and the cytological assessment is limited to raising suspicions. This suspicion was raised in 2 of our negative biopsies, so if suspicion is considered a sufficient indicator of test quality, the sensitivity could be calculated at 60%. However, this is still a low sensitivity in detecting lymphomas compared to some reports, so it remains a matter that requires further attention from our part. It is a case to be made that the implementation of flow cytometry can improve the diagnostic yield of EBUS-TBNA in these cases.

An obvious limitation of the study is its retrospective nature. The analysis of records from more than two years ago is not an optimal way to determine the parameters of a diagnostic test. Designing and conducting a prospective study with histopathological verification for all subjects would be an optimal approach, providing objectively the most accurate numerical values for the test parameters. Certainly, such a form would allow one to determine the specificity of the test, which we did not undertake in this analysis. The construction of our study, by accepting cytological diagnoses of tumors as certain and noncaseating epithelioid cell granulomas without necrosis as significant for the diagnosis of sarcoidosis, and the lack of secondary intervention in these patients, precluded the existence of false positive test results. Therefore, instead of accepting a specificity of 100%, it was better for us to refrain from determining this indicator with these limitations.

The study population in our center, representing a regional population of around 2 million people, in terms of cytopathological diagnoses, seems quite typical. Sangorini et al. described a similar cross section of patients in their analysis, with nearly 53% having cancer diagnoses, 1% lymphomas and 39% benign lesions, including sarcoidal ones.[10] Zhang et al. in their study presented a population with a comparable distribution: cancer – 43%, sarcoidosis – 42%, reactive nodes – 13% and tuberculosis – 1.5%.[11] On the other hand, Usluer et al. reported a smaller percentage of cancer and sarcoidosis diagnoses in favor of reactive nodes (39%).[12] Cetinkaya and his team, as the EBUS-TBNA diagnoses included tuberculosis – 35%, sarcoidosis – 35%, carcinoma - 25%, and lymphoma – 5%.[13] This large percentage of tuberculosis patients may be due to culture and other microbiological tests performed simultaneously. Nevertheless, it is uncommon to see such significant proportion of tuberculous disease reported, especially considering not even one percent in our study group. Ortakoylu et al. described a more standard cross section of results, consisting of 31% cancer, 36% sarcoidosis, 14% tuberculosis, 16% reactive/normal nodes.[14] The variability in results is small over the available studies, and only a significant proportion of sarcoidosis diagnoses juxtaposed with an exceptionally low percentage of tuberculosis may seem intriguing in our region, encouraging further research on granulomatous diseases in our center.

Conclusion

EBUS-TBNA is an effective method for diagnosing the cause of mediastinal lymphadenopathy, allowing a definitive diagnosis in 86.92% of patients in the first intervention and demonstrating high sensitivity to detect metastatic malignant lymph node involvement (approximately 89%).

Declarations

Funding

There is no funding to disclose.

Author contributions

Conceptualization, P.Z.; Methodology, P.Z.; Software, P.Z.; Validation, W.K. and E.K.; Formal Analysis, P.Z.; Investigation, P.Z. and W.K.; Resources, E.K.; Data Curation, P.Z. and E.K.; Writing – Original Draft Preparation, P.Z.; Writing – Review & Editing, P.Z. and E.K.; Visualization, P.Z.; Supervision, E.K.; Project Administration, E.K.

Conflicts of interest

The author(s) declare no conflict of interest.

Data availability

The data sets generated and/or analyzed during the current study are not publicly available due to their nature as medical records collected from a hospital information system. However, anonymized records derived directly from these data supporting the findings of this study are available from the corresponding author [PZ] upon reasonable request.

Ethics approval

This study was approved by the Bioethics Committee of the University of Rzeszów (KB 08/2025).

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