DISSERTATION ON

THE ROLE OF FIBEROPTIC BRONCHOSCOPY
IN EVALUATING CAUSES OF UNDIAGNOSED
PLEURAL EFFUSION

Dissertation submitted to the
TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY,
In Partial fulfillment of the requirements
for the degree of Doctor of Medicine in
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Madras Medical College & Rajiv Gandhi Government General Hospital

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY
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APRIL 2012
DECLARATION BY THE SCHOLAR

I hereby declare that the dissertation entitled “THE ROLE OF FIBEROPTIC BRONCHOSCOPY IN EVALUATING CAUSES OF UNDIAGNOSED PLEURAL EFFUSION” submitted for the Degree of Doctor of Medicine in M.D, DEGREE EXAMINATION Branch XVII PULMONARY NEDICINE is my original work and the dissertation has not formed the basis for the award of any degree, diploma, associate ship, fellowship or similar other titles. It had not been submitted to any other university or institution for the award of any degree or diploma.

Place: Chennai
Date:

Signature of the scholar
Name: Dr. K. ANBANANTHAN
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As they say, dissertation is an amateur’s foray into the world of clinical research. I as a postgraduate enjoyed this learning process and would like to thank my known and unknown teachers, who taught the basics of clinical research. I thank the guidance, encouragement, motivation and constant supervision extended to me by my respected Director & H.O.D Prof. Dr. N. Meenakshi.

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BACKGROUND:
The role of Fiberoptic bronchoscopy in the investigation of pleural effusion is not well defined. Although the inclusion of bronchoscopy as a part of routine evaluation of all such patients is frequently advocated, evidence to support this is sparse.

In an attempt to clarify the role of Fiberoptic bronchoscopy in the investigation of undiagnosed pleural effusion a study was conducted to evaluate the diagnostic merits of Fiberoptic bronchoscopy.

AIMS AND OBJECTIVES:

To evaluate the diagnostic merit of Fiberoptic bronchoscopy in evaluating the causes of undiagnosed pleural effusion.

MATERIALS AND METHODS: An observational study involving 110 individuals, both males and females, coming to the outpatient department of Institute of Thoracic medicine & Madras Medical College, with diagnosis of pleural effusion, between January and September 2011. All eligible and consenting patients were subjected to routine investigations and pleural fluid analysis. In patients who had exudative pleural effusion and initial investigations were inconclusive, Pleural biopsy and Fiberoptic bronchoscopy were done and specimens were sent for microbiological, cytological and histopathological analysis.
RESULTS:

Among 110 patients with pleural effusion, after initial work up, diagnosis was made in 43 (39.09%) patients. In the remaining 67 patients, 3 patients were not willing for bronchoscopy. Out of 64 patients whose diagnosis was not made by initial work up, FOB was useful in making diagnosis in 18 (28.1%) cases. Pleural biopsy helped in diagnosing 26 (40.62%) cases.

CONCLUSION:

Fiberoptic bronchoscopy is useful in patients with exudative effusion still undiagnosed after pleural fluid cytology and biopsy and with parenchymal abnormalities on chest skiagram or with hemoptysis.
INTRODUCTION

Pleural effusion is an abnormal collection of fluid in the pleural space. It is not a disease but rather a complication of an underlying illness. Effusion can occur for a variety of reasons. Common classification systems divide pleural effusions into two categories of (1) Transudative pleural effusions and (2) Exudative pleural effusions.

Determining the cause of a pleural effusion is greatly facilitated by analysis of the pleural fluid. Thoracentesis is a simple bedside procedure that permits fluid to be rapidly sampled, visualized, examined microscopically and quantified. A systematic approach to analysis of the fluid in conjunction with the clinical presentation should allow the clinician to diagnose the cause of an effusion.

A definitive diagnosis is provided by the finding of malignant cells or specific organisms in the pleural fluid can be established in approximately 25% of patients.

Pleural effusion remains undiagnosed after routine tests in pleural fluid in many patients. So, we need a simple and safe investigative tool to evaluate undiagnosed effusion.
This study is designed to diagnose the cases of undiagnosed effusions by using Fiberoptic bronchoscope, where pleural fluid analysis and closed pleural biopsy were inconclusive.

Fiberoptic bronchoscopy is seemed to be justified in the diagnostic work-up of pleural effusions of unknown origin, since neoplasm is frequently the cause of a pleural effusion that remains undiagnosed after analysis of pleural fluid and closed pleural biopsy.
AIM OF THE STUDY

To evaluate the diagnostic merits of Fiberoptic bronchoscopy in evaluating the causes of undiagnosed pleural effusion.
REVIEW OF LITERATURE

INTRODUCTION

Pleural fluid accumulates when pleural fluid formation exceeds pleural fluid absorption. Normally fluid enters the pleural space from the capillaries in the parietal pleura and is removed via the lymphatics situated in the parietal pleura. Fluid can also enter the pleural space from the interstitial spaces of the lung via visceral pleura or from peritoneal cavity via small holes in the diaphragm. The lymphatics have the capacity to absorb 20 times more fluid than is normally formed. Accordingly, a pleural effusion may develop when there is excess pleural fluid formation or when there is decreased fluid removal by the lymphatics.

When a patient is found to have a pleural effusion, an effort should be made to determine the cause.

The first step is to determine whether the effusion is a transudate or an exudate. Light’s criteria were used to differentiate exudative pleural effusion from transudative pleural effusion.
Exudative pleural effusions meet at least one of the following criteria, whereas transudative pleural effusions meet none:

- Pleural fluid protein divided by serum protein greater than 0.5
- Pleural fluid LDH divided by serum LDH greater than 0.6
- Pleural fluid LDH greater than two thirds of the upper limit of normal serum LDH.

A transudative pleural effusion occurs when systemic factors that influence the formation and absorption of pleural fluid are altered. The leading causes of transudative pleural effusions are left ventricular failure and cirrhosis. An exudative pleural effusion occurs when local factors that influence the formation and absorption of pleural fluid altered. The leading causes of exudative pleural effusions are Tuberculosis, bacterial pneumonia, malignancy, viral infection, and pulmonary embolism. The primary reason to make this differentiation is that additional diagnostic procedures are indicated with exudative effusions to define the cause of the local disease.

Thoracentesis for pleural fluid analysis and closed pleural biopsy are the two fundamental diagnostic procedures in approaching the underlying entity of a pleural effusion of unknown origin.
However, a significant number of patients still have no definite diagnosis after the above methods.

Fiberoptic bronchoscopy is seemed to be justified in the diagnostic work-up of pleural effusions of unknown origin, since neoplasm is frequently the cause of a pleural effusion that remains undiagnosed after analysis of pleural fluid and closed pleural biopsy(1,2,3).
COMMON CAUSES OF PLEURAL EFFUSION

TRANSUDATIVE PLEURAL EFFUSIONS

Congestive heart failure
Cirrhosis
Nephrotic syndrome
Superior vena caval obstruction
Urinothorax
Peritoneal dialysis Glomerulonephritis
Myