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Comparison of EBUS-TBNA and surgical evaluation in mediastinal lymphatic staging of non-small cell lung cancer

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Abstract
Mediastinal lymph node involvement is the most important factor which determines the treatment and prognosis in NSCLC. In this study, the role of EBUS-TBNA was examined in evaluating intrathoracic lymph node in patients diagnosed with preoperative NSCLC. EBUS-TBNA was performed on fourty-four male cases (average age 59.8) diagnosed with preoperative NSCLC between March 2010-January 2012. Thorax-CT and PET-CT were performed on all patients before staging. Hystopathological evaluation results of lymph nodes which were dissected during the surgery were compared with citopathological evaluation results of the lymph nodes which were taken through EBUS-TBNA. Sixteen right paratracheal (36, 4%), 23 left paratracheal (52, 3%) and 40 subcarinal (90, 9%) lymph nodes were sampled through EBUS-TBNA. On the other hand, paratracheal lymph nodes were removed from 41 cases (93, 2%) and subcarinal lymph nodes were removed from 43 cases (97, 7%) through surgical procedure. Ultrasonograhic sizes of the right paratracheal lymph nodes which were sampled through EBUS-TBNA was 8,88mm, left paratracheal lymph nodes was 9,23mm and subcarinal lymph nodes was 11,66mm. As a result of the statistical analysis, sensitivity, specifity, PPV, NPV and accuracy of the EBUS-TBNA in NSCLC were identified as 66.7%, 100%, 100%, 97.6% and 97.7% respectively. Thus, in addition to clinician experience, tomographic, bronchoscopic and ultrasonograhic correlation of the lymph node which will be sampled and sufficient number of aspiration, EBUS-TBNA can be preferred as an alternative to invasive techniques due to its high diagnostic accuracy and accurate staging in NSCLC patients.

Keywords: Lung Cancer, Staging, EBUS, TBNA

Introduction
Fifty percent of the patients with non-small cell lung cancer (NSCLC) have mediastinal lymph node involvement at the time of the diagnosis and 30 per cent of them are suitable for surgical resection. Mediastinal lymphatic staging is the most important factor in determining prognosis in NSCLC [1].

In the evaluation of mediastinal lymph nodes; besides the conventional imaging techniques such as computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET), interventional procedures such as transbronchial and transtracheal needle biopsies, endobronchial-endoesophageal ultrasonography guided lymph node biopsy, cervical mediastinoscopy, mediastinotomy and video-assisted lymph node staging are commonly used.

While Thorax-CT, the first method used to evaluate mediastinal lymph nodes, may show size increase in mediastinal lymph nodes, it has limited sensitivity and selectivity in the detection of metastasis [2]. On the other hand, mediastinoscopy, which has excellent sensitivity and selectivity in staging mediastinal lymph node evaluation and is accepted as the standart gold standard, has the disadvantage of being invasive. Therefore, there is a growing interest in non-invasive and minimally invasive techniques and research has been concentrated in this direction. PET, which is one of the non-invasive techniques and endobronchial ultrasongography (EBUS) guided transbronchial needle aspiration (TBNA), which is one of the minimally invasive technique, have become increasingly used methods.

EBUS is an ultrasound method developed for imaging the structures adjacent to the airways and on the airway wall. As a result of the search for a minimally invasive procedure that can be preferred to mediastinoscopy, which is an invasive procedure for cytopathological lymph node evaluation and has the same sensitivity and selectivity, EBUS has been increasingly used in recent years. Besides, research conducted in that direction show that EBUS-TBNA, which has 87% sensitivity and 100% selectivity, has now became the focus of interest [3].

Our aim in our study is to determine EBUS-TBNA'a sensitivity, selectivity, negative prediction value, positive prediction value and accuracy rates in mediastinal staging by comparing the mediastinal lymph node evaluation findings of patients with NSCLC and radiological staging with the histopathological evaluation of the lymph nodes after the operations.

