

TRANSBRONCHIAL LUNG BIOPSY: TWO YEARS EXPERIENCE OF A TERTIARY CARE CENTRE

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ABSTRACT

Objective: To determine the outcome and safety of transbronchial lung biopsy (TBLB) in various pulmonary disorders.

Methodology: This study was carried out at the Department of Pulmonology, Shaikh Zayed Hospital, Federal Postgraduate Medical Institute (FPGMI) Lahore, Pakistan. It was a case series consisting of 50 TBLB procedures conducted via flexible fiberoptic bronchoscope (among >200 diagnostic and therapeutic bronchoscopic procedures) over 24 months (April 2015 to April 2017). The data were entered and analyzed by using SPSS version 20.0.

Results: Fifty TBLB procedures yielded results in 45 patients (90%), while 5 (10%) remained inconclusive. Among all patients, pulmonary sarcoidosis was diagnosed in 12 (24%), malignant disease in 9 (18%), pulmonary tuberculosis (PTB) in 5 (10%), chronic hypersensitivity pneumonitis (CHP) in 4 (8%), organizing pneumonia (OP) in 3 (6%), slowly resolving bacterial pneumonia in 5 (10%), non-specific interstitial pneumonia (NSIP) in 4 (8%) and others in 3 (6%) of patients. Per procedural bleeding after TBLB occurred in around 13 (30%) but none developed a pneumothorax, hemodynamic instability or death during the procedure.

Conclusion: TBLB is a safe bronchoscopic procedure and carries a high diagnostic yield in disorders involving the pulmonary parenchyma.

Key Words: Flexible bronchoscopy, Lung biopsy, Transbronchial lung biopsy

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INTRODUCTION

Bronchoscopy consists of two main types including the rigid bronchoscopy (done under general anesthesia in operation theatre) and flexible fiberoptic bronchoscopy (done in bronchoscopy suite under conscious sedation and analgesia)¹. Flexible bronchoscope having a great diagnostic and therapeutic yield is used in many airways and pulmonary parenchymal disorders^{1,2}. Besides bronchial washing, broncho-alveolar lavage (BAL) and endobronchial biopsy, bronchoscope is also utilized to obtain biopsy from the lung parenchyma known as transbronchial lung biopsy. Specimens can be obtained through TBLB blindly, with fluoroscopic guidance, or with ultrasound or other navigational (e.g. virtual or electromagnetic) guidance².

Guidance procedures confirm proper placement of the forceps, which is particularly helpful if the lesion or area of interest is small and peripheral (Figure 1a and 1b)³. It is associated with an improved diagnostic yield, although it does not appear to reduce the chances of pneumothorax⁴. In contrast, the blind approach is suffi-

cient for a diffuse process because the area of interest is widespread (e.g. sarcoidosis or disseminated malignancy)⁵.

The purpose of the study was to retrospectively evaluate the yield of TBLB in patients presenting with various pulmonary disorders in a tertiary care pulmonology unit. TBLB requires some training on part of pulmonologists and if utilized during bronchoscopy, can help in the diagnosis of various pulmonary disorders without requiring surgical lung biopsy thus avoidance of patients from invasive surgical lung biopsy.

METHODOLOGY

It was a case series consisting of 50 TBLB procedures based on temporal sample size in duration of 24 months from April 2015 to April 2017. The aim of this study was to retrospectively evaluate the diagnostic yield of TBLB for various pulmonary disorders which remained undiagnosed after initial diagnostic work up including sputum analysis and chest radiology. An informed consent was taken from these patients for procedure as

well as for using data for research purpose. More than 200 diagnostic and therapeutic bronchoscopic procedures were conducted during this time frame and 50 patients required TBLB in isolation or in addition to other bronchoscopic procedures which included bronchial washings, BAL, transbronchial needle aspiration (TBNA) and endobronchial biopsies. Patients using aspirin were allowed to continue and those on clopidogrel were advised to stop the antiplatelet drug at least 5-7 days before TBLB procedure.

Procedures were conducted at interventional bronchoscopy and medical thoracoscopy unit of the Department of Pulmonology at Shaikh Zayed Hospital, FPGMI Lahore, Pakistan. Data of the patients were saved in the computer placed in the procedural suite including history, radiology, biopsy results, complications and any further interventions. Lignocaine 4% was used to spray nose and throat for local anesthesia; lignocaine gel was used to lubricate the nasal passage during scope insertion and lignocaine 2% was used to anesthetize the airways during bronchoscope insertion and inspection through the vocal cords and lower airways. Procedural analgesia & sedation was achieved using midazolam (1-5 mg) + fentanyl (25-100 mcg). Pulse oximetry was used to monitor heart rate and oxygen saturation (SpO₂) during the bronchoscopic procedures.

