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Comparison of cytologic accuracy of endobronchial ultrasound transbronchial needle aspiration using needle suction versus no suction

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Abstract

Background and Objectives:

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is a relatively new procedure initially used for lung cancer diagnosis, staging and re-staging and extended to benign diseases such as sarcoidosis and other mediastinal lesions. Previously, multiple studies evaluated the use of needle biopsy with no aspiration that did not change the diagnostic accuracy compared with needle biopsy aspiration.

Materials and Methods:

All adult subjects who were scheduled to undergo EBUS-TBNA to sample mediastinal lesions were eligible. We evaluated two methods of sampling mediastinal lesions. The first method was the application of negative pressure syringe for needle suction aspiration. The second was with no suction. For every patient and every biopsy site in the same patient, we had two samples using each method.

Results:

Among the 26 participants, 24 patients had adequate tissue using both methods (92.3%, $P = 1.00$). Among the 24 patients with adequate tissue using both methods, 14 patients (58.3%) had benign pathology using both methods, whereas ten patients (41.7%) had malignant pathology using both methods ($P = 1.00$). Among the 32 sites that were sampled, 30 sites had adequate tissue using both methods (93.8%, $P = 1.00$). Among the thirty sites with adequate tissue using both methods, 17 (56.7%) had benign pathology using both methods; 12 (40.0%) had malignant pathology using both methods; and one site (3.3%) had malignant pathology using suction, but benign pathology using no suction ($P = 1.00$).

Conclusion:

In patients undergoing EBUS-TBNA to sample mediastinal lesions, the diagnostic yield with the application of suction to needle biopsy was not statistically significant compared to no suction.

Keywords: Endobronchial ultrasound, mediastinal, suction, transbronchial needle aspiration

INTRODUCTION

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is a relatively novel, rapidly growing diagnostic modality that allows accurate sampling of mediastinal lymph nodes (LNs) and other peribronchial lesions. EBUS-TBNA is a minimally invasive, safe and cost effective technique, with high yield cytologic diagnosis.[1] Although it is mainly used for lymph-node staging and diagnosis of lung cancer, EBUS-TBNA might also be used for the diagnosis of unexplained mediastinal and hilar lymphadenopathy, as well as other mediastinal lesions.[2,3,4] Since its introduction in 2004,[3] EBUS-TBNA use is becoming widely variable and includes restaging lung tumors, diagnosing sarcoidosis and evaluation of patients with extrathoracic malignancies. EBUS-TBNA has a high yield for diagnosing and staging lung cancer that ranges from 89% to 98%,[2,3,5,6] and better when compared to computed tomography (CT) and positive emission tomography (PET) scan.[5] It also reduces the need for surgical mediastinal staging. EBUS-TBNA was diagnostic in 88-93% of patients with sarcoidosis and mediastinal lymphadenopathy,[1] and provided superior diagnostic yield compared to conventional TBNA.[7] Cytologic studies that included data on patients who underwent EBUS-TBNA revealed adequate samples rate ranging from 60% to 95%. Although it is the gold standard, and relatively safe procedure, mediastinoscopy is more invasive and compared to EBUS-TBNA, it carries higher complication and mortality rates.[8] Additionally, few studies revealed higher diagnostic yield for EBUS-TBNA compared to cervical mediastinoscopy.[9,10]

Endobronchial ultrasound-guided transbronchial needle aspiration is performed under real-time US guidance, which leads to significant diagnostic improvement compared to conventional TBNA.[7,11] The EBUS bronchoscope is equipped with a conventional bronchoscopic fiberoptic component to identify airway anatomy, a linear US scanning probe for real-time imaging and a biopsy channel for a 22 or 21 gauge aspiration needle. The integrated color Doppler allows easy identification of vascular structures. Technically, once the LN or mass has been clearly identified with EBUS, the needle is inserted through the working channel under real-time US guidance. The stylet of the needle is left in place on the first puncture; once the needle tip is inside the lesion, the stylet is used to clean the tip of the needle from any bronchial contamination. After removing the stylet, the standard of care is to apply suction using a negative pressure syringe (20 mL) and the needle is stabbed multiple times. The needle is removed, and the specimen is expelled onto glass slides using a 10 or 20 mL air-filled syringe or by reinserting the stylet. The slides are then air-dried, or alcohol fixed or sent as cellblock specimen.