Materials and Methods
Patients diagnosed as preoperative NSCLC between March 2010 and January 2012, who underwent thoracic-CT and

PET-CT as well as EBUS-TBNA for staging purposes were evaluated retrospectively. The patients who had no contraindication for fiberoptic bronchoscopy and had pathological involvement (SUVMax> 2.5) in PET-CT or those with a short axis of 1 cm or more on thorax-CT were included in the evaluation.

All cases were evaluated by anamnesis, physical examination, pulmonary function tests, electrocardiography, biochemistry, hemogram, coagulation tests, chest radiographs, thorax-CT and PET-CT. Age, sex, the method of preoperative diagnosis of NSCLC, localization of the mass, intrathoracic lymph nodes showing pathologic size increase (> 1cm) in thorax-CT, SUVmax values of the mass and all lymph nodes on PET-CT, lymph nodes sampled with preoperative EBUS-TBNA, operation performed, lymph nodes sampled / excised in the operation, tumor size, cytological and histopathological examination results of the sampled lymph nodes and tumor type were recorded in the database for all the cases included in the study.

EBUS-TBNA procedure was performed on all patients by the same team in the interventional bronchology unit. Patients abstained from food for eight hours before the procedure. Following the monitoring of vital findings by the anesthesiologist in the procedure room before the procedure, sedation was performed.

Mediastinal lymph nodes showing radiological pathological size increase were evaluated according to Wang map. Lymph nodes were classified at 5 mm intervals. TBNA was performed on the right / left paratracheal and subcarinal lymph nodes. TBNA was repeated 3 times on average for each station. Since there was no pathologist involved in the procedure, the adequacy of the material was decided by the physician performing the bronchoscopy.

Pathological evaluation of all preparations was performed by the same pathologist as a single blind. Materials were divided into two groups as pathologically sufficient and insufficient samples. The preparations diagnosed with definite malignancy were evaluated as positive enough and those with abundant lymphocytes but not malignancy were considered negative enough. Suspicious preparations containing bronchial epithelium or cellular atypia were accepted as insufficient samples.

Data analysis was performed using SPSS for Windows version 11.5. Descriptive statistics were shown as mean ± standard deviation (minimum - maximum) for continuous variables and as number of cases (%) for nominal variables. Sensitivity, selectivity, positive and negative predictive values and diagnostic accuracy rates were calculated in order to investigate the diagnostic performance of EBUS in the classification of benign and malignant lymph nodes according to surgical pathology. Fisher's exact chi-square test was used to determine whether EBUS-TBNA was key to differentiating malignant and benign lymph nodes. P values less than 0.05 were considered statistically significant.

Results

All 44 cases (100%) included in the study were male. The mean age of the patients ranged between 39-74 years was 59.8 ± 7.8 years. All of the patients included in the study had lymph nodes with a short axis of 1 cm or more on thorax-CT. PET-CT results for pathological involvement of lymph nodes were not sought in these patients. EBUS-TBNA was applied to the paratracheal and subcarinal lymph nodes.

The analysis of tumor localization revealed lesions in the right lung in 19 cases (43.2%) and in the left lung in 25 cases (56.8%). Of the tumors located in the right lung, 8 (18.2%) were in the upper lobe, 3 (6.8%) were in the middle lobe and 8 (18.2%) were in the lower lobe. Of the tumors located in the left lung, 8 (18.2%) were in the upper lobe and 17 (38.6%) were in the lower lobe.

Lobectomy was performed in 24 (54.5%), pneumonectomy in 19 (43.2%) and mediastinoscopy in 1 (2.3%) of 44 patients who underwent EBUS-TBNA for staging following the preoperative NSCLC diagnosis. Right upper lobectomy was performed in 7 cases (15.9%), right lower lobectomy in 4 (9%), bilobectomy inferior in 2 (4.5%), right pneumonectomy in 5 (11.4%), left upper lobectomy in 4 (9%), left lower lobectomy in 7 (15.9%) and left pneumonectomy in 14 cases (31.8%).

The mass SUVmax values in PET-CT ranged from 4 to 30.8, with a mean SUVmax of 12.1 ± 5.5. Mass sizes ranged from 46 to 160 mm, with a mean of 48.9 ± 31.6 mm.

