Original Article

Conventional transbronchial needle aspiration: From acquisition to precision

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Abstract:

INTRODUCTION: Conventional transbronchial needle aspiration (C-TBNA) is a minimally invasive, safe, and cost-effective technique in evaluating mediastinal lymphadenopathy. Previously we reported that the skills for C-TBNA can be acquired from the books. We studied the learning curve for C-TBNA for a single bronchoscopist at a tertiary-care center where ultrasound technology remains difficult to acquire.

METHODS: We prospectively collected results of the first 99 consecutively performed C-TBNA between December 2009 and 2013. Patients were divided into 3 groups: (I): First 33, (II): Next 33 and (III): Last 33. Results were categorized as malignant, non-malignant or non-diagnostic. Diagnostic yield (DY), sensitivity (SEN), specificity (SPE), positive and negative predictive values (PPV, NPV), and accuracy (ACC) were calculated to learn the learning curve for C-TBNA.

RESULTS: Total 99 patients (M:F = 62:37), mean age 58.2 ± 11.5 years, mean LN diameter 26.9 ± 9.8 mm underwent C-TBNA. Sixty-nine patients had lymph nodes (LNs) >20 mm in diameter. Final diagnoses were established by C-TBNA in 44 (yield 44.4%), mediastinoscopy 47, transthoracic needle aspiration 5, endobronchial biopsy 2 and peripheral LN biopsy 1. C-TBNA was exclusively diagnostic in 35.4%. Group I: DY: 42.4%, 64.7% in malignancies, 19% in benign conditions ($P = 0.008$). SEN, SPE, PPV, NPV, ACC = 70%, 100%, 100%, 66.6%, 78.7%, respectively. Group II: DY: 54.5% (36.4% exclusive), 88.2% in malignancies and 19% benign conditions ($P = 0.000$). SEN, SPE, PPV, NPV, ACC=72%, 100%, 100%, 53.3%, 78.7%, respectively. Group III: DY: 36.3% (27% exclusive), 100% in malignancies and 16% in benign conditions. SEN, SPE, PPV, NPV, ACC = 92.3%, 100%, 100%, 95.2%, 97%, respectively. No difference was found in relation to LN size or location and TBNA yield.

CONCLUSION: C-TBNA can be easily learned and the proficiency can be attained with <66 procedures. In selected patients, its exclusivity could exceed 35%.

Key words:

C-TBNA, EBUS-TBNA, flexible bronchoscopy, learning curve

Conventional transbronchial needle aspiration (C-TBNA) has been proven to be a minimally invasive, safe and cost-effective technique in establishing the diagnosis of mediastinal lymphadenopathy (MLA). Despite its advantages, it still remains underutilized. The limited acceptance of C-TBNA is presumed to be due to the lack of in-depth training and a fear of complications.[1]

We previously reported that the C-TBNA can be successfully learned without a formal training that is offered by the Interventional Pulmonology (IP) fellowship programs. In other words, C-TBNA can be learned "by the books"; postgraduate courses, workshops or hands-on courses can certainly add more to the initial exposure to the procedure.[2] Even in the era of endobronchial (EBUS) and the esophageal ultrasounds (EUS), acquiring skills to perform C-TBNA is essential. The availability of the ultrasound accessories and acquiring the necessary skills remain elusive in the developing world.[3]

Previous investigators have reported their learning curve for the C-TBNA in their sample groups.[3-9] In most of these studies, the learning curve was assessed among a group of pulmonologists with different experiences. In the present study, we aimed to study the learning curve for the C-TBNA for a single bronchoscopist at a tertiary care center where ultrasound technology remains difficult to acquire.

Methods

Prior to the study

Başkent University School of Medicine is a tertiary care center in the capital of our country. Approximately 600 conventional diagnostic bronchoscopies are performed annually at our institution. We gathered working knowledge of C-TBNA by reviewing the literature,[10-14] watching video tapes, and participating on an inanimate model for TBNA and in a hands-on training course offered by an international society. After feeling confident about the C-TBNA technique on the lung model, we started

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performing the actual procedure in December 2009, according to the method described by Wang *et al*.[15] The lymph nodes (LNs) were considered enlarged if the diameter was larger than 10 mm in its short axis. Chest computed tomography (CT) was reviewed by both the pulmonologist as well as the radiologist in detail to identify the location and to gauge the size of the LNs. The procedure was performed on all patients presenting with MLA on chest CT. The location was described according to Mountain's classification.[16] Patients in whom bronchoscopy was contraindicated were excluded from the study.