In general, bronchoscopists apply negative pressure to needle sampling except when rapid-on-site evaluation is requested, and the first sample returned bloody materials. In this case subsequent samples are taken without suction to minimize the risk of inadequately bloody specimen. Since its first introduction in 1930,[12] aspiration biopsy was latter described by many authors as modified fine-needle aspiration (FNA) without aspiration in diagnosing breast, thyroid and lung lesions.[13,14] Currently, there are no data showing that applying negative pressure to FNA needle biopsy leads to higher diagnostic accuracy. However, several studies showed that FNA without suction resulted in better specimen adequacy. [13,14,15,16] This was explained by decreased tissue trauma and blood cell return into the needle when no suction was applied. The objective of our study is to compare cytologic diagnostic accuracy between EBUS-TBNA samples using suction versus no suction.

MATERIALS AND METHODS

This is a non-inferiority study between EBUS-TBNA suction and no suction techniques. We prospectively enrolled consecutive patients presenting to our endoscopy suite for EBUS-TBNA between February and November 2011. All procedures were performed by K.H. and (M.C.) and only patients to be performed by these 2 doctors were enrolled in the study. All patients were adults and have an outpatient chest CT scans that were reviewed prior to the procedure, and some of the patients had PET scan as well. All lesions to be biopsied were measured in their short axis. Only LNs that were above 1 cm in size were included in the study.

Our institutional review board approved the study, and written consent was obtained for all patients undergoing the bronchoscopic procedure. The study did not carry any additional risk compared to routine EBUS-TBNA procedure. Patients were medicated with midazolam and meperidine for the procedure. In all patients, local anesthesia was performed with 4% lidocaine; 2 cc were injected in each nostril and 4 cc were used for gargling then swallowed. All patients were given 2 L/min of oxygen via nasal cannula and increased as needed during the procedure. The procedure was performed using the US bronchoscope Olympus BF-UC160F-OL8 connected to US processor EU-C60; Olympus. Transbronchial aspiration was performed using a 22-gauge-needle (Olympus NA-201SX-4022) in all patients. Real-time US was used in all EBUS-TBNA, and when indicated, colored Doppler was used to prevent accidental vascular punctures. The LNs to be biopsied localized methodically based on their stations. Each site was punctured using 2 methods. The first method is when we apply negative pressure using 20 mL syringe for needle suction and we called it EBUS-TBNA and suction (EBUS-TBNA-S), and the second is when no needle suction is applied after needle site puncture and we called it EBUS-TBNA and no suction (EBUS-TBNA-NS). Needle punctures were performed using the jabbing method followed by the stylet withdrawal then “to and fro” movement inside the lesion for 10 times. The stylet was removed in both methods. The aspirates were expelled onto slide glass using a 20 mL air-filled syringe then fixed with alcohol (95% ethanol). Every site was punctured four times, twice for each technique. In the EBUS-TBNA-S group, the second puncture was performed with a suction even if the first one yielded bloody specimen. The EBUS-TBNA-NS was performed first to prevent needle contamination with cancerous cells and thus prevented false results. In addition, two or more punctures using 20 cc syringe suction were performed and sent as cellblock specimen. The additional punctures were not included in the analysis and were used for clinical purposes only. The collected samples were sent for the cytopathological evaluation, and all pathologists were blinded to sampling methods by using labeling the specimen with alphabetic letters. Rapid on-site evaluation was not performed in all cases. We collected our pathology data using our institutional electronic system. The biopsy was considered adequate if there were lymphocytes or specific diagnosis such as malignancy reported by the Cytopathologist. The biopsies were considered inadequate if there were no lymphocytes or specific diagnosis seen on any slides. The primary outcomes are the diagnostic yield and specimen adequacy of EBUS-TBNA with and without suction for mediastinal lymphadenopathy. We excluded patients who were not able to complete the EBUS procedure for any reason.