The mean SUVmax value of right paratracheal lymph nodes was 1.56, the average SUVmax value of left paratracheal lymph nodes was 0.77, and the average SUVmax value of subcarinal lymph nodes was 2.07 on PET-CT.

Sixteen (36.4%) right paratracheal, 23 (52.3%) left paratracheal and 40 (90.9%) subcarinal lymph nodes were sampled by EBUS-TBNA. Lymph nodes were sampled at least 3 times in all cases with EBUS-TBNA except one case. During the operations, paratracheal lymph node dissection was performed in 41 (93.2%) cases and subcarinal lymph node dissection was performed in 43 (97.7%) cases.

The diameters of the lymph nodes were evaluated by EBUS and subjected to statistical analysis. Accordingly, the mean ultrasonographic diameter of the right paratracheal lymph nodes sampled was 8.88 mm, the left paratracheal lymph nodes were 9.23 mm and the subcarinal lymph nodes were 11.66 mm (Table I).

Table 1: Ultrasonographic diameters of lymph nodes evaluated by EBUS

Variables	Average (mm)	Standard Deflection	Mean	Smallest	Biggest
EBUS diameter 4R	8,88	3,54	8,25	4,60	18,00
EBUS diameter 4L	9,23	3,94	8,00	5,20	19,20
EBUS diameter 7	11,66	4,85	10,50	4,50	26,00

Tumor cell types were identified according to histopathological results obtained after the operations performed. Squamous cell carcinoma 27 (61.36%), adenocarcinoma 9 (20.45%), adenosquamous carcinoma 3 (6.82%), carcinosarcoma 2 (4.54%), atypical carcinoid tumor 1 (2.27%), large cell carcinoma 1 (2.27%) and combined squamous + large cell carcinoma 1 (2.27%) were detected.

Cytopathologic examination revealed metastatic lymph nodes in 1 (6.3%) of 16 cases whose right paratracheal lymph node was evaluated by EBUS-TBNA. Whereas none of the 23 cases whose left paratracheal lymph node had

cytopathologic metastasis. Cytopathologic metastasis was identified in 1 (2.5%) of 40 cases whose subcarinal lymph node was evaluated by EBUS-TBNA.

Histopathological examination of 41 paratracheal lymph nodes dissected after the operations revealed metastatic lymph nodes in 2 cases (4.9%). Metastatic lymph nodes were detected in 1 (2.3%) of 43 cases that underwent subcarinal lymph nodes dissection.

In the evaluation of paratracheal lymph nodes, histopathologic examination of the right paratracheal lymph nodes following the operation revealed metastatic lymph nodes in 2 cases and one of these cases (50.0%) was found to be metastatic as a result of the cytopathological evaluation the lymph nodes sampled with EBUS-TBNA. All of the 14 patients (100%) whose surgical pathology results were benign were also found to be non-metastatic with EBUS. Hystopatholofical result of 1 case (100%) that was identified as metastatic following the cytopathologic evaluation of lymph nodes sampled by EBUS-TBNA was also metastatic. Surgical pathology of 14 (93.3%) of 15 case, which were evaluated as non-metastatic by EBUS-TBNA, was also non-metastatic. In the evaluation of right paratracheal lymph nodes, the sensitivity of EBUS-TBNA was 50%, selectivity was 100%, PPV was 100%, NPV was 93.3% and accuracy was 93.8%. EBUS was not found to be statistically significant in the detection of metastatic and non-metastatic lymph nodes ($p = 0.125$).

Histopathological examination of the left paratracheal lymph nodes revealed non-metastatic lymph nodes in all cases. All 23 cases (100%) whose surgical pathology results were non-metastatic were also identified as non-metastatic as a result of cytopathological evaluation after EBUS-TBNA. The selectivity of EBUS-TBNA was 100%, NPV was 100% and accuracy was 100%. Because of the lack of metastatic lymph nodes and sufficient number of cases, the determination of EBUS-TBNA in detecting metastatic and non-metastatic lymph nodes could not be statistically analyzed.