Most patients had bronchoscope insertion through right or left nostril and per-oral insertion only in 3-4 subjects was utilized due to bilateral nasal narrowing/obstruction (polyps, hypertrophied turbinates or ulcerations). Thirty patients (60%) had the procedure done under fluoroscope guidance and 20 (40%) subjects with diffuse lung disease had their TBLB done blindly (without fluoroscope guidance). Both diagnostic (2 mm channel) and therapeutic (3.2 mm channel) bronchoscopes (Fujinon® EB-200 video-bronchoscope system) were utilized and cupped/alligator biopsy forceps were used to obtain pulmonary parenchymal tissue/TBLB (6-10 bites/specimens).

After identifying the appropriate sub-segment of a lung lobe (as seen on CT scan of chest), biopsy forceps were advanced in the forward direction until it got stuck (stopped moving further) in the lung parenchyma. At this point, the biopsy forceps were pulled an inch back, opened and moved to and fro and slightly advanced to reach the lung parenchyma followed by closing (grasping the lung tissue) during patients' exhalation thus taking a bite through lung tissue followed by pulling and removal of the forceps. At least 6 and maximum 10 bites were taken to ensure adequacy of the specimen. The biopsy specimens were placed in the small containers containing formalin solution and sent for histopathology. If needed, the bleeding sub-segment of lung through which biopsy forceps was advanced was wedged with the bronchoscope and ice cold saline and

epinephrine (1:1000) were also used topically to help cease bleeding. Follow up chest radiograph was taken immediately (dyspnoeic patient) or in the evening (stable patient) following procedure to rule out a pneumothorax. Histopathology report was collected and saved in patient's data. Data were entered and analyzed by using SPSS version 20.0. Data for age was expressed by using mean and standard deviation. Data for gender and diagnosis was presented by frequency and percentages. Pie chart was formed for ratio of different diagnosis among cases using MS excel.

RESULTS

Fifty cases included 30 males (60%) and 20 females (40%), having ages between 22-82 years (mean age 48 years). TBLB procedures yielded results in 45 patients (90%) while 5 (10%) remained inconclusive (inconclusive or showed non-specific/diagnostic inflammation/findings on histopathology). Among all patients, pulmonary sarcoidosis was diagnosed in maximum cases (24%), followed by malignancy (18%), pulmonary tuberculosis (PTB) in (10%), and slowly resolving bacterial pneumonia in (10%) (Figure 2). All biopsies showed presence of alveolar lung tissue on histopathology suggestive of accuracy of the pulmonary specimens.

Among types of pulmonary malignancies, adenocarcinoma was most common type diagnosed in 7 (77.7%) patients (Table 1). Chronic non-caseating granulomas were seen in 12 patients with sarcoidosis and vaguely formed granulomas were appreciated in 4 patients with the compatible diagnosis of CHP. Five patients who suffered from disseminated tuberculosis had TB sputum smear negative (therefore underwent bronchoscopy) and were found to have chronic granulomatous inflammation with caseation necrosis on histopathology of the biopsy specimens as well as acid fast bacilli (AFB) smear positivity on bronchial washings/lavage specimen. Five patients (10%) who were diagnosed to have slowly/non-resolving pneumonia on TBLB had infiltrates on chest radiograph/HRCT which mimicked lung cancer or were suspicious of having PTB. One patient who was diagnosed to have CEP had mild eosinophilic infiltration with chronic non-specific inflammation on TBLB but was found to have 41% eosinophils on BAL differential cell counts. Another patient who had non-caseating granulomas on histopathology was also found to have positive antineutrophilic cytoplasmic antibodies (ANCA) consistent with the diagnosis of GPA (formerly Wegener's granulomatosis). Last patient with an atypical HRCT who underwent TBLB was surprisingly diagnosed as having IPF showing areas of fibroblastic foci, mild honey combing and intervening normal lung parenchyma on histopathology.

There were fewer complications associated with TBLBs. All patients experienced mild to moderate cough

and chest discomfort during the procedure that was controlled well with topical sprays of 2% lignocaine; mild bleeding (10-30 ml) after TBLB occurred in 15 (30%) individuals (ceased with topical epinephrine and

cold saline sprays), and fortunately none of our patients developed a pneumothorax, hemodynamic instability or death during the procedure.