STATISTICA ANALYSIS

Patient and LN characteristics [Table 1] were reported by mean and range for continuous variables, and the frequency and relative frequency for categorical variables. Sensitivity and specificity are estimated with Wilson 95% confidence intervals. McNemar test was used to check the equality of sensitivities between the two diagnostic techniques at a significance level of 0.05.

RESULTS

Among the 26 participants, one of the patients (3.8%) had no adequate tissue using both methods; one patient (3.8%) had adequate tissue using suction, but no adequate tissue using no suction; and 24 patients had adequate tissue using both methods (92.3%, $P = 1.00$). Among the twenty-four patients with adequate tissue using both methods, 14 patients (58.3%) had benign pathology using both methods, while ten

patients (41.7%) had malignant pathology using both methods ($P = 1.00$). Considering suction to be the golden method, the sensitivity and specificity of no suction were 100% [Figure 1]. The 95% CI for sensitivity and specificity, are 0.72-1.00 and 0.78-1.00 respectively.

Among the 32 sites, which were sampled, one site (3.1%) had no adequate tissue using both methods; one site (3.1%) had adequate tissue using suction but no adequate tissue using no suction; and 30 sites had adequate tissue using both methods (93.8%, $P = 1.00$). Among the thirty sites with adequate tissue using both methods, 17 (56.7%) had benign pathology using both methods; 12 (40.0%) had malignant pathology using both methods; and one site (3.3%) had malignant pathology using suction, but benign pathology using no suction ($P = 1.00$). Considering suction to be the golden method, the no suction had a sensitivity = 92.3% (95% CI: 0.67-0.99) and specificity = 100% (95% CI: 0.77-1.00) [Figure 2]. For the site that had no adequate tissue with no suction, but adequate tissue with suction, the no suction specimen was totally dry, and we were unable to obtain any specimen.

Of the 32 sites punctured, 16 were at the station 7 (50%), 12 were at station 4R (37.5%), 2 were 10R (6.2%), 1 was at station 4L (3.1%), and one was lung mass (3.1%) [Table 1]. Of the 26 patients enrolled in the study, 10 patients (38.4%) had a diagnosis of malignancy, of which 4 (40%) were small cell lung cancer and 6 (60%) were non-small lung cancer. Only one of the 10 patients with malignancy had a positive result with EBUS-TBNA-S and negative with EBUS-TBNA-NS. This was at the subcarinal (station 7) LN site and therefore did not affect the adenocarcinoma lung staging in this patient as the patient had EBUS-TBNA-S and EBUS-TBNA-NS both positive for malignant cells at another N2 LN stage (4R). 21 of 26 patients had underlying lung lesions in association with the mediastinal LNs. All 10 patients diagnosed with malignancy had lung lesions mainly in the upper lobes (5/10). Of the other 14 patients with adequate tissue using both methods, 5 patients did not have underlying lung lesions, of which one was diagnosed with sarcoidosis with EBUS-TBNA, 2 had some non-specific peripheral lung opacities and ended up having usual interstitial pneumonia as final diagnosis and two patients were considered non-malignant after decreasing size with subsequent chest CT follow-ups. Only 1 of the 14 patients with benign biopsies using both methods yielded to a specific diagnosis (7.1%), which was sarcoidosis. Three of these patients didn't follow-up in our office, and we did not know the final diagnosis. One patient was diagnosed with small cell carcinoma based on Immunohistochemical analysis of the cellblock specimen.