Histopathological evaluation of the subcarinal lymph nodes revealed metastatic lymph nodes in one patient and metastatic lymph nodes were detected as a result of cytopathological examination after EBUS-TBNA procedure (100%). All 39 cases (100%) whose surgical pathology results were non-metastatic were also identified as non-metastatic by EBUS-TBNA. The sensitivity, selectivity, PTD, NTD and accuracy of EBUS-TBNA were 100% in the evaluation of subcarinal lymph nodes. EBUS-TBNA was found to be statistically significant in distinguishing between metastatic and non-metastatic lymph nodes ($p = 0.025$).

In general, the evaluation of N2 lymph node stations showed that 2 (66.7%) of the 3 cases whose histopathological examination revealed metastatic lymph nodes were also found to be metastatic after EBUS-TBNA and 1 patient was found to be false negative with EBUS-TBNA. It was. All 41 cases (100%) whose surgical pathology results were non-metastatic were also identified as non-metastatic by EBUS-TBNA. Pathology results of 2 cases which were identified as non-metastatic by EBUS-TBNA revealed metastatic lymph nodes. Surgical pathology results of 41 (97.6%) of 42 cases who were evaluated as non-metastatic by EBUS-TBNA were also non-metastatic. The sensitivity of EBUS-TBNA was 66.7%, selectivity was 100%, PTD was 100%, NTD was 97.6% and accuracy was 97.7%. EBUS-TBNA was found to be statistically significant in differentiating between metastatic and non-metastatic lymph nodes ($p = 0.003$).

Table II provides diagnostic performance indicators of EBUS-TBNA in determining metastatic and non-metastatic lymph node groups according to postoperative histopathological evaluations.

Table 2: Diagnostic Performance Indicators of EBUS in Distinguishing Malignant and Benign Groups According to Surgical Pathology

Indicators	Definitions	EBUS 4R	EBUS 4L	EBUS 7	N2
Number of cases	N	16	23	40	44
Sensitivity	TP/(TP+FN)	1/2 (%50)	-	1/1 (%100)	2/3 (%66,7)
Specificity	TN/(TN+FP)	14/14 (%100)	23/23 (%100)	39/39 (%100)	41/41 (%100)
PPV	TP/(TP+FP)	1/1 (%100)	-	1/1 (%100)	2/2 (%100)
PV	TN/(FN+TN)	14/15 (%93,3)	23/23 (%100)	39/39 (%100)	41/42 (%97,6)
Accuracy	(TP+TN)/(N)	15/16 (%93,8)	23/23 (%100)	40/40 (%100)	43/44 (%97,7)

Discussion

Surgical resection is the best accepted method for the treatment of lung cancer. Accurate staging is crucial in identifying prognosis as most of the cases have mediastinal lymph node involvement and distant metastasis at the time of diagnosis. The study by Herth *et al.* [4], which showed that EBUS-guided TBNA was more effective and successful in sampling lymph nodes that show pathological size increase on CT than the conventional TBNA procedure, was among the first studies showing the meaning of EBUS in TBNA. The sensitivity of EBUS-TBNA is higher in patients with lymph node enlargement (shorter diameter greater than 1 cm) on thorax-CT. In a similar study, the sensitivity increases from 15% to 38% when only the presence of lymph nodes showing pathologic size increase on CT is accepted as the criteria [5]. While Utz *et al.* [6] reported positive TBNA in 36% of 88 patients with lung cancer, this value was 43% in 67 cases where pathologic lymph node size increase could be detected radiologically, and %10 in 21 patients who underwent subcarinal lymph node evaluation and did not show any pathological size increase radiologically. In our study, which included cases whose lower paratracheal and subcarinal lymph nodes were sampled by EBUS-TBNA, there were 7 cases with a short diameter of less than 1 cm on CT. In all of these cases, sufficient material for diagnosis and sampling was obtained by EBUS-TBNA. In only 1 case, the lymph node was evaluated as false negative with EBUS-TBNA.

