

Diagnostic Value and Effective Factors on Transbronchial Lung Biopsy Using Cup and Alligator Forceps

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Background: Lung biopsy through the airways by using a flexible bronchoscope (transbronchial lung biopsy: TBLB) is a suitable method for obtaining tissue specimens. This study aimed at evaluating the factors influencing TBLB results in order to increase the diagnostic power of this method.

Materials and Methods: This was a prospective double blind observational study. We had a total of 44 patients with pulmonary lesions who underwent biopsy and 4 specimens were obtained from each patient. A total of 176 specimens were obtained from all patients. Biopsy specimens were taken using cup and alligator forceps alternatively. Characteristics of the obtained specimens including size, floatation, alveolarity, and bleeding were thoroughly studied. After sending to the pathologist, specimens were divided into 2 groups of diagnostic and non-diagnostic specimens.

Results: Of a total of 176 specimens, 37 (21%) were diagnostic and 139 (79%) were non-diagnostic. From 88 specimens obtained by the alligator forceps, 16 were diagnostic while from the same number of specimens taken by the cup forceps 21 had diagnostic value. However, this difference was not statistically significant ($P>0.05$). Of the small specimens (57 cases), 12 (21.1%) were diagnostic while among the 66 medium specimens, 12 (18.2%) and from the 53 large specimens, 13 (24.5%) were diagnostic. No statistically significant difference was detected in this respect ($P>0.05$). Among specimens floating on the surface of the liquid (48 cases), 6 (12.5%) had diagnostic value. Of the 12 specimens suspended in the liquid, 2 (16.7%) and among the 116 specimens precipitated at the bottom, 29 (25%) were diagnostic. These differences were not significant either ($P>0.05$). Of the 84 specimens with more than 20 alveoli, 31 (36.9%) were diagnostic. Among 26 specimens with less than 20 alveoli 5 (19.2%) were diagnostic. This correlation was statistically significant indicating that the higher the number of alveoli in the biopsy specimen, the greater the chance of being diagnostic.

Conclusion: This study failed to find a significant correlation between the diagnostic power of TBLB and type of forceps, sample size or floatation of the specimen in the liquid. However, number of alveoli present in the tissue specimens was significantly correlated with its diagnostic value. Increasing the number of specimens to four can increase the chance of diagnosis.

Key words: Diagnostic, Lung biopsy, Transbronchial

INTRODUCTION

Transbronchial lung biopsy is the method of choice for diagnosis of pulmonary lesions and can be used for diagnosis of a wide range of pulmonary diseases such as interstitial lung diseases, vascular diseases, small airway

diseases, malignancies such as disseminated form of the alveolar cell carcinoma and infections. Since 1970, TBLB with a flexible fiberscope has been widely accepted as a conventional method for lung biopsy (1,2).

In general, TBLB is a safe procedure with an overall mortality rate of 0.1%, which is way lower than that surgical lung biopsy (1%). Since it does not require general anesthesia, it is commonly used for out patients (3). Small size of TBLB specimens is a major factor that contributes to the acceptability of TBLB as a diagnostic modality for pulmonary conditions (4,5).

Type of forceps, number of specimens and size of specimens can affect the diagnostic value of TBLB. Determination of the adequate number of biopsy specimens can be very helpful to prevent unnecessary biopsy and decreased diagnostic value of TBLB. Several studies have evaluated the quality of specimens in terms of size and alveolarity and number of biopsies (1,6-8). However, no suitable criteria have been set for obtaining specimens with higher quality (9). This study aimed to assess the factors affecting the diagnostic value of TBLB.

MATERIALS AND METHODS

This prospective, double blind observational study was conducted on patients referred to the Bronchoscopy Department of Masih Daneshvari Hospital.

After local anesthesia via nasal inhalation of 2cc of 5% lidocaine, bronchoscopy was performed by an interventional pulmonologist and data were recorded by a pulmonology fellow. All specimens were evaluated by a pathologist. Both pathologist and fellow were blinded to the type of forceps. A total of 44 patients underwent biopsy and 4 specimens were taken from each patient (a total of 176 specimens). There were 21 males (47.7%) and 23 females (52.3%). The specimens were obtained by the cup and alligator forceps randomly and alternately (88 specimens were taken by each forceps).

Characteristics of each specimen:

A: Size

Small: specimens were classified as small if they did not fill the forceps

Medium: specimens were classified as medium if they filled the forceps

Large: specimens were classified as large if they spilled over the surface of the forceps

B: Floatation (in formalin):

1: The specimen was floating on the surface of liquid

2: Somewhere between 1 and 3

3: The specimen precipitated at the bottom of the tray

Specimens were then sent to the Pathology Department.

