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Evaluation of Pathological Outcomes of EBUS-TBNA in Southern Iran: A Single Center Experience

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Abstract

Background: Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) has become an essential minimally invasive procedure for diagnosis and staging of lung cancer and unexplained mediastinal lymphadenopathy. Limited data exist on its clinical utility and outcomes in southern Iran.

Methods: This retrospective study was conducted on the results of pathologic reports of 128 patients who underwent EBUS-TBNA at Shiraz University of Medical Sciences, Shiraz, Iran, between 2017 and 2023. Patient demographics, anesthesia type, sedative medications, procedure-related complications, and pathology results were recorded and analyzed. Descriptive statistics were used to summarize continuous and categorical variables as mean ± standard deviation and frequency (percentage), respectively.

Results: Of the 128 patients (mean age 57.5 ±14.14 years; 81 (63%) male), 40.6% were diagnosed with malignancies, including primary lung cancers and metastatic diseases, while other cases involved benign conditions like sarcoidosis, tuberculosis, and anthracosis. Most procedures (99.2%) were conducted under general anesthesia, with minor complications reported in only six cases, including mild dyspnea and hypoxia. The majority of patients (88%) were discharged the same day.

Conclusion: EBUS-TBNA is a safe and effective diagnostic tool in southern Iran, with a high diagnostic accuracy for malignancies. Its low complication rate and outpatient feasibility reinforce its role as a first-line diagnostic approach for evaluating mediastinal lymphadenopathy and lung lesions. Future research should aim to standardize procedural techniques and further evaluate long-term outcomes in a larger, more diverse patient population.

Keywords: Endobronchial Ultrasound, Transbronchial Needle Aspiration, EBUS-TBNA, Thoracic Disease, Lymphadenopathy, Lung Cancer, Iran

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Introduction

Due to the high societal impact of malignant lung diseases in terms of mortality and disability-adjusted life years (DALYs), rapid and accurate diagnosis through sampling of affected lymph nodes is essential (1). Thus, endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) has emerged as an acceptable method for obtaining samples from mediastinal lymph nodes (2). This technique is widely utilized and recommended by American cancer guidelines for diagnosing and staging lung cancer, making it an indispensable tool for pulmonologists and thoracic surgeons (3, 4).

With increasing experience in performing EBUS-TBNA, it has emerged as a less invasive yet effective alternative to mediastinoscopy, the gold standard for mediastinal lymph node evaluation in lung cancer, with high sensitivity, specificity, and positive predictive value (5, 6). American College of Chest Physicians (ACCP) reports that EBUS-TBNA has a 91% sensitivity in establishing

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Key Messages:

↑What is "already known" in this topic:

EBUS-TBNA is a minimally invasive and highly effective technique for diagnosing and staging mediastinal and thoracic diseases, particularly lung cancer. Previous studies have demonstrated its high diagnostic accuracy and favorable safety profile compared with more invasive procedures such as mediastinoscopy.

→What this article adds:

This study provides the first comprehensive report of EBUS-TBNA outcomes from southern Iran, demonstrating its real-world diagnostic utility in malignancies, granulomatous diseases, and anthracosis. It also highlights its safety profile, outpatient feasibility, and unique regional disease patterns in a resource-limited clinical setting.

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the diagnosis of non-small cell lung cancer (NSCLC) as compared with 81% for cervical mediastinoscopy (7).

Besides lung cancer staging, EBUS-TBNA allows real-time visualization of airway walls, lungs, and mediastinal structures, aiding in the accurate diagnosis of undiagnosed thoracic lymphadenopathy causes such as malignant lymphoma, tuberculosis, and sarcoidosis (8). A 2019 study on 327 patients found that 231 were diagnosed with malignancies, while others had benign or infectious diseases (9). EBUS-TBNA is also used for sampling pulmonary nodules and assessing airway changes due to esophageal and thyroid cancers (10). Although it is generally low-risk, potential complications include fever, cough, chest pain, and hypoxia, but serious adverse effects are rare. So, benefits typically outweigh risks, particularly in the context of thorough patient assessment and procedural expertise (11, 12).

Although limited studies have been conducted on EBUS-TBNA and its diagnostic yield in specific conditions and diseases in Iran, comprehensive studies evaluating its clinical use and outcomes are notably scarce (13, 14). Given the revolutionary impact of EBUS-TBNA on diagnosing and treating respiratory and mediastinal disorders, it is crucial to assess its application, performance, and outcomes. This study aims to present the results of EBUS-TBNA at Shiraz University of Medical Sciences, addressing a significant gap in research from southern Iran. Publishing such outcomes enhances transparency, supports informed decision-making, fosters research, and ultimately leads to improved patient care and elevated healthcare standards.