According to research, simultaneous needle aspiration and cytopathological evaluation (ROSE) increased the diagnostic performance of conventional TBNA up to 71% and this rate was 25% in sampling without ROSE [7]. That the use of ROSE increases the diagnostic performance of TBNA was also confirmed by Davenport *et al.* [8] (56% vs. 31%) and Diette *et al.* [9] (81% versus 50%). The ROSE process is not implemented in every clinic as it requires

support personnel. In a study of 242 patients with mediastinal lymph node (mean diameter 1.7) which showed increased pathologic size on CT and EBUS-TBNA, adequate material was obtained in 86% of the cases and malignant lymph node involvement was detected in 72% [10]. The fact that 100% material adequacy was obtained in our study may be related to the good detection of lymph node localizations by EBUS. We believe that the conventional TBNA experience of practitioners plays a role in the rate of adequate material, and that ROSE will not contribute to the diagnostic success.

In our study with 44 cases which aims to investigate the efficacy of EBUS-TBNA in determining the presence of N2 which detects prognosis in mediastinal staging in NSCLC, 2 (66.7%) of the 3 cases with metastatic lymph nodes found following the histopathological examination after the surgery, were also found to be metastatic after EBUS-TBNA procedure and 1 patient was found to be false negative with EBUS-TBNA. All 41 cases (100%) who were found to be non-metastatic following the surgical pathology were also evaluated non-metastatic by EBUS-TBNA. The pathology result of 2 cases which were identified as metastatic by EBUS-TBNA was also metastatic. Surgical pathology results of 41 (97.6%) of 42 cases which were identified as non-metastatic by EBUS-TBNA, were also non-metastatic. In the statistical analysis performed with these results, the sensitivity of EBUS-TBNA was 66.7%, selectivity %100, PPV 100%, NPV 97.6% and accuracy %97.7. In the meta-analysis published in ACCP in 2007, the results of EBUS-TBNA in mediastinal staging were examined. In this meta-analysis, the mean sensitivity was found to be 90% (79-95%), while the overall false-negative rate was 24%. Although not confirmed by further interventions, selectivity and false positivity rates were 100% and 0%, respectively (Table III) [11].

Table 3: Efficacy of EBUS-TBNA in mediastinal staging in the literature

Article	n	Technic	Sensitivity (%)	Specificity (%)	FP (%)	FN (%)	Accuracy (%)
Yasufuku 2004	70	RT-US fob (22 ga)	95	100	0	10	67
Yasufuku 2005	108	RT-US fob (22 ga)	95	100	0	11	69
Vilmann 2005	31	RT-US fob (22 ga)	85	100	0	28	65
Rintoul 2005	20	RT-US fob (22 ga)	79	100	0	30	70
Kanoh 2005	54	Radial prob (19 ga)	86	100	0	37	81
Herth 2006	502	RT-US fob (22 ga)	94	100	0	89	98
Plat 2006	33	Radial prob (Histo Dana 2.2 mg)	93	100	0	25	82
Herth 2006	100	RT-US fob (22 ga)	94	100	0	10	17
Total	908		90	100	0	20	68

When the ACCP 2007 meta-analysis results were compared with the results of our study, the sensitivity was lower, the selectivity was the same and the accuracy was higher. While the cytopathological results of the lymph node of 1 patient which was sampled with EBUS-TBNA were reported as non-metastatic, its histopathological evaluation after surgery was found to be metastatic. When this case was examined, it was seen that less than 3 samples were taken from this lymph node by EBUS-TBNA. Low sensitivity was thought to be caused by insufficient sampling of the lymph node by TBNA.

