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Endobronchial Ultrasound Transbronchial Needle Aspiration for the Diagnosis of Paratracheal and Peribronchial Central Parenchymal Lesions

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Abstract

Objectives: Obtaining qualitative, sufficient material for the diagnosis of malignancies in cases with normal endoscopic findings in patients with suspected lung cancer and hilar and mediastinal lymphadenopathy is challenging.

Materials and methods: Endobronchial ultrasound (EBUS) was used to control a transbronchial needle biopsy (TBNA) for the first time in our country. From 2015 to 2018, TBNA with a convex probe EBUS was performed on 57 patients [41 men, 16 women, mean age 56.10 (range 37-77 years)] with mediastinal lesions found on CT scan. We used the Hitachi Aloka - ProSound Alpha 7 and BF-UC180F (Olympus) 21G and 22G needles Ultrasound System. In 22 of the cases, we performed a biopsy of hilum lesions (9 on the left and 13 on the right), in 13 - of subcarinal lesions, and in 4 - of lesions located on the right paratracheal lymphatic chain.

Results: EBUS-TBNA confirmed lung cancer in 48 patients (84.2%). In 33 of them, it was non-small cell lung cancer: spinocellular in 13 cases and adenocarcinoma in 17 cases; three cases were without accurate verification. Small cell lung cancer was found in 15 cases. In two cases, the biopsies were negative for tumor (3.5%), and in seven - non-specific inflammatory process (12.3%).

Conclusions: This study confirms the high diagnostic success rate of EBUS-TBNA reported in similar studies developed on a daily routine basis without adhering to a specific protocol. EBUS-TBNA is an interventional procedure with high sensitivity in diagnosing hilar and mediastinal lesions in negative conventional bronchoscopy and thus is useful in patients with paratracheal and peribronchial lesions. The results could be improved with training and experience.

Keywords

INTRODUCTION

Lung cancer is a leading worldwide cause of mortality, with approximately 2 million deaths per year.[1] In the United States, more than 170000 people are diagnosed with lung cancer and about 130000 die of lung cancer annually. The new cases registered in Bulgaria in 2015 were 3794 of which 81.2% were men.[2]

In suspicious patients, histological confirmation is required to make the diagnosis. In addition to diagnosis, it is needed for staging, therapy guide, and prognosis.

Bronchological examination is a major method for the diagnosis of pulmonary neoplasms. Bronchoscopic biopsies are the only material in more than 80% of patients with non-small cell lung cancer.[3]

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Many biopsy techniques have been developed with different success rates and diagnostic values depending on the location[4,5] and size[6] of the lesion, macroscopic characteristics, number and size of the biopsy taken[7,8], and last but not least - the experience of the interventional pulmonology specialists.[9]

The peribronchial central tumors (bulky lesions that do not alter the tracheobronchial tree) present a diagnostic challenge with conventional techniques including transbronchial needle aspiration biopsy because of the lack of real-time control of the sampling.

Endobronchial ultrasound (EBUS) is a combination of bronchoscopy and ultrasound in real-time and thus enhances the visibility of suspicious peribronchial structures, reducing biopsy sampling errors due to superior site selection sampling.[10] For this purpose, a biopsy technique under endobronchial ultrasound guidance with needle puncture aspiration biopsy (EBUS-TBNA) has been developed. Using EBUS, it is possible to take adequate samples for immunohistochemistry and DNA analysis of the tissue obtained needed for further examination when preparing the patient for targeted therapy.[11] Although the utility of EBUS in diagnosing parenchymal lesions in cases of non-diagnostic conventional bronchoscopy has been recognized there are limited reports about its application for this purpose[12-15] and none in Bulgaria.

AIM

This study aims to assess the diagnostic yield of endobronchial ultrasound transbronchial needle aspiration biopsy in patients with paratracheal and peribronchial central parenchymal lesions.

MATERIALS AND METHODS

Study design

A study of the diagnostic yield of EBUS-TBNA for four years (2015 – 2018) in patients with central lesions suspected for pulmonary neoplasm after negative bronchoscopy was conducted. A total of 57 consecutive patients were enrolled. Informed consent was obtained from all participants for the procedures. The Ethics Committee of the Clinical Center for Pulmonary Diseases approved the study (No 38/25.11.2015).

Procedure

EBUS-TBNA was performed by three qualified specialists, with the BF UC180F Olympus Ltd. videobronchoscope, Tokyo, Japan incorporating the Hitachi Aloka ProSound Alpha 7 ultrasonic processor.

The examination was performed under general anesthesia and intubation with a Storz No. 8.5 rigid bronchoscope or with an I-gel supraglottic airway device. TBNA was performed with 21G and 22G biopsy needles SonoFlex FNA-B02-2218 and Olympus NA-201SX4021. Subsequently, the acquired biopsy material was prepared on microscopic glass, dried and after fixation with 95% alcohol was sent for histopathological investigation in a specialized unit.

Additional immunohistochemical and genetic studies were performed if necessary at the discretion of a pathologist. Positive results from EBUS-TBNA were not verified by surgical intervention or histological examination. Negative results were followed by VATS and histological examination.