DISCUSSION

In 1987, Zajdela *et al.*[14] introduced a modified technique of performing FNA. They compared the diagnostic yield in two groups of patients who underwent FNA for breast tumors. Both groups included benign and malignant diagnoses. In the first group, the FNA was performed with application of negative pressure created by a syringe and the second was when the FNA was performed without applying negative pressure after puncturing the breast lesion. The cellular yield in suction and no suction group was 6% and 5.5% respectively, which was not statistically significant. Additionally, Santos and Leiman[17] described the use of non-aspiration use of FNA with the same conclusion. Yue and Zheng[16] were the first to report the use of FNA without aspiration for lung lesions. Fifteen patients underwent transthoracic lung biopsies, 11 of them had FNA without suction and 4 with suction. The diagnostic accuracy was comparable between both techniques. The samples with no aspiration contained less blood, and the cytologic diagnosis was easier to make. Moreover, Bhutani *et al.*[18] studied two metastatic LNs that were dissected at autopsy. One of these LNs was metastatic with transitional cell bladder cancer, and the other was non-small cell lung cancer. They used a 21-gauge needle to perform FNA with the application of suction using 10 mL, 20 mL and 30 mL. The specimens were evaluated blindly by two Pathologists. The cellularity and the quality of the FNA were better with less suction using the 10 mL negative pressure syringe.

In late 2000, Wallace *et al.*[15] were first to compare two endoscopic US FNA techniques. They used the 22-gauge needle FNA with and without suction at the center and at the edge of the LNs. Totally 43 patients were included in the final analysis, and all patients had a primary cancer most commonly lung cancer.

They used a 20 mL syringe for suction. Most of the LNs sampled were subcarinal (N7). 39% if the LN were malignant. Suction significantly increased the cellularity of the samples as well as the amount of blood. The authors did not find any significant difference concerning the diagnostic yield between the suction versus no suction as well as between the centered versus edge directed FNA samples. Casal *et al.* [19] were the first study to evaluate the EBUS needle sampling with and without suction. There were no differences in adequacy, diagnosis, and quality between samples obtained using either way.

Our study aimed to compare the EBUS-TBNA with and without suction. It showed no significant difference in diagnosing malignant and benign diseases, which was consistent with all previous studies.[14,15,16,17] We chose to obtain 4 passes per site based on previous data,[20,21,22] and we always had at least two additional specimens for the cellblock the results of which were used for clinical purposes. For the TBNA-NS specimen that was dry, the TBNA-S was positive for malignancy, therefore, one will conclude that the application of suction should be applied only in cases where a dry specimen is obtained with TBNA-NS or FNA without suction in cases of other types and sites of tissue biopsies. Our study had a few limitations. We did not evaluate the LN characteristics such as shape, echogenicity, margin, presence of necrosis sign and central hilar structure. Although that we tried to take both the TBNA-S and TBNA-NS samples from the exact same location in the LN, some location variability still exist but thought to be insignificant. Furthermore, all our punctures were in the center of the lymph and were not taken at the edge. We did not compare the time of the procedure with TBNA-NS versus TBNA-S and our patients' malignancy was limited to lung cancers with small sample size. Finally, we did not compare the sample adequacy for molecular testing between the two techniques.

CONCLUSION

Endobronchial ultrasound-guided transbronchial needle aspiration with suction and EBUS-TBNA without suction are both acceptable techniques for the diagnosis of mediastinal lymphadenopathy. The diagnostic sensitivity, specificity, and specimen adequacy were not statistically significant between the two methods. Large trials evaluating this matter are warranted and till then the choice of the technique should be left to the personal preference of the bronchoscopist.

Footnotes

Source of Support: Nil.

Conflict of Interest: None declared.