Methods

Study Design

This study was a retrospective descriptive study of all patients who underwent the EBUS-TBNA procedure at Shiraz University of Medical Sciences between April 2017 and March 2023. The study protocol underwent a thorough review by a dedicated review board and received approval from the respected ethics committee at Shiraz University of Medical Sciences (SUMS) with the ethics code IR.SUMS.MED.REC.1402.397.

Indications for EBUS-TBNA

The procedure indications included a diverse range of conditions, such as individuals with primary lung cancer, unexplained mediastinal lymphadenopathy/masses, and metastatic cancers. All outpatient and inpatient hospital admissions who underwent EBUS-TBNA during the study period were included, with no exclusion criteria.

Data collection

Pre-operative diagnoses were determined based on operation notes. We recorded patients' age, gender, the type of anesthesia they received, and the specific sedative medications used during the procedure. Detailed notes regarding the drugs used for hypnosis, analgesia, amnesia, and muscle relaxation were recorded. We also documented any complications experienced after the procedure, noting any challenges they faced during their recovery. We carefully recorded how long each patient stayed in the hospital, both overall and on specific wards. Additionally, we reviewed the technical details of the procedure, such as the type of ventilation tubes used. Our aim was to comprehensively document each patient's experience of EBUS-TBNA from start to finish.

All pathologic records were prepared at the pathology laboratory of Namazi Hospital in Shiraz.

Data Analysis

Collected data were entered into a Microsoft Excel spreadsheet for organization and analysis. Descriptive statistics were used to summarize the findings, including means ± standard deviations for continuous variables and frequencies and percentages for categorical variables. As this study was primarily descriptive in nature, no inferential statistical tests were performed.

Results

Our study involved 128 patients, comprising 47 females (37%) and 81 males (63%) with a mean age of 57.5 ± 14.14 years. Almost all patients (99.2%) received general anesthesia, with only one undergoing conscious sedation (Table 1). The primary anesthetic agents used included Propofol and Sodium Thiopental (STP), Midazolam, Fentanyl, and Atracurium. The combinations of Midazolam, Fentanyl, STP, and Atracurium (47 cases) and Midazolam, Fentanyl, Propofol, and Atracurium (29 cases) were most commonly used. All procedures were started initially with fiberoptic bronchoscopy and performed with Convex Probe Endobronchial Ultrasound (EBUS, EB-530US Fuji) using a dedicated 21-gauge aspiration needle from various companies. Rapid on-site (ROSE) evaluation was not available.

The mean hospital stay was 1.4 ± 6.17 days (The high standard deviation is due to the large variability in the data regarding the length of hospital stay), with 88% of patients being discharged on the same day of the procedure. Fourteen patients were hospitalized due to their underlying conditions rather than the procedure itself (Table 1). Most patients were diagnosed with malignancies, including 52 cases of various cancers such as primary lung cancer (33 cases), breast cancer, renal cell carcinoma, lymphoma, and other malignancies (Table 1).

Preoperative diagnoses most frequently included primary lung cancer, lymphoma, metastasis, and granulomatous diseases like sarcoidosis and tuberculosis (TB).

Pathologic results (Table 2) identified 52 malignancies, including 13 cases of primary lung cancer. This group comprised 5 adenocarcinomas, 3 small cell lung cancers, and 2 squamous cell carcinomas (SCC). One case initially suspected as renal cell carcinoma (RCC) metastasis was confirmed as an undefined type of lung cancer. Out of 35 metastatic malignancies, 26 were confirmed as lung metastases, including 16 adenocarcinomas, 5 SCLC cases, and 5 undefined types. Other metastatic cancers included 2 cases of breast cancer, medullary thyroid carcinoma, and neuroendocrine malignancy. Five cases had metastasis with an undefined origin.

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Table 1. Basic demographic data of participants and their underlying diseases

Variable	Category	N (%)
Participants, n(%)	Men	81 (63%)
	Women	47 (37%)
Age, mean ± SD (years)		57.7 ± 14.14
Type of anesthesia, n(%)	General	127 (99.2%)
	Sedation	1 (0.8%)
Ventilation technique, n(%)	Endotracheal Tube	103 (80%)
	Laryngeal Mask	25 (20%)
Type of admission, n(%)	Outpatient	113 (88%)
	Inpatient	15 (12%)
Underlying diseases, n(%)	Malignancies	
	Lung cancer	35 (27.3%)
	Breast cancer	4 (3.1%)
	Renal cell carcinoma	3 (2.3%)
	Lymphoma	3 (2.3%)
	Uterine cancer	2 (1.5%)
	Colon cancer	1 (0.7%)
	Neuroendocrine tumor	1 (0.7%)
	Medullary thyroid carcinoma	1 (0.7%)
	Ophthalmic melanoma	1 (0.7%)
	Laryngeal cancer	1 (0.7%)
	Chronic Obstructive Pulmonary Disease	7 (5.4%)
	Asthma	5 (3.9%)
	previous Tuberculosis	6 (4.7%)

