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Original research paper

A study on the sensitivity, specificity, positive predictive value and negative predictive value of EBUS TBNA yield with that of conventional bronchoalveolar lavage

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Abstract

EBUS-TBNA plays a vital role in diagnosis of lymphoma. Mediastinoscopies or thoracotomies have been performed as the standard procedure to obtain a histologic diagnosis in patients with mediastinal lymphadenopathy and suspected lymphoma. These procedures require general anesthesia and carry immense risks. Mediastinoscopy also has limited access to perihilar lymph nodes. Conventional TBNA, though superior to mediastinoscopy, has been shown to be inferior to EBUS-TBNA due to a lower specificity and sensitivity. At Apollo Hospital, on an average 1-2 patients undergo EBUS-TBNA every week. Based on this statistic, we got about 72 patients who underwent EBUS TBNA during my study period. About 58 patients were eligible for the study satisfying the inclusion criteria, allowing for some who did not give consent for the study. Every effort was made to screen and recruit the maximum possible number of patients for the study.
With the use of Chi square test, we found that EBUS TBNA had sensitivity 88.88%, specificity 87.75%. Positive predictive value 57.11% and negative predictive value 97.72% for malignant cytology.

Keywords: EBUS TBNA, conventional bronchoalveolar lavage, mediastinoscopy

Introduction

In recent years, endoscopic ultrasound (EUS)-guided tissue sampling either through the esophagus (EUS) or endobronchial (endobronchial ultrasound) has come up as safe and accurate method for achieving etiological diagnosis [1]. The advent of endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) in the early 1990's in Japan has now revolutionized the investigation of patients with mediastinal lymphadenopathy. EBUS-TBNA facilitates a fairly noninvasive way by which lymph nodes whether enlarged or not-positioned at stations 2, 4, 7, 10 and 11 of the Mountain and Dressler classification can most typically be sampled-usually under light sedation as a day case procedure. Moreover, when combined with endoscopic ultrasound, these minimally invasive procedures complement one another and facilitate near complete mediastinal staging in lung cancer [2].

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Routine bronchoscopic assessment of patients with mediastinal lymphadenitis can be attempted. Bronchoalveolar Lavage can be taken and cultures can reveal some infectious pathology and cytology may sometime point towards malignant etiology or rarely conditions like sarcoidosis. BAL is safe and inexpensive but is a very low yield procedure, previously necessitating surgical biopsy (cervical mediastinoscopy) to achieve microbial diagnosis in such case. Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is a minimally invasive technique allowing sampling of mediastinal lymph nodes via fine needle aspiration under direct sonographic visualization. It has a low rate of morbidity and good diagnostic yield [3, 4].

Another important and clinically very useful indication of LINEAR EBUS is in patient with mediastinal lymphadenopathy of unknown etiology. Apart from providing structural information about the airway wall and surrounding structures, central and peripheral lung histological specimens can be obtained under sonographic guidance improving diagnosis and patient management. EBUS in a setup already using bronchoscopy is a very cost-effective, feasible, and highly effective mode to evaluate mediastinal lymphadenopathy [5].

EBUS-TBNA plays a vital role in diagnosis of lymphoma. Mediastinoscopy or thoracotomies have been performed as the standard procedure to obtain a histologic diagnosis in patients with mediastinal lymphadenopathy and suspected lymphoma. These procedures require general anesthesia and carry immense risks. Mediastinoscopy also has limited access to perihilar lymph nodes. Conventional TBNA, though superior to mediastinoscopy, has been shown to be inferior to EBUS-TBNA due to a lower specificity and sensitivity. EBUS can be performed for a histologic diagnosis in suspected lymphoma and fluorescence in situ hybridization can also be done on the samples obtained by EBUS to further characterize lymphoma subtypes [6].

Methodology

Study population

In patients and out patients undergoing EBUS-TBNA, at Apollo Hospital during the study period.

Study design

Cross sectional comparative study.

Study sample size with justification

The diagnostic yield of EBUS-TBNA was found to be 92% from the previous study done by Tanushree Gahlot *et al*., Ujjwal Prakash *et al*., and Neeraj Jain *et al*. Considering the 95% level of confidence interval (Z=1.96) with 7% precision (d=0.07) the minimum required sample size is 58.