Inclusion criteria

The study included patients with previous bronchoscopy without endoscopic data for bronchial involvement and CT data for peribronchial or central lesion **(Fig. 1)**.

Statistical analysis

The data were analyzed using the SPSS software package (v. 20) and MS Excel. The prevalence, results and variables are described as numbers and percentages.

Figure 1. Representative sample patient - a 49-year-old woman with CT data of peribronchial right-sided lesion (A) and an ultrasound image of performing TBNA (B).

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RESULTS

For the first time in Bulgaria, EBUS has been used to control transbronchial needle aspiration biopsy in central lesions without infiltration of the bronchial mucosa. The demographic data and CT characteristics of the target tumor are presented in **Table 1**.

Table 1. Demographic data and location of the tumor

Patients, N	57
Age, mean years	56.1 (±4.2)
Males, N (%)	41 (71.9)
Smokers, N (%)	51 (89.4)
Mean size, mm	28.5 (±10.7)
Tumor location, N (%)	
Hilar region, left	12 (21.1)
Hilar region, right	20 (35.1)
Subcarinal	17 (29.8)
Paratracheal, right	8 (14.0)

A pulmonary neoplasm was confirmed in 48 patients (84.2%, **Table 2**): 33 patients were diagnosed with NSCLC (13 with squamous cell cancer, 17 with adenocarcinoma, and 3 were undifferentiated). SCLC was found in 15 patients. In 9 patients, the malignancy was not confirmed by EBUS-TBNA - 2 were negative and 7 with non-specific inflammation. They were referred to a surgical department for subsequent diagnostic work-up. Video-assisted thoracoscopy was performed which confirmed SCLC in 1 patient with negative histology, adenocarcinoma in 1 patient, sarcoidosis in 2 patients, and benign mesenchymal tumor in 1 patient. The sensitivity and specificity of the method were calculated and presented in **Table 3**.

Table 2. The pathological results from EBUS-TBNA

Non-small cell lung cancer, N (%)	33 (57.9)
Squamous cancer, N (%)	13 (22.8)
Adenocarcinoma, N (%)	17 (29.8)
NSCLC – not otherwise specified, N (%)	3 (5.3)
Small cell lung cancer, N (%)	15 (26.3)
Nonspecific inflammation, N (%)	7 (12.3)
Undiagnosed, N (%)	2 (3.5)
Total	57 (100)

Table 3. Sensitivity and sensibility of EBUS-TBNA in the study

Measure	Value	95% CI
Sensitivity	94.12%	83.76% to 98.77%
Specificity	90.00%	55.50% to 99.75%
Positive Likelihood Ratio	9.41	1.46 to 60.50
Negative Likelihood Ratio	0.07	0.02 to 0.20

No procedure-related complications were registered in 24 hours and the patients were discharged on their regular therapy for comorbidities.

DISCUSSION

EBUS-TBNA has several advantages in central lesions - the ability to observe the object of interest in real-time, the precise selection of a biopsy site, and the avoidance of surrounding structures using Doppler. The use of TBNA without ultrasound control in central lesions increases the risk of affecting surrounding structures – such as large vessels, resulting in low diagnostic success. Combined with the Rapid On-Site Cytology exam (ROSE) method, it increases success but also requires additional qualification or a cytomorphology specialist on-site during the study.

The possibility of diagnosing a tumor process is transthoracic true-cut biopsy which has a high success rate in peripheral, especially lesions that are attached to the chest wall. In central lesions, the risk of bleeding and pneumothorax is increased due to the underlying parenchyma.[16]

Diagnostic yield depends on the location and size of the tumor. In cases of endobronchial central localization, it reaches up to 95%. In contrast, it is diagnostic up to 65% in peripheral lesions even under X-ray control.[4] In the case of submucosal or peribronchial localization of the lesions, the use of forceps biopsy has low diagnostic sensitivity due to the lack of mucosal infiltration.

A study by Verma et al. demonstrated that the conventional methods – mucosa sampling and TBNA in cases of peribronchial lesions has a diagnostic yield of 13.5% compared to 86.4% with EBUS-TBNA.[15]

Tournoy et al. demonstrated the high sensitivity of the method (82%) in patients with central lesions and diagnostic failure of prior conventional bronchoscopy. As a result, in 47% of patients, a further diagnostic transthoracic needle biopsy and 30% surgical intervention was not necessary. There were no complications associated with the procedure. The authors recommend EBUS-TBNA in patients with central lesions after negative conventional bronchoscopy.[12]

In another study by Nakajima et al., patients with central lesion without endobronchial involvement were diagnosed with EBUS-TBNA in 94.1% of cases. These authors also recommend biopsy with real-time endobronchial ultrasound control for diagnostic purposes.[13]

Lee et al. retrospectively examined the success of the method in 126 patients with X-ray suspected pulmonary neoplasm. 118 of them were without endobronchial involvement, but EBUS-TBNA was diagnostic in 92.1% (116/126) of patients.[14]