Table 2. Final pathology reports of participants who underwent EBUS-TBNA in Shiraz, Iran, 2017-2023

Final pathology results	Sub-group	No, %
Malignancy (n,%)		52/128 (40.6%)
	Metastatic lung malignancy	35/52 (67.3%)
	Primary lung cancer	13/52 (25%)
	lymphoproliferative disorders	4/52 (7.7%)
Granulomatous disease (n,%)		17/128 (13.3%)
	Sarcoidosis	13/17 (76.5%)
	Tuberculosis	3/17 (17.6%)
	Foreign body granuloma	1/17 (5.9%)
nonspecific inflammation (n,%)		39/128 (30.5%)
	With underlying disease*	21/39 (53.8%)
	Without underlying disease	18/39 (46.2%)
Anthracosis (n,%)		4/128 (3.1%)
	With underlying disease*	2/4 (50%)
	Without underlying disease	2/4 (50%)
Insufficient sampling (n,%)		16/128 (12.5%)
	With underlying disease*	7/16 (43.7%)
	Without underlying disease	9/16 (56.3%)

*Including any kind of cancer or respiratory diseases

Among all patients with lung cancer, only 5 cases underwent EBUS-TBNA for staging, all of which revealed N2 or N3 lymph node involvement.

Four cases involved lymphoproliferative disorders, including a suspected lymphoma diagnosed as B-cell lymphoma and one case classified as non-Hodgkin's lymphoma.

Within the observed cases, 39 were classified as non-specific inflammation**.** Of these, 21 had known underlying diseases, such as lung cancer, lymphoma, breast cancer, rheumatoid arthritis, RCC, and uterine cancer. These patients underwent the procedure to rule out of metastasis or malignancy, but none showed any malignant cells.

Out of the patients studied, 17 were identified as having granulomatous diseases. This included 13 cases of sarcoidosis, with three initially investigated for malignancy but later confirmed as sarcoidosis. Three cases were diagnosed as tuberculosis (TB), and one case involved a foreign body granuloma.

There were 16 instances of insufficient sampling. Among these, seven cases had underlying diseases. This included three known cases of lung cancer, where only one had atypical cells in the inadequate sample. Other cases with insufficient sampling involved small cell lung cancer (SCLC), uterine cancer, malignant ophthalmic melanoma, and a mediastinal mass suspected of malig-

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nancy. In the case of malignant ophthalmic melanoma, only some melanin pigment was observed in the inadequate sample. Additionally, there were nine patients without underlying diseases. Of these, five were investigated to rule out malignancy but had insufficient sampling; one showed few atypical cells. Two cases were assessed for granulomatous diseases, and one each for lung cancer and differentiation between tuberculosis and lymphoma, but sampling was inadequate for diagnosis.

Lastly, four cases of pulmonary anthracosis were observed. Two of these were known cases of malignancies (one case each of colon cancer and renal cell carcinoma (RCC)) initially assessed to exclude metastasis, with results ultimately indicating anthracotic mediastinal lymphadenopathy. Additionally, one case initially suspected of malignancy was confirmed as pulmonary anthracosis. Finally, one case primarily suspected of anthracosis was confirmed to show extensive anthracosis upon final examination.

Complications were mostly minor, with no major complications reported. Six patients experienced complications including mild post-procedure dyspnea (2 cases), pain (1 case), bradycardia (1 case), tachycardia (1 case), post-procedure hypoxemia (1 case), and prominent cough (1 case).

Three patients with lung cancer passed away during hospital stay, but their deaths were not attributed to the procedure (Table 1).

Discussion

This is the first comprehensive study offering important insights into the clinical use and outcomes of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) at Shiraz University of Medical Sciences, highlighting its significant role in diagnosing thoracic pathologies (15, 16). Our results are consistent with global findings, demonstrating that EBUS-TBNA is an effective and safe diagnostic tool, particularly in detecting malignancies and lymph node sampling. In contrast to alternative diagnostic approaches such as mediastinoscopy or CT-guided biopsy, its minimally invasive nature and quicker recovery time, coupled with a high diagnostic accuracy, make it a practical and safe option, especially for patients at higher surgical risk (17).

While the procedure result was non-diagnostic in some cases compared to highly diagnostic studies (6, 9, 16-19) it is still acceptable for real-world clinical settings, where patient factors, procedural expertise, and disease heterogeneity can influence outcomes (10, 20).