At Apollo Hospital, on an average 1-2 patients undergo EBUS-TBNA every week. Based on this statistic, we got about 72 patients who underwent EBUS TBNA during my study period. About 58 patients were eligible for the study satisfying the inclusion criteria, allowing for some who did not give consent for the study. Every effort was made to screen and recruit the maximum possible number of patients for the study.

Inclusion criteria

- Patients undergoing EBUS TBNA.

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- Patients aged between 10-80yrs.
- Patients of both genders.
- Presence of mediastinal lymphadenopathy in CT chest/PET CT/CXR.
- Informed Consent.
- Patients who are hemodynamically stable.
- Patients with no baseline hypoxemia.
- Patients without recent myocardial infarction.
- Patients without any evidence of uremia.

Exclusion criteria

- Pregnant females.
- Patients who are not hemodynamically stable.
- Patients with altered coagulation profile.
- Patients aged less than 10yrs and more than 80yrs.
- Patients having baseline hypoxemia.
- Patients who had recent myocardial infarction within six weeks.
- Patients with evidence of severe uremia.
- Poor performance status.
- Patients who are found unfit for general anesthesia.

Results

In our study, out of 58 patients who underwent BAL, 20.69% had infectious etiology, 15.52% had malignancy, 13.79% had noninfectious etiology and 50% were inconclusive.

Table 1: Showing study outcome of BAL

BAL	No. of Cases	Percentage
Inconclusive	29	50.00%
Infectious	12	20.69%
Malignancy	9	15.52%
Non-Infectious	8	13.79%
Total	58	100%

Inconclusive results in 1/2 of the patients.
In the remaining 1/2, majority had infectious etiology.

Table 2: Comparision of EBUS TBNA outcome with BAL

		BAL				Total
		Inconclusive	Infectious	Malignancy	Non- Infectious	
EBUS TBANA	Inconclusive	9	2	1	0	12
	Infectious	11	10	0	0	21
	Malignancy	6	0	8	0	14
	Non- Infectious	3	0	0	8	11
Total		29	12	9	8	58

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Chi-Square Tests

	Value	DF	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	8.854	1	.003		
Continuity Correction	7.270	1	.007		
Likelihood Ratio	9.630	1	.002		
Fisher's Exact Test				.005	.003
Linear-by-Linear Association	8.701	1	.003		
N of Valid Cases	58				

P value is .003 [<0.05], hence significant.

Table 3: 2x2 table comparing EBUS TBNA with BAL for culture positivity [BAL is taken as the gold standard assuming the pathology is affecting both lung parenchyma and mediastinal lymph nodes]

EBUS TBNA	Bal		Total
	Positive	Negative	
Positive	10	11	21
Negative	2	35	37
Total	12	46	58

	Bal	
EBUS TBNA	Positive	Negative
Positive	83.33%	23.92%
Negative	16.67%	76. 08%

Sensitivity	83.33%
Specificity	76.08%
PPV	47.61%
NPV	94.59%

With the use of Chi square test, we found that EBUS TBNA had sensitivity 83.33%, specificity76.08%. Positive predictive value 47.61% and negative predictive value 94.59% for culture positivity.

Table 4: 2x2 table comparing EBUS TBNA with BAL for malignant cytology [BAL is taken as the gold standard]

EBUS TBNA	Bal		Total
	Positive	Negative	
Positive	8	6	14
Negative	1	43	44
Total	9	49	58

	Bal	
EBUS TBNA	Positive	Negative
Positive	88.88%	12.25%
Negative	11.12%	87.75%

Sensitivity	88.88%
Specificity	87.75%
PPV	57.11%
NPV	97.72%

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With the use of Chi square test, we found that EBUS TBNA had sensitivity 88.88%, specificity 87.75%. Positive predictive value 57.11% and negative predictive value 97.72% for malignant cytology.

Discussion

Lymph nodes are seen in all three functional compartments of the mediastinum. These are the draining site for lymph along with absorption of dietary fat and fluid homeostasis. Lymph originates when blood plasma leaks out of capillaries and into the interstitial space. Along with the normal macromolecules and lymphocytes within plasma, tumor cells can also leak out and enter lymph nodes. There is high chance for mediastinal lymph node involvement in lung malignancy. Lymph node involvement determines staging of lung cancer as well. Hence N staging in lung cancer is important for diagnosis and prognosis.