The study protocol was approved by the Ethics Committee and all the patients signed an informed consent before the procedure.

The study was carried out and data were gathered in a prospective fashion.

C-TBNA procedure

All the procedures were performed under conscious sedation and local anesthesia. A 19- and/or a 21-gauge Smooth Shot Needles (Olympus®, Japan) were used at the discretion of the bronchoscopist. The 19-gauge needle was chosen if a benign condition was included in the differential diagnosis. Once a 19-gauge needle was inserted, it was moved back and forth by 2-3 mm through the tracheobronchial wall to obtain a core of the specimen for histological examination. On the contrary, following the insertion of a 21-gauge needle to its fullest length, the catheter was agitated while applying suction at the proximal end using a 50 ml syringe to obtain loose cells for a cytological examination. At least four satisfactory specimens were obtained during each bronchoscopy procedure; minimum of two from each desirable location in cases of multiple stations involvement. Tissue specimens were prepared according to the description by Wang *et al*.[15]

C-TBNA was performed on all N2 and N3 lesions (if present) for staging of suspected lung cancer, and at N1 location for the purpose of making the diagnosis. Rapid on-site cytology examination (ROSE) was not available.[17] In cases where the LNs from more than one location were sampled, the one with the largest size was taken into consideration for the calculations.

"Leak Test" was performed following each TBNA procedure to rule out any damage to the bronchoscope.

Study population

Patients were consecutively recruited and divided into 3 groups: Group I included the first 33 patients, Group II included the next 33 patients, and Group III included the last 33 patients. The C-TBNA results were categorized into the following groups: Malignant, non-malignant or non-diagnostic. Diagnosis of malignancy was established based on cytology and/or histology findings. When a tissue representative of a benign diagnosis was present, the results were considered "confirmatory" for the non-malignant condition. Both, malignant and benign diagnoses were considered "true positive" if they matched our clinical suspicion, else further diagnostic step was considered to rule out "false positive" results. The results were considered non-diagnostic if no material was obtained (Dry Tap) or if the procured material was not representative of any of the above two groups. In cases where the C-TBNA was either non-diagnostic or showed only normal lymphocytes, the final diagnosis was established by mediastinoscopy, transthoracic needle aspiration (TTNA), peripheral LN or endobronchial biopsies (EBB). The aspirates with normal lymphocytes were considered "true negative" if no definite diagnosis was established by any of the above methods.

Statistical analyses

Diagnostic yield (DY), sensitivity (SEN), specificity (SPE), positive predictive value (PPV), negative predictive value (NPV) and accuracy (ACC) were calculated using published definition.[2] The influence of size and anatomical location of the LN on the outcome of C-TBNA was analyzed using χ^2 test. All statistical tests were 2-sided and $P < 0.05$ was considered statistically significant. All data were analyzed with a statistical software package (SPSS, version 11.5 for Windows; SPSS Inc. Chicago, IL).

Results

Overall results

Ninety-nine patients (M:F = 62:37) with mean age of 58.2 ± 11.5 (27-78) years underwent C-TBNA using either 21 g or 19 g (or both) Smooth Shot Olympus® needles for MLA. Demographic data according to the groups and the suspected and final diagnoses are depicted in Table 1.

Sixty-nine patients had LNs larger than 20 mm (Mean: 30.8 ± 9.2 mm) and the remainder between 10-20 mm (Mean: 17.8 ± 2.1 mm). Mean diameter for all LNs was 26.9 ± 9.8 mm. Locations of the target LNs were: Right paratracheal (30), subcarinal (43) and right or left hilar (26).