Despite the excellent visualization provided by real-time endobronchial ultrasound, the complexity of certain lymph nodes or masses, particularly those affected by fibrosis or necrosis, can hinder adequate tissue sampling. The lack of definite post-procedural diagnosis for benign undiagnosed conditions and insufficient sampling in our study underscore this procedural challenge associated with EBUS-TBNA. These findings are consistent with prior reports indicating that EBUS-TBNA has higher diagnostic accuracy for malignancies compared to other conditions (20, 21). and emphasize the need for careful patient selection and the potential utility of adjunctive techniques such as ROSE and elastography to enhance diagnostic accuracy (8, 13).

The high rate of malignancy diagnoses (40.6%) and the ability of EBUS-TBNA to provide accurate staging information for lung cancer (as seen in five cases) underline the value of this procedure in clinical practice. EBUS-TBNA has become a cornerstone in the diagnostic pathway for lung cancer, particularly non-small cell lung cancer (NSCLC), where accurate lymph node staging is critical for determining treatment strategy (3, 4). However, despite its common use in developed countries for staging lung cancer post-CT scan, we found that EBUS-TBNA was primarily used for diagnosing primary lung cancer (22). This difference is mainly due to the high proportion of advanced, inoperable lung cancer at presentation in our country (23, 24). This makes it a frontline tool in assessing mediastinal lymphadenopathy in patients with malignancy (18).

Findings related to granulomatous diseases, particularly sarcoidosis and tuberculosis, further highlight the versatility of EBUS-TBNA. In resource-limited settings, where access to advanced imaging and invasive procedures may be restricted, EBUS-TBNA offers a valuable diagnostic option for differentiating between benign and malignant causes of lymphadenopathy (10, 20). Additionally, we observed a notable incidence of anthracosis in our patient population (4 cases), which is consistent with findings from regions with high rates of environmental or occupational exposure to dust and pollution. This observation is supported by Abedini et al (13), who highlighted the utility of EBUS-TBNA in diagnosing anthracosis, particularly in populations with significant exposure to pulmonary irritants. Given the geographical and environmental context of southern Iran, the relatively high prevalence of anthracosis in our study is not unexpected.

The lack of significant difference in outcomes of patients who underwent general anesthesia or moderate sedation reported in recent studies allows for greater patient accessibility and comfort and supports the use of moderate sedation as a viable alternative to general anesthesia (25-28). However, most of our patients underwent general anesthesia with a variety of drugs, selected due to patient-specific conditions, underlying diseases, varying anesthesiologists' experiences, and drug potencies.

The overall complication rate in our study was low, with only six patients experiencing mild complications, such as transient hypoxia and post-procedure pain, which is in line with existing literature that emphasizes the safety profile of EBUS-TBNA, making it a preferred option for both patients and clinicians (12, 28, 29). The absence of major complications and the relatively short hospital stays (average 1.4 ± 6.17 days) further support the procedural safety of EBUS-TBNA in both inpatient and outpatient settings.

Even though we intended to also investigate drug dosages and procedure timing, we faced some limitations. Inconsistencies and potential inaccuracies in hospital records, along with reliance on incomplete pathologic results, impacted the precision of our study. The retrospective nature of the study limited our ability to control variables,

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verify results, and assess long-term outcomes accurately. Poor patient follow-up and selection bias compounded these issues, and variability in how EBUS-TBNA was performed and documented by physicians introduced further inconsistencies (21, 30). Future research should focus on specific dosage regimens, precise procedure timing, and diverse patient demographics with larger sample sizes to improve applicability. Long-term monitoring post-EBUS-TBNA could provide insights into efficacy and recurrence. Standardizing sedation protocols, exploring advancements in imaging technology, and investing in healthcare provider training could enhance procedural precision, safety, and patient care. These improvements have the potential to refine EBUS-TBNA practices and enhance patient outcomes in pulmonary medicine.

Conclusion

In conclusion, our study reaffirms the role of EBUS-TBNA as a key diagnostic tool in managing thoracic diseases. The high diagnostic accuracy and safety profile support its use as a first-line procedure for evaluating unknown lymphadenopathies, lung and other chest region masses, primary malignancies and metastases, and even benign conditions such as infections and granulomatous diseases.

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Conflict of Interests

The authors declare that they have no competing interests.

Authors' Contributions

All authors have made substantial contributions to the conception, design, analysis, and interpretation of data, and have approved the final manuscript.

Ethical Considerations

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study protocol was thoroughly reviewed and approved by the Ethics Committee of Shiraz University of Medical Sciences (SUMS) (Approval No.: IR.SUMS.MED.REC.1402.397), and informed consent was obtained from all participants.

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Data Availability

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

AI Use Statement

The authors did not use artificial intelligence or AI-assisted technologies in the preparation of this manuscript.

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