C: Alveolarity

1: Presence of more than 20 alveoli: Alveolated

2: Presence of less than 20 alveoli: Non-alveolated

3: No alveoli: Unsatisfactory specimen

RESULTS

In this study, 44 patients were evaluated out of which 21 (47.7%) were males and 23 (52.3%) were females. The mean age of patients was 46.6±14.6 yrs. Of 176 specimens, 57 were small (32.4%), 66 were medium (37.5%) and 53 were large (30.1%) (Table 1).

Table 1. Evaluation of specimens according to size and pathologic diagnosis

Specimen	Size			Total
	Small	Moderate	Large	
Diagnostic	12(21.1%)	12(18.2%)	13(24.5%)	37(21%)
Non-diagnostic	45(78.9%)	54(81.8%)	40(75.5%)	139(79%)
Total	57	66	53	176

In terms of floatation, 48 specimens (27.3%) floated on the surface of liquid, 12 specimens (6.8%) were somewhere between 1 and 2 and 116 (65.9%) precipitated at the bottom of the tray.

In terms of alveolarity, 84 specimens (47.7%) were alveolated, 26 (14.8%) were non-alveolated and 66 (37.5%) were unsatisfactory.

A. Type of forceps and diagnostic value:

Of a total of 176 specimens, 37 (21%) were diagnostic and 139 (79%) were non-diagnostic. Since each forceps yielded 88 specimens, in specimens taken by alligator forceps, 16 (18.2%) were diagnostic and 72 (81.8%) were non-diagnostic. In specimens taken by cup forceps, 21

(23.9%) were diagnostic and 67 (76.1%) were non-diagnostic. According to the chi square test, no association existed between type of forceps and diagnostic value of specimens ($p=0.355$).

B. Size and diagnostic value:

As mentioned earlier, of a total of 176 specimens, 37 were diagnostic. Of the 57 small specimens, 12 (21.1%) were diagnostic. Of the 66 medium specimens, 12 (18.2%) and of the 53 large specimens, 13 (24.5%) were diagnostic. Chi square test did not find a significant correlation between the size of specimen and its diagnostic value ($p=0.700$).

Number of small, medium and large specimens among diagnostic specimens was almost the same. In other words, no significant correlation existed between the size of specimen and its diagnostic value ($p=0.700$).

C. Floating and diagnostic value:

Although overall 37 specimens (21%) were diagnostic, the frequency of diagnostic specimens based on their floating was as follows:

Of the 48 specimens floating on the surface, 6 (12.5%) were diagnostic. Of the 12 specimens suspended in the liquid, 2 (16.7%) and of the 116 specimens precipitated at the bottom, 29 (25.5%) were diagnostic. Despite the fact that the percentage of diagnostic specimens in the third group was twice the rate in the first group, chi square test failed to find a significant correlation in this respect ($P=0.188$).

D. Alveolarity and diagnostic value

Of 84 alveolated specimens, (more than 20 alveoli) 31 (36.9%) were diagnostic. Of the 26 specimens with less than 20 alveoli, 5 (19.2%) were diagnostic. Of 66 specimens with no alveoli, 1 (1.5%) was diagnostic. Percentage of diagnostic cases was significantly higher in group 1. This difference was statistically significant according to the chi square test ($P<0.005$). In other words, a specimen with more alveoli has a greater chance of being diagnostic.

E. Size of specimen and alveolarity:

The frequency of number of alveoli based on the size of specimens was as follows:

Of 57 small size specimens, 23 (40.4%) had more than 20 alveoli, 9 (15.8%) had less than 20 alveoli and 25 (43.9%) had no alveoli. Of 66 medium size specimens, 30 (45.5%) had more than 20 alveoli, 12 (18.2%) had less than 20 alveoli and 24 (36.4%) had no alveoli. Of 53 large-size specimens, 31 (58.5%) had more than 20 alveoli, 5 (9.4%) had less than 20 alveoli and 17 (32.1%) had no alveoli. According to chi square test, the difference between size of specimens and number of alveoli was not significant ($P=0.326$).

F. Floating and alveolarity:

The frequency of alveolarity based on floating of specimens was as follows:

Of a total of 48 floating specimens, 23 (47.9%) had more than 20 alveoli, 5 (10.4%) had less than 20 alveoli and 20 (41.7%) had no alveoli. Of 12 specimens suspended in the liquid, 9 (75%) were alveolated, 1 (8.3%) was non-alveolated and 2 (16.7%) did not have alveoli. Of 116 precipitated specimens, 52 (44.8%) had more than 20 alveoli, 20 (17.2%) had less than 20 alveoli and 44 (37.9%) had no alveoli. The numerical values in the three groups were close. Chi square test found no significant correlation between floating and alveolarity ($P=0.275$).