In 2004 Yasufuku *et al*. [7] published first study report of EBUS-TBNA in mediastinal LN staging in lung cancer showed sensitivity of 94.5%, specificity and PPV of 100%, NPV of 89.5% and diagnostic accuracy of 96.3%. The prevalence of mediastinal nodal metastasis was 63%. In 19% of patients, in addition to offering staging information, EBUS-TBNA provided diagnostic information, eliminating the need for further invasive tests

In 2011 Ting Ye *et al*. [8] did a prospective analysis on The role of Endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) for qualitative diagnosis of mediastinal and hilar lymphadenopathy in 101 patients with lung carcinoma and found that with respect to the correct diagnosis of mediastinal and hilar lymphadenopathy, EBUS-TBNA had a sensitivity of 95.08%, specificity of 100%, positive predictive value of 100%, negative predictive value of 93.02%, and overall accuracy of 97.02%.

In 2014 Daniel *et al*. [9] conducted a study on diagnostic yield of EBUS TBNA in mediastinal lymphadenopathy of extrapulmonary malignancies and found that EBUS-TBNA found malignancy in 24 out of 47 (51%) patients. Sensitivity, negative predictive value and accuracy of EBUS-TBNA were 83% (CI95% 64-94), 78% (CI95% 56-92) and 89.

Recently, in 2015 Wada *et al*. [10] reported on performance of a prototype thin convex probe-EBUS (TCP-EBUS) in a porcine lung. The TCP-EBUS has a smaller external diameter of 5.9 mm and grater bending angle of 170° up than the current CP-EBUS (6.9 mm external diameter and 120° up angulation).

In 2016 Daisuke Minami *et al*. [11] conducted a study on Endobronchial ultrasound-guided transbronchial needle aspiration of hilar and mediastinal lymph nodes detected on 18F-fluorodeoxy glucose positron emission tomography/computed tomography and concluded that EBUS TBNA accurately diagnoses N1/N2 disease detected on 18F-fluorodeoxyglucose positron emission tomography/computed tomography. A definitive diagnosis was made by endobronchial ultrasound-guided transbronchial needle aspiration in 39 patients out of 5O patients.

Mediastinal lymphadenopathy is a common finding in patients with extra thoracic malignancies and is a frequent diagnostic dilemma for respiratory physicians and oncologists. Enlarged mediastinal nodes are often discovered at the time of initial staging when the demonstration of mediastinal metastases may significantly alter treatment and prognosis. Alternatively, mediastinal lymphadenopathy may be discovered after treatment and require pathological evaluation to exclude or confirm disease recurrence.

In 2011 Jinkyeong Park *et al*. [12] did a study on the effectiveness of EBUS TBNA Biopsy for Diagnosis of Mediastinal Lymphadenopathy in Patients with Extra thoracic Malignancy. A total of 88 lymph nodes was analyzed. EBUS-TBNA findings indicated malignancies in 34 patients (57.6%). The EBUS-TBNA sensitivity and specificity for the detection of mediastinal malignancy in patients with a previous extra thoracic malignancy were 96.3% and 100%, respectively.

Table 5: Showing comparison of sensitivity, specificity, PPV, NPV of reference study with present study.

EBUS TBNA	Erer of *et al*.	Present study
Sensitivity	87.5%	85.71%
Specificity	98.5%	54. 05%
PPV	91.4%	51.43%
NPV	98%	86.96%

While for BAL we obtained, 29 adequate samples, hence the diagnostic yield is only 50%. Among these 29 patients, 41.3% had infective pathology, 31% had malignancy and 27.5% had reactive pathology. Similarly, in a study done by Nimit V Khara [82] *et al*. diagnostic yield of fiberoptic bronchoscopy and BAL was only 55.7%. The most common pathology in their study was malignancy [68.5%] followed by tuberculosis [37.7%].

Conclusion

In this study population, the diagnostic yield of EBUS TBNA was 79.3%.The sensitivity, specificity and NPV of EBUS TBNA for infections were 83.33%, 76.08%, 47.61% and 94.59% while for malignancy it was found to be 88.88%, 87.75%, 57.11% and 97.72% respectively.

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