In the literature, the rate of diagnosis in tumors located in the right lung is higher than in tumors located in the left lung in staging performed with EBUS-TBNA [12]. The sensitivity of EBUS-TBNA was 92% for the right lung, 56% for the left lung, and 76% in total. Harrow *et al*. [13] found that the sensitivity of EBUS-TBNA was higher in right lung localized tumors compared to the left lung localized tumors. Similarly, right paratracheal and subcarinal lymph node aspirates had higher positivity than left paratracheal aspirates. In their study, Patelli *et al*. [14] found that the total sensitivity in detecting mediastinal lymph node metastasis was 71% in 194 TBNA procedures, with a sensitivity of 52% in the left paratracheal stations, which was lower compared to the right paratracheal (84%) and subcarinal (84%) stations. In their 2008 study with 66 cases Ernst *et al*. [3] compared EBUS-TBNA with mediastinal lymphadenopathy and mediastinoscopy, and particularly investigated the effect of lymph node localization on the diagnostic success. The diagnostic accuracy rate of EBUS-TBNA was 91% while that of mediastinoscopy was 78%. In addition, EBUS-TBNA was found to be more effective than mediastinoscopy in samples taken from subcarinal lymph node. In our study, the sensitivity of EBUS-TBNA was 50% in the evaluation of right paratracheal lymph nodes, selectivity 100%, PPV 100%, NPV 93.3% and accuracy 93.8%. EBUS was not found to be statistically significant in the detection of metastatic and non-metastatic lymph nodes ($p = 0.125$). The selectivity of EBUS-TBNA in the evaluation of left paratracheal lymph nodes was 100%, NPV was 100% and accuracy rate was 100%. Since there was no variability, the efficacy of EBUS-TBNA in detecting metastatic and non-metastatic lymph nodes could not be statistically analyzed. In the evaluation of subcarinal lymph nodes, the sensitivity, selectivity, PPV, NPV and accuracy rates of EBUS-TBNA were 100%. EBUS-TBNA was found to be statistically significant in distinguishing between metastatic and non-metastatic lymph nodes ($p = 0.025$). We think that the difference between the statistical results obtained in our study and the rates in the literature is due to the small number of cases included in our study.

Lymph node size is another factor that increases the sensitivity of TBNA. In their study on conventional TBNA, Harrow *et al*. [13] showed that a linear increase in malignancy-positive aspirates was observed as the lymph node size increased from 1 cm to 2.5 cm. The most comprehensive study with EBUS-TBNA and real-time linear screening was performed by sampling 572 lymph nodes from 502 patients. 535 (94%) lymph node sampling were diagnostic. Sampling was made from all accessible lymph node stations by EBUS-TBNA. The mean size of the lymph nodes was found to be 1.6 cm (0.8-3.2 cm), sensitivity 92%, selectivity 100%, and positive diagnosis rate 93%. A study comparing the success of EBUS-TBNA among patients with different lymph node sizes has not been

published [15]. In one of their studies, Herth *et al*. [16] sampled mediastinal lymph nodes smaller than 1 cm short axis on radiological CT with EBUS. In 100 patients, 119 lymph nodes with an average size of 8.1 mm (4mm-10mm) were identified and sampled. Malignancy was detected in 19 patients, but false negativity was detected in 2 patients. All diagnoses were confirmed by surgery. The sensitivity of EBUS-TBNA in detecting malignancy was 92.3%, selectivity was 100% and negative diagnosis rate was 96.3%. In our study, the mean ultrasonographic diameter of the right paratracheal lymph nodes, which were visualized by EBUS and sampled with TBNA, was 8.88mm, the left paratracheal lymph nodes were 9.23mm and the subcarinal lymph nodes were 11.66mm. The statistical analysis showed that there was a significant increase in the sensitivity along with the increasing diameter, confirming the existing literature.

One of the factors that increase the sensitivity of the technique is the number of aspirations performed at each lymph node station. Chin *et al*. [7] performed consecutive EBUS-TBNA procedure in 79 patients with suspected lung cancer and suggested that at least four aspiration samples should be taken to obtain sufficient material from each lymph node station and that seven samples were the most effective factor in the diagnosis. In our study, all lymph nodes were sampled in more than 3 samples except 1 lymph node which was sampled twice due to technical difficulties. In the cytopathological evaluation of this lymph node, false negative results were obtained, leading to a decrease in sensitivity. In conclusion, we think that EBUS-TBNA procedure should have high sensitivity rates and aspiration should be done at least 3 times from each lymph node.