Final diagnosis was established by C-TBNA in 44 (DY: 44.4%), mediastinoscopy in 47, transthoracic needle aspiration in 5, peripheral LN biopsies in 1 and EBB in 2 patients. The C-TBNA was exclusively diagnostic in 35 patients (35.4%). In 4 patients, diagnosis was made by TBNA+EBB while the diagnosis was established by TBNA+brushing in 3 and TBNA+bronchial

Table 1: Demographic data of the groups with final diagnoses

Group	Gender (male/ female)	Age (mean)	LN Size (mm, mean)	LN size mm: (number)	Final diagnosis
I	22/11	54.7±12	2.7+1	10-20 (11) >20 (22)	Lung cancer:15 Met:1 Lymphoma:1 Sarcoidosis:3 Tuberculosis:1 Reactive LN:12
II	26/7	61±9	2.7+1	10-20 (15) >20 (18)	Lung cancer:16 Met:1 Sarcoidosis:7 Tuberculosis:1 Reactive LN:8
III	14/19	58±12	2.5	10-20 (4) >20 (29)	Lung cancer:8 Sarcoidosis:3 Tuberculosis:2 Reactive LN:20

washings (BW) in 2 patients. Thus, C-TBNA prevented further diagnostic testing, including mediastinoscopy in more than 30% (35) of our patients including in 61.5% (24/39) with lung cancer. Satisfactory C-TBNA specimens were obtained from all aspirates except one (Dry tap).

C-TBNA revealed definitive diagnosis in 44 patients; lung cancer 32, metastatic cancer 1, lymphoma 1, sarcoidosis 7, tuberculosis (TB) 2, and reactive lymphadenopathy 1. The only reactive lymphadenopathy diagnosed with C-TBNA was confirmed by mediastinoscopy. This patient was suspected to have TB or sarcoidosis based on the clinical grounds and was subjected to a close follow up. Hence we considered this result as "true negative," similar to reactive lymphadenopathy in other patients.

We didn't encounter any damage to the flexible bronchoscope during the study period.

Results according to each group

Group I

In Group I, C-TBNA was diagnostic in 14 (42.4%). Final diagnosis was established in 14 patients by mediastinoscopy, in 3 by TTNA, in 1 by peripheral LN biopsies and in 1 by EBB. There was a significant difference in the DY of C-TBNA (P = 0.000) based on the size of the LNs; (>21 mm vs. <20 mm) but not based on the LN location (P > 0.05) [Table 2]. The DY of C-TBNA was significantly higher when a malignant diagnosis over benign condition was suspected (64.7% vs. 18.8 %, P = 0.008) [Table 3].

Group II

In Group II, C-TBNA was diagnostic in 18 (54.5%) patients, being exclusively diagnostic in 13 (39.3%). In 12 patients, the diagnosis was established by mediastinoscopy, in 3 by TBNA + EBB, 2 by TTNA, and one each by EBB and TBNA + brushing and TBNA + BW. There was no significant difference in the DY based on the LN size or its location (P = 0.12 and 0.08, respectively) [Table 2]. The DY of C-TBNA was significantly higher when a malignant diagnosis over benign condition was suspected (88.2% vs. 18.8 %, P = 0.000) [Table 3].

Group III

In Group III, C-TBNA was diagnostic in 12 (36.3%) patients; being exclusively diagnostic in 8 (24.2%). In 21 patients, diagnosis was established by mediastinoscopy, in 1 by TBNA + BW, in 2 by TBNA+brushing and in 1 by TBNA+EBB. There was no significant difference in the DY based on either the LN size or the location (P > 0.05) [Table 2]. The DY of C-TBNA was significantly higher when a malignant diagnosis over benign condition was suspected (100 vs. 16 %, P = 0.000). C-TBNA was positive in 8/8 patients when only a malignant diagnosis was suspected (DY = 100%) [Table 3].

The TP, TN, FN values and DY, SEN, SPE, PPV, NPV, ACC of C- TBNA for all patients with benign as well as malignant conditions are depicted in Table 4. Also the same values of C-TBNA for patients suspected to have lung cancer are represented in Table 5.

Table 2: Comparison between the LN size/location and C-TBNA results

Group		TBNA diagnosis (+)	TBNA diagnosis (–)	*P*
I	Location			
	Paratracheal	6	8	0.43
	Subcarinal	6	5	
	Hilar	2	6	
	Size			
	<20 mm	0	11	0.000*
	>20 mm	14	8	
II	Location			
	Paratracheal	7	1	0.08
	Subcarinal	6	9	
	Hilar	5	5	
	Size			
	<20 mm	6	9	0.12
	>20 mm	12	9	
III	Location			
	Paratracheal	2	6	0.67
	Subcarinal	8	9	
	Hilar	2	6	
	Size			
	<20 mm	2	2	0.54
	>20 mm	10	19	