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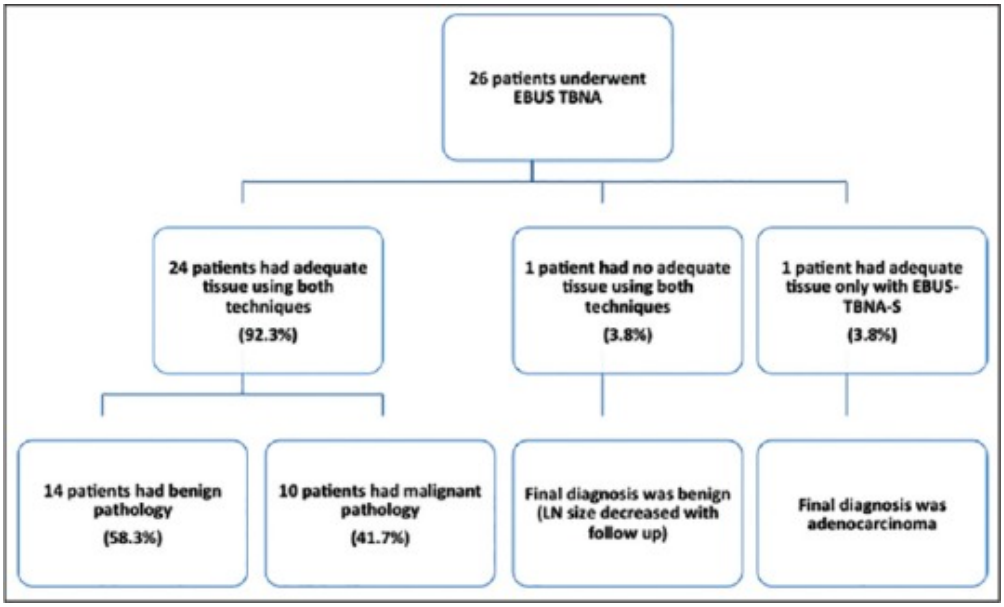
Figures and Tables

Table 1

Characteristics	Value (%)
Number of patients	26
Age, mean (range), year	61.4 (38-81)
Sex	
Women	14
Men	12
Number of lymph nodes	32
Number of lymph node size, mean (range), cm	1.95 (1-4)
Lymph node station (stage)	
1 (N0)	1 (3.1)
10R (N1)	2 (6.2)
4R (N2)	12 (37.5)
7 (N2)	16 (50)
4L (N2)	1 (3.1)

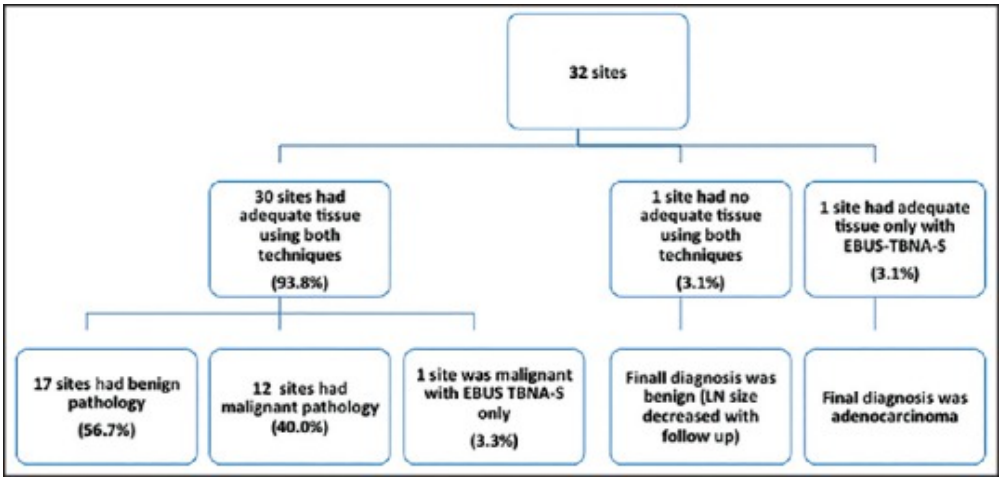
Baseline characteristics of patients and lymph nodes

Figure 1



Results by patient: Tissue adequacy and diagnostic yield comparing the two methods (transbronchial needle aspiration and suction and endobronchial ultrasound-guided transbronchial needle aspiration and no suction)

Figure 2



Results by site: Tissue adequacy and diagnostic yield comparing the 2 methods (transbronchial needle aspiration and suction and endobronchial ultrasound-guided transbronchial needle aspiration and no suction)