In their 2009 study with 226 cases, Szlubowski *et al*. [17] investigated the diagnostic performance of the technique in patients who underwent EBUS-TBNA for NSCLC staging. TEMLA was applied to the lymph nodes which were evaluated non-metastatic in cytopathological evaluations following the EBUS-TBNA procedure. As a result, the sensitivity of EBUS-TBNA in the evaluation of mediastinal lymph nodes was 89%, the selectivity was 100%, the PPV was 100%, the NPV was 83.5% and the accuracy was 92.9%. In our study, the sensitivity of EBUS-TBNA was 66.7%, the selectivity was 100%, the PPV was 100%, the NPV was 97.6% and the accuracy was 97.7%. EBUS-TBNA was found to be statistically significant in differentiating between metastatic and non-metastatic lymph nodes ($p = 0.003$). While the results were similar, low sensitivity was thought to be due to insufficient number of cases and insufficient lymph node aspiration in one case.

Herth *et al*. reported that EBUS-TBNA should be considered in the preoperative staging of all NSCLC cases regardless of the presence of pathological lymph node in CT and mediastinal activity involvement in PET. (18) In their study published in 2008, the sensitivity, selectivity and NPV of EBUS-TBNA were reported as 89%, 89%, and 98.9%, respectively. In our study, sensitivity was 66.7%, selectivity was 100%, PPV was 100%, NPV was 97.6%.

The literature review shows that EBUS-TBNA is mostly performed under general anaesthesia [19]. In our study, EBUS-TBNA was performed under local anesthesia and sedation, not under general anaesthesia. The study by Scherer *et al*. [20] is among the literature where EBUS-TBNA was performed under local anaesthesia and according to that study cough was reported in 15-20% of the cases, and in contrast to our study, it resulted in premature termination of the procedure in 8-12% of the cases. In 10% of the cases, the process was continued after the balloon was deflated due to desaturation and oxygenation was achieved. In their study of 70 patients 62 of whom underwent local anaesthesia and 8 under general anaesthesia, Falcone *et al*. [21] observed full compliance in 93.6% of the cases and partial compliance in 6.4% cases due to cough, haemoptysis and hypoxia. None of the patients required early termination of the procedure. Preparing the patient before the procedure and sedation during the procedure became the routine method used in the interventional bronchology unit of our hospital. EBUS-TBNA was used to reach 96 lymph node localizations of 44 patients and these localizations were easily reached. No complication was detected in any of the cases except minimal haemorrhage at the procedure sites. All the patients were in compliance with the procedure, and none of the patients experienced cooperation issues requiring discontinuation of the procedure.

Conclusion

Accurate evaluation of mediastinal lymph nodes is crucial in patients with NSCLC for whom surgery offers potential chance of cure. Identification of N2 or N3 involvement in NSCLC is critical for case management.

Our study, which investigated the efficacy of EBUS-TBNA in mediastinal staging in NSCLC, showed that this method can be used effectively by experienced clinicians and can be an alternative to invasive methods. However, there are other issues that need to be considered when performing EBUS-TBNA procedure in addition to clinician experience. These are detection of the localization of the lymph node to be sampled tomographically, bronchoscopically and ultrasonographically, and ensuring adequate aspiration (aspiration at least 3 times from each lymph node).

In addition, it was found that as the lymph node diameter increased, the sensitivity rate of the procedure increased.

In conclusion, EBUS-TBNA provides a high sensitivity, selectivity and accuracy rate and makes it safe to perform the procedure. Its high diagnosis rate and efficacy in staging NSCLC cases, it makes invasive methods redundant. It should be kept in mind that lymph nodes that are reported as non-metastatic after EBUS-TBNA procedure but which are clinically and radiologically suspected metastatic should be evaluated with more invasive methods.