Figure 1: (a) A middle aged male with cough, dyspnea and pyrexia having bilateral airspace shadowing in peripheral lung fields and (b) TBLB through peripheral right lung lesion (in the same subject) under fluoroscope guidance proved to be cryptogenic organizing pneumonia

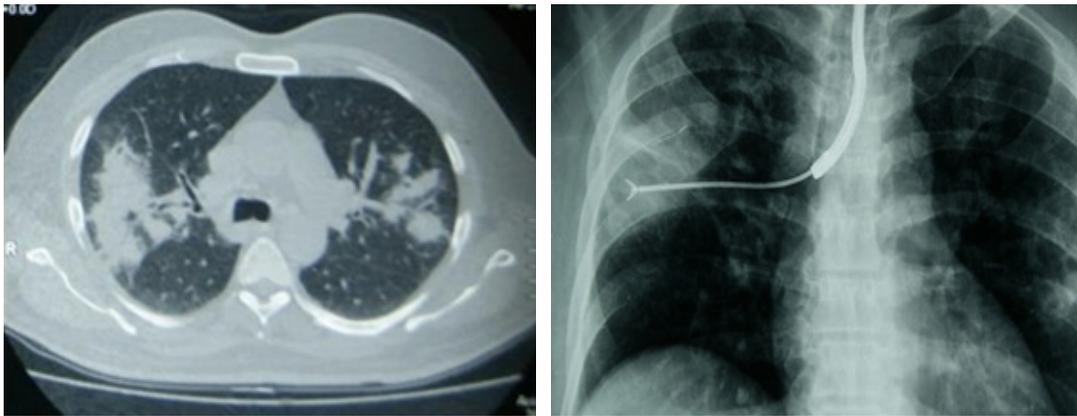


Figure 2: Frequency and type of pulmonary disorders diagnosed with transbronchial lung biopsy using fiberoptic flexible bronchoscope

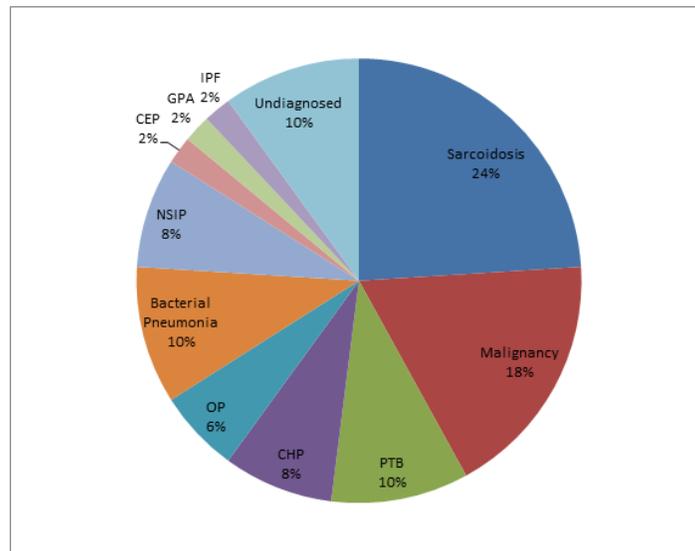


Table 1: Frequency and type of malignancy on transbronchial lung biopsy

Type	Number	Percentage
Adenocarcinoma Lung	07	77.7 %
Squamous Cell Carcinoma	01	11.1 %
Undifferentiated	01	11.1 %
Total	09	100%

DISCUSSION

We analyzed 50 TBLB procedures carried out in 30 males and 20 female patients. The youngest was a 22-year-old female who underwent TBLB (febrile slowly/non-resolving community acquired pneumonia) in the suspicion of pulmonary TB because of poor resolution of infiltrates on chest radiograph. The eldest patient who had TBLB (under fluoroscopy) was an 82-year-old male suffering from severe chronic obstructive pulmonary disease and had an opacity on chest CT (round pneumonia in a peripheral right lower lobe location) that was even reported as lung cancer by the radiologist. Histopathology of lung tissue was consistent with the diagnosis of resolving pneumonia (sub-acute inflammation). In our study, the overall diagnostic yield of TBLB was 90%. International data also supports the high utility of TBLB (6-10 bites/specimens) in the evaluation of diffuse parenchymal lung disease particularly in lymphangitis carcinomatosa, chronic eosinophilic pneumonia, sarcoidosis, rejection after lung transplantation, hypersensitivity pneumonitis and mycobacterial and invasive fungal infection⁶.