G. Type of forceps and diagnostic value of specimen:

In 44 patients, biopsy led to diagnosis in 21 cases (47.7%) while a diagnosis was not made in 23 patients (52.3%). Of 21 patients with diagnosis, alligator forceps had been used in 9 (40.9%) and cup forceps in 12 (54.5%). No correlation was noted between type of forceps and diagnostic value of specimen ($P=0.365$). Thus, regardless of the first specimen, which was diagnostic alone in 55% of the cases, each of the second to fourth specimens increased the diagnostic value by 15% and had equal efficacy in this respect (Table 2).

Table 2. Diagnostic features based on order of specimens

Specimen 1	Specimen 2	Specimen 3	Specimen 4	No.	Diagnostic%
+	+	+	+	2	10
+	+	+	-	2	10
+	+	-	+	0	0
+	+	-	-	0	0
+	-	+	+	1	5
+	-	+	-	0	0
+	-	-	+	2	10
+	-	-	-	4	20
-	+	+	+	0	0
-	+	+	-	1	5
-	+	-	+	0	0
-	+	-	-	2	10
-	-	+	+	2	10
-	-	+	-	1	5
-	-	-	+	3	15
				20	100

DISCUSSION

This study was designed to assess the effect of factors such as type of forceps, number of specimens, size of specimens and their alveolarity on the diagnostic value of TBLB. Of 176 specimens 37 (21%) were diagnostic. This rate was 22.9% in a study by Liam et al (10). In another study by Schreiber and McCrory, this rate was 21-84% (11). Thus, difference in the diagnostic value of specimens can be due to expertise of the operator, more accurate pathological analysis and higher quality of specimens (12,13).

Of the 88 specimens obtained by each forceps, 18 specimens taken by the alligator forceps (18.2%) and 21 specimens (23.9%) taken by the cup forceps were diagnostic. A significant difference was not detected in this respect. Study on a larger population may reveal a significant association between type of forceps and diagnostic value of specimens. Controversy exists in this respect among other studies. Some authors believe that type of forceps has no effect on diagnostic value of specimens (10-14) while some others (6, 15) such as Lee et al. believe that type of forceps had a significant effect on diagnostic value of specimens and specimens taken by alligator forceps have higher diagnostic quality (15).

In contrast to a study by Curley et al, (6) we did not find a significant association between size of specimens and their diagnostic value. In other words, larger specimens do not necessarily have higher diagnostic value. A total of 21% of specimens were diagnostic. This rate was 21.1% in small, 18.2% in medium and 24.5% in large specimens. However, Curley et al concluded that specimens that filled the entire forceps space (adequate) had a significant correlation with diagnostic value (6). Some other authors concluded that larger specimens are more diagnostic. Berbescu et al. believed that if clinical and radiographic findings match, small specimens have high diagnostic value as well. But if clinical and radiographic findings do not match, a larger specimen would be more diagnostic (7).

Although the percentage of diagnostic specimens precipitated at the bottom (25%) was twice the specimens floating on the surface (12.5%), this difference was not statistically significant. In other words, in contrast to the study by Anders et al, (9) we found no significant association between floating and diagnostic value of specimens. However, a significant correlation may be found in a larger population. On the other hand, in our study most of the specimens (65.9%) precipitated at the bottom of tray in contrast to the afore-mentioned study.

Specimens with higher number of alveoli had a greater chance of being diagnostic. In specimens with more than 20 alveoli 36.9% were diagnostic. This difference was statistically significant. Therefore, we can conclude that increased number of alveoli increases the chance of being diagnostic. This has also been reported in previous studies and many researchers have emphasized that higher number of alveoli in specimens increases the diagnostic value (7,8,16).

No significant association was noted in our study between size of specimen and number of alveoli. In other words, a larger specimen does not necessarily mean higher number of alveoli and higher diagnostic value. Similar to the study by Anders et al, (9) and in contrast to some previous studies, we found no significant association

between number of alveoli and floating of specimens. In other words, floating test is not suitable for assessment of adequacy and quality of specimens.

In our study, TBLB in 21 out of 44 patients (47.71%) resulted in diagnosis. In other words, the diagnostic sensitivity of TBLB was about 50%. Poletti et al. reported that TBLB had 64% sensitivity and 86% specificity.

Despite the fact that in over half the patients (55%) who were diagnosed, the first specimen was diagnostic (highlights the significance of first specimen in diagnosis), the second and third specimens resulted in diagnosis each in 15% of the cases. In other words, they added 15% to the diagnostic value. The fourth specimen was the first and only diagnostic specimen also in 15% of the cases. Thus, further specimens may increase the chance of diagnosis. Thus, optimal number of specimens could not be determined in our study. Curely et al. stated that the fifth and next specimens did not increase the chance of diagnosis and the first and second specimens had the greatest share in diagnosis. Specimens after the fourth one had an insignificant share in diagnosis (6). However, others (1,8,15,17) concluded that increasing the number of specimens to 5 or 6 increases the chance of diagnosis. Griff et al. (16) and Balzar et al. (18), used 2 to 4 specimens in their studies for diagnosis and suggested that further increasing the number of specimens (more than 4) increases the quality of diagnosis. Thus, it can be suggested that by increasing the number of specimens to more than 4, the quality of diagnosis can be enhanced.