References

1. Pearson FG. Lung Cancer. Pearson FG Thoracic Surgery. Churchill Livingstone. 2002 second edition. P 772-924.
2. Yildiz OO, Ozkan S. The role of thorax-CT in mediastinal staging of the nonsmall cell lung cancer, revive our memories. J Clin Anal Med. 2018; 9(1):13-7
3. Ernst A, Anantham D, Eberhardt R, Krasnik M, Herth FJ. Diagnosis of mediastinal adenopathy-real-time endobronchial ultrasound guided needle aspiration versus mediastinoscopy. J Thorac Oncol. 2008; 3(6):577-82
4. Herth F, Becker HD, Ernst A. Conventional vs endobronchial ultrasound-guided transbronchial needle aspiration a randomized trial. Chest. 2004; 125(1):322-5.
5. Shure D, Fedullo PF. The role of transcarinal needle aspiration in the staging of bronchogenic carcinoma.

Chest. 1984; 86(5):693-6.
6. Utz JP, Ashok MP, Edell ES. The role of transcarinal needle aspiration in the staging of bronchogenic carcinoma. Chest. 1993; 104(4):1012-16
7. Chin R, McCain TW, Lucla MA. Transbronchial needle aspiration in diagnosing and staging lung cancer. How many aspirates are needed? Am J Respir Crit Care Med. 2002; 166(3):377-81.
8. Davenport RD. Rapid on-site evaluation of transbronchial aspirates. Chest. 1990; 98(1):59-61.
9. Diette GB, White P Jr, Terry P, Jenckes M, Rosenthal D, Rubin HR. Utility of on-site cytopathology assessment for bronchoscopic evaluation of lung masses and adenopathy. Chest. 2000; 117(4):1186-90.
10. Herth FJF, Ernst A, Schulz M, Becker HD. Endobronchial ultrasound reliably differentiates between airway infiltration and compression by tumor. Chest. 2003; 123(2):458-62.
11. Detterbeck FC, Jantz MA, Wallace M, Vansteenkiste J, Silvestri GA. Invasive Mediastinal Staging of Lung Cancer. ACCP Evidence-Based Clinical Practice Guidelines (2nd Edition) Chest. 2007; 132:s202-220.
12. Wang KP, Terry PB. Transbronchial needle aspiration in the diagnosis and staging of bronchogenic carcinoma. Am Rev Respir Dis. 1983; 127(3):344-7.
13. Harrow EM, Abi-Saleh W, Blum J. The utility of transbronchial needle aspiration in the staging of bronchogenic carcinoma. Am J Respir Crit Care Med. 2000; 161(2):601-7.
14. Patelli M, Agli LL, Poletti V. Role of fiberscopic transbronchial needle aspiration in the staging of N2 disease due to non-small cell lung cancer. Ann Thorac Surg. 2002; 73(2):407-11.
15. Herth FJF, Eberhardt R, Vilmann P, Krasnik M, Ernst A. Real time endobronchial ultrasound-guided transbronchial needle aspiration: a new method for sampling mediastinal lymph nodes. Am J Respir Crit Care Med. 2005; 49(2):157-8
16. Herth FJF, Ernst A, Eberhardt R, Vilmann P, Dienemann H, Krasnik M, *et al.* Endobronchial ultrasound-guided transbronchial needle aspiration of lymph nodes in the radiologically normal mediastinum. Eur Respir J. 2006; 28(5):910-4.
17. Szlubowski A, Kuzdzal J, Kolodziej M. Endobronchial ultrasound-guided needle aspiration in the non-small cell lung cancer staging. Eur J CTS. 2009; 35(2):332-6
18. Herth FJ, Eberhardt R, Krasnik M, Ernst A. Endobronchial ultrasound-guided transbronchial needle aspiration of lymph nodes in the radiologically and PET normal mediastinum in patients with lung cancer. Chest. 2008; 133(4):887-91.
19. Sihoe AD, Yim AP. Lung cancer staging. J Surg Res. 2004; 117(1):92-106
20. Scherer T, Klinger K, Barandun J, Inderbitzi R. Initial experience in the application of endobronchial ultrasound. ERS-Olympus Satellite Symposion on "Bronchoscopic disease management of lung cancer" Proceedings of the ERS-Congress, Madrid, 1999; P.6-8
21. Falcone F, Fois F, Grosso D. Endobronchial ultrasound. Respiration. 2003; 70 (2):179-94.