In a Chinese study addressing the diagnostic value of TBLB (under fluoroscopic guidance) in solitary pulmonary nodules utilizing 170 patients, 120 (70.6%) had lung cancer, 40 (23.5%) patients had pulmonary TB and the remaining 10 (5.9%) patients had other benign pulmonary lesions⁷. The results of our study were different from this study as we enrolled patients with localized and diffuse lung diseases; majority of our patients had sarcoidosis (24%), followed by malignancy (18%) and TB (10%) and the remaining suffered from other benign lung diseases.

In another Polish study, TBLB was performed in 243 patients with bilateral diffuse pulmonary shadows and histological diagnosis was established in only 54.4% which was much lower compared to our study having 90% success⁸. In a recent meta-analysis regarding diagnostic yield and safety of cryoprobe transbronchial lung biopsy in diffuse parenchymal lung diseases, pooled diagnostic yield of cryo-transbronchial lung biopsy was 76.9% (95% CI 67.2-85.3) still lower than our results⁹. Our results are comparable to reported diagnostic yields of 85 to 92 percent for surgical lung biopsy¹⁰.

Most of our patients had sarcoidosis which in reported series has a high diagnostic yield (79%) on TBLB¹¹. TBLB is often the biopsy procedure of choice when the diffuse lung disease is likely to have a centrilobular location and when a diagnosis can be established using small samples of lung tissue⁶. We could make diagnosis in patients with sarcoidosis, PTB, CHP, OP, and CEP; the diseases with predominantly centrilobular distribu-

tion. Although surgical lung biopsy is recommended for patients with suspected COP, a TBLB with typical histopathologic findings might be sufficient in the appropriate clinical and radiologic context like in 3 (6%) out of 50 patients in our study¹². TBLB is not recommended in idiopathic interstitial pneumonias because of small size of specimen and poor diagnostic yield. We could still diagnose one patient with IPF who underwent the procedure because of atypical radiological appearances on HRCT. Among three patients who were diagnosed to have OP, two actually had cryptogenic organizing pneumonia (COP) and one had OP as a pulmonary manifestation of underlying rheumatoid arthritis (Figure 1).

While TBLB is rarely sufficient to make a histopathological diagnosis of IPF, a properly performed and interpreted TBLB does increase the post-test probability of IPF in patients who already have a high pre-test probability of this disease¹³. In this study, 4 (8%) of our patients were diagnosed to have NSIP on TBLB, they also had a high pre-test probability of NSIP but were not agreed to undergo surgical lung biopsy which is the recommended procedure for confirmation of diagnosis¹³. Occasionally, transbronchial lung biopsy may be performed in selected group of patients who are not good candidates for surgical lung biopsy¹⁰.

In our country patients are generally reluctant to have surgical lung biopsy because of invasiveness and cost issues and none of our patients agreed to undergo a surgical lung biopsy including 5 (10%) cases which remained undiagnosed after TBLB.

None of our patients died as a complication of the intervention; TBLB is a safe procedure with an estimated mortality of <0.05 percent¹⁴. Complications of TBLB include pneumothorax and hemorrhage and presence of pulmonary hypertension increases the risk of bleeding. TBLB is safe in patients receiving aspirin, but clopidogrel should be withheld 5-7 days before the test. Insignificant bleeding occurred in 13 (30%) of our patients but no one developed a pneumothorax, which is estimated to occur in 0.7 to 2 percent, although rates up to 10 percent have been reported^{10,13,14}.

LIMITATIONS OF STUDY

The limitations of our study include small sample size of the subgroups which may have impact on the reliability of the results. Another important limitation to our study is its retrospective design in which chances of missing information is more compared to a prospective study. However, we are confident that our assessment of interventions is reliable because all the necessary records were maintained; there is still a possibility that minor intervention related complications may have been missed.

CONCLUSION

Transbronchial lung biopsy is a safe and ultimately useful tool in the armamentarium of interventional pulmonologists having an excellent yield in the diagnosis of various pulmonary disorders including but not limited to sarcoidosis, interstitial lung diseases, malignancies & lung infiltrative and infectious diseases.

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CONTRIBUTORS

TM conceived the idea, planned the study and drafted the manuscript. MS helped acquisition of data critically revised the manuscript. MA did data entry, statistical analysis and results interpretation. All authors contributed significantly to the submitted manuscript.