*p < 0.05 is considered significant

Table 3: Comparison between C-TBNA diagnosis and malignant *vs.* benign diseases

Group		TBNA diagnosis (+)	TBNA diagnosis (–)	*P*
I	Malignant	11	6	0.008*
	Benign	3	13	
II	Malignant	15	2	0.000*
	Benign	3	13	
III	Malignant	8	0	0.000*
	Benign	4	21	

*p < 0.05 is considered significant

Table 4: SEN, SPE, PPV, NPV, ACC and DY of C-TBNA for all patients

Groups	TP	TN	FN	SEN (%)	SPE (%)	NPV (%)	PPV (%)	ACC (%)	DY (%)	*P* value SEN, SPE, ACC
Group 1*	14	12	6	70	100	66.6	100	78.7	42.4	>0.05
Group 2	18	8	7	72	100	53.3	100	78.7	54.5	>0.05
Group 3	12	20	1	92.3	100	95.2	100	97	36.3	>0.05
Overall	44	40	14	75.8	100	74	100	84.8	44.4	

*There is one inadequate sample in Group I with final diagnosis of lung cancer, TP = True positive, TN = True negative, FN = False negative, SEN = Sensitivity, SPE = Specificity, NPV = Negative predictive value, PPV = Positive predictive value, ACC = Accuracy, DY = Diagnostic yield

Table 5: SEN, PPV and DY of C-TBNA for lung cancer*

Lung Cancer	TP	FN	SEN (%)	PPV (%)	DY (%)
Group I**	10	4	71.4	100	66.6
Group II	14	2	87.5	100	87.5
Group III	8	0	100	100	100
Overall	32	6	84.2	100	82

*Based on number of patients suspected of having Lung Ca, **There is one inadequate sample in Group I with final diagnosis as lung ca, TP = True positive, FN = False negative, SEN = Sensitivity, PPV = Positive predictive value, DY = Diagnostic yield

Figures 1 and 2 depict our learning curve in relation to the SEN and ACC. Note the proficiency at C-TBNA plateaus around 60 procedures.

Discussion

In our previous publication, we reported that C-TBNA can be learned by the books.[2] This information is very valuable for the settings where the formal training in IP is not available and the ultrasound technology is not affordable. DY of EBUS-TBNA is certainly superior to C-TBNA while evaluating the MLA, yet the latter is still acceptable considering its low cost and the ease of the technique. Besides, it has also been shown that the DY of C-TBNA is based on the prevalence of the malignant disease in the community under scrutiny.[10] It is not hard to believe that the prevalence of malignant conditions involving the mediastinum is also high in the developing world.

Several studies have claimed that it takes over 100 EBUS-TBNA procedures to acquire adequate skills.[18-21] Its DY continues to improve till a sufficient number of procedures are performed.[20,21] Such a scenario is rather difficult in the developing world as well as at the low volume diagnostic centers. Under the circumstances, our findings further support the notion that, C-TBNA can be easily learned and the proficiency can be attained with less than 66 procedures. As shown in Table 4, there was no significant difference in SPE, SEN and ACC among the groups. In other words, we were able to attain proficiency with C-TBNA within 33-66 procedures. The difference in the DY among our group is mainly related to the prevalence of malignancy in the respective groups. Our results also parallel those published in the literature; most recommending 50 procedures.[4,7,9]

Interestingly, most of these studies involved more than one bronchoscopy team involving several physicians and medical personnel. In one study, it was shown that after 24 months of training and months of a post-training period, the diagnostic ACC of C-TBNA increased from 38% to 80%. Two separate bronchoscopists were involved in performing the procedure. Authors concluded that the number of C-TBNA procedures to become proficient is variable, but at least 50 TBNA procedures may be necessary to achieve comparable results with those reported in the literature and to be considered competent on the technique.[4] In another study, a group of thoracic surgeons and several bronchoscopists demonstrated an increase in the DY and the ACC of C-TBNA and attributed this to decrease in the inadequate samples with experience. Authors concluded that an experienced bronchoscopist should require a training period of approximately 50 procedures to become proficient with C-TBNA.[9] Few other articles have reported that increasing experience with C-TBNA can enhance its role in the diagnosis and staging of bronchogenic carcinoma but did not specify a number. The authors affirmed that the satisfactory results can be obtained immediately after the implementation of the program and that there is no significant learning curve for C-TBNA.[5,6,8] Tutar *et al*.,[7] retrospectively evaluated results of their first 66 C-TBNA procedures performed by a single bronchoscopist within an 8-month period. The diagnostic ACC increased from 72% to 96% between the fist 30 and the last 30 patients. However, they did not obtain a statistically significant difference based on the LN size. They attributed these results to their small sample size and the lower number of passes. The median number of the passes was only 2 in their study group, which was lower than what is mentioned in the literature. In the present study, the sample size was higher and the numbers of passes were at least 4 for each TBNA procedure.