Zhao et al. performed EBUS-TBNA in 66 patients with negative prior bronchoscopy, and confirmed malignancy in 59, achieving a diagnostic success rate of 89.4%. Despite the high success rate of the method, false-negative cases were up to 42.9%, which requires subsequent surgical intervention in negative EBUS-TBNA cases.[6]
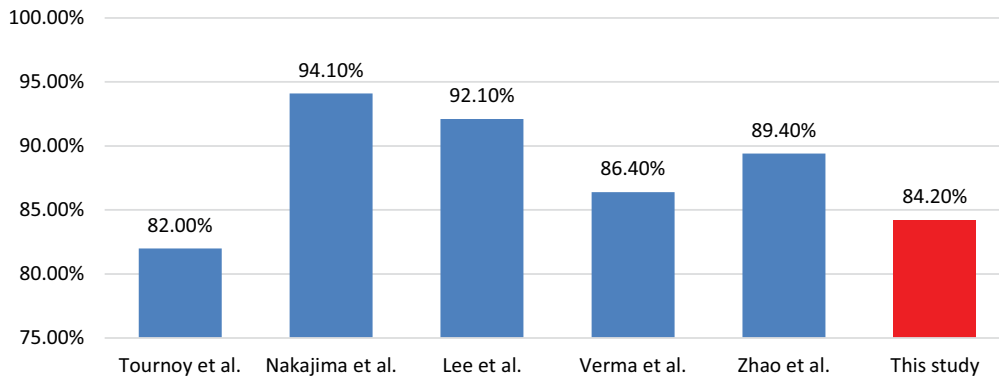
Figure 2. Diagnostic yield of EBUS-TBNA.

This study confirms the high diagnostic success rate of EBUS-TBNA published in similar studies developed on a daily routine basis without adhering to a specific protocol **(Fig. 2)**. Our results are similar to those from other bronchological centres and support the utility of the method in the diagnosis of peribronchial central lesions.

Despite the high results, we recognize a 5-10% lower diagnostic yield compared to the other centres. The explanation could not be straightforward. Many physicians lack adequate training and experience in the first place and because of the expensive equipment and consummative, the quality level is hard to be sustained. Also, there is no additional professional fee reimbursement and no additional facility fee reimbursement above standard bronchoscopy.[17] Because of all these facts, our results are hard to be compared with foreign interventional centres that perform above 100 procedures per year.

CONCLUSIONS

This study confirms the high diagnostic success rate of EBUS-TBNA reported in similar studies developed on a daily routine basis without adhering to a specific protocol. EBUS-TBNA is an interventional procedure with high sensitivity in diagnosing hilar and mediastinal lesions in negative conventional bronchoscopy and thus is useful in patients with paratracheal and peribronchial lesions. The results could be improved with training and experience.

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Эндобронхиальное ультразвуковое исследование с трансбронхиальной иглой для диагностики паратрахеальных и перибронхиальных центральных паренхиматозных поражений

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Резюме

Цели: Получение качественного и достаточного материала для диагностики злокачественных новообразований при нормальных результатах эндоскопических исследований у пациентов с подозрением на рак лёгкого и внутригрудную и средостенную лимфаденопатию является сложной задачей.

Материалы и методы: Эндобронхиальное ультразвуковое исследование (ЭБУИ) было использовано для контроля трансбронхиальной игольной биопсии (ТБИБ) впервые в нашей стране. С 2015 по 2018 год ТБИБ с выпуклым зондом для ЭБУИ была проведена 57 пациентам (41 мужчина, 16 женщин, средний возраст 56,10 (диапазон 37-77 лет)) с поражениями средостения, обнаруженными при КТ. Мы использовали Hitachi Aloka – ProSound Alpha 7 BF-UC180F (Olympus) 21G и игольную ультразвуковую систему 22G needles Ultrasound System. В 22 случаях мы выполнили биопсию очагов поражения ворот лёгких (9 слева и 13 справа), в 13 – биопсию очагов субкраниальных поражений и в 4 – поражений, расположенных на правой паратрахеальной лимфатической цепи.

Результаты: ЭБУИ – ТБИБ подтвердил рак лёгких у 48 пациентов (84.2%). У 33 из них была обнаружена немелкоклеточная карцинома лёгкого: плоскоклеточная карцинома в 13 случаях и аденокарцинома в 17 случаях; три случая остались без точной проверки. Мелкоклеточный рак обнаружен в 15 случаях. В двух случаях биопсия была отрицательной на опухоль (3.5%), а в 7 – неспецифической на воспалительный процесс (12.3%).

Заключение: Это исследование подтверждает высокий процент успешного применения ЭБУИ – ТБИБ, установленный при аналогичных исследованиях, проведённых на повседневной рутинной основе без соблюдения определённого протокола. ЭБУИ – ТБИБ – это высокочувствительная интервенционная процедура для диагностики внутригрудных и средостенных поражений в случаях отрицательной стандартной бронхоскопии, поэтому она полезна для пациентов с паратрахеальными и перибронхиальными поражениями. Результаты можно улучшить с помощью обучения и опыта.

Ключевые слова

бронхология, ЭБУИ, эндобронхиальное УЗИ, рак лёгких