CONCLUSION

In terms of diagnostic value of specimens, no significant difference was noted between the two types of forceps. Only number of alveoli in each specimen had a significant correlation with diagnostic value. Number of alveoli was correlated with floating of specimens but no association was found between size of specimens and number of alveoli. Size and floating had no significant

association with diagnostic value. Increasing the number of specimens to four can increase the chance of diagnosis. Thus, we cannot determine the adequacy of specimen based on its size or floating. Optimal number of specimens would be more than 4; although a definite number could not be determined in our study.

REFERENCES

1. Visner GA, Faro A, Zander DS. Role of transbronchial biopsies in pediatric lung diseases. *Chest* 2004;126(1):273-80.
2. Sasada S, Ogata Y, Kobayashi M, Hirashima T, Kawahara K, Matsui K, Kawase I. Angled forceps used for transbronchial biopsy in which standard forceps are difficult to manipulate: a comparative study. *Chest* 2006;129(3):725-33.
3. Margaritopoulos GA, Wells AU. The role of transbronchial biopsy in the diagnosis of diffuse parenchymal lung diseases: con. *Rev Port Pneumol* 2012;18(2):61-3.
4. Pajares V, Torrego A, Puzo C, Lerma E, Gil De Bernabé MA, Franquet T. Transbronchial lung biopsy using cryoprobes. *Arch Bronconeumol* 2010;46(3):111-5.
5. American Thoracic Society; European Respiratory Society. American Thoracic Society/European Respiratory Society International Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonias. This joint statement of the American Thoracic Society (ATS), and the European Respiratory Society (ERS) was adopted by the ATS board of directors, June 2001 and by the ERS Executive Committee, June 2001. *Am J Respir Crit Care Med* 2002;165(2):277-304.
6. Curley FJ, Johal JS, Burke ME, Fraire AE. Transbronchial lung biopsy: can specimen quality be predicted at the time of biopsy? *Chest* 1998;113(4):1037-41.
7. Berbescu EA, Katzenstein AL, Snow JL, Zisman DA. Transbronchial biopsy in usual interstitial pneumonia. *Chest* 2006;129(5):1126-31.
8. Poletti V, Cazzato S, Minicuci N, Zompatori M, Burzi M, Schiattone ML. The diagnostic value of bronchoalveolar lavage and transbronchial lung biopsy in cryptogenic organizing pneumonia. *Eur Respir J* 1996;9(12):2513-6.
9. Anders GT, Linville KC, Johnson JE, Blanton HM. Evaluation of the float sign for determining adequacy of specimens

- obtained with transbronchial biopsy. *Am Rev Respir Dis* 1991;144(6):1406-7.
10. Liam CK, Pang YK, Poosparajah S. Diagnostic yield of flexible bronchoscopic procedures in lung cancer patients according to tumour location. *Singapore Med J* 2007;48(7):625-31.
 11. Schreiber G, McCrory DC. Performance characteristics of different modalities for diagnosis of suspected lung cancer: summary of published evidence. *Chest journal* 2003;123(1_suppl):115S-28S.
 12. Cox CE, Davis-Allen A, Judson MA. Sarcoidosis. *Med Clin North Am* 2005;89(4):817-28.
 13. Shorr AF, Torrington KG, Hnatiuk OW. Endobronchial biopsy for sarcoidosis: a prospective study. *Chest* 2001;120(1):109-14.
 14. Prakash UB, Cortese DA, Stubbs SE. Technical solutions to common problems in bronchoscopy. *Bronchoscopy*. New York: Raven. 1994:111-33.
 15. Lee P, Mehta AC, Mathur PN. Management of complications from diagnostic and interventional bronchoscopy. *Respirology* 2009;14(7):940-53.
 16. Griff S, Ammenwerth W, Schönfeld N, Bauer TT, Mairinger T, Blum TG, Kollmeier J, Grüning W. Morphometrical analysis of transbronchial cryobiopsies. *Diagn Pathol* 2011;6:53.
 17. Descombes E, Gardiol D, Leuenberger P. Transbronchial lung biopsy: an analysis of 530 cases with reference to the number of samples. *Monaldi Arch Chest Dis* 1997;52(4):324-9.
 18. Balzar S, Wenzel SE, Chu HW. Transbronchial biopsy as a tool to evaluate small airways in asthma. *Eur Respir J* 2002;20(2):254-9.