Our study has several strengths. We feel that our results are more meaningful as it involves a single, consistent bronchoscopy team; one of each, bronchoscopist, bronchoscopy assistant, radiologist and a cytopathologist, eliminating interpersonal technical variation. We believe that this information is more applicable to any individual setting. It is prospective in nature and all the patients were recruited consecutively. Besides, the final diagnosis was established in every patient, by means of even invasive testing, when required. The exclusivity of C-TBNA of over 35% is also of significant value. We also feel that number of patients recruited in the study is also appropriate as larger groups may not have outlined the learning curve more precisely. In our opinion, thorough understanding of the mediastinal anatomy, refinement of the technique and the preparation of the specimen were the major determinants of the learning curve and to arrive at precision.

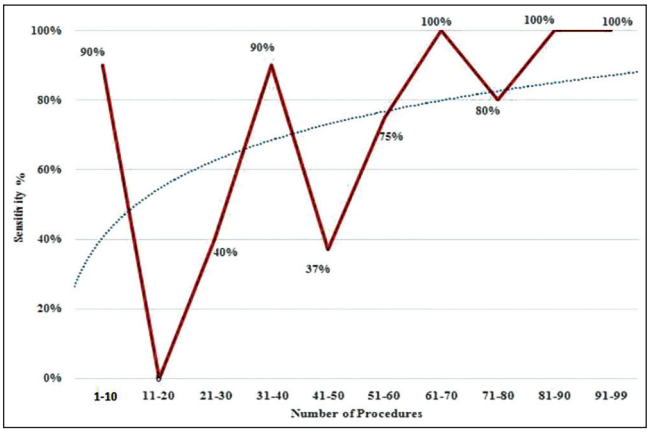

Figure 1: Learning curve for C-TBNA in relation to sensitivity. Note: The sensitivity plateaus around 60 procedures

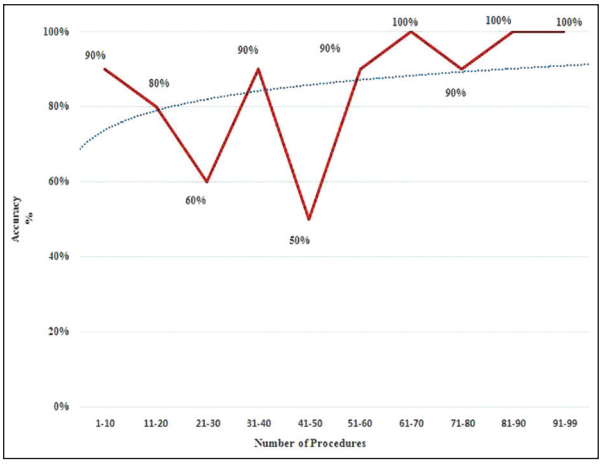

Figure 2: Learning curve for C-TBNA in relation to accuracy. Note: The accuracy plateaus around 60 procedures

Interestingly, majority of our patients had LN larger than 20 mm in their short axis and we did not need to sample the LNs in the left paratracheal location. This may be construed as a weakness of our study, yet this is the reality of our practice. Most patients present late in the course of their illness with large LN involving multiple stations. We also had a very low prevalence of malignant disease in Group III curtailing our DY. Incidentally, we encountered relatively large number of patients with reactive lymphadenitis. This may be related to the local epidemiological factors. Majority of them underwent mediastinoscopy to rule out TB or sarcoidosis and had adequate follow up to qualify them as true negatives.

In summary, C-TBNA can be easily learned outside the IP fellowship program and it has a very short and steep learning curve. In our opinion, every bronchoscopist in the developing world as well as those who cannot acquire the EBUS-TBNA skills should learn to perform C-TBNA. While dealing with mediastinal LNs of over 20 mm in short axis, in hilar, subcarinal or right paratracheal location, its exclusivity could exceed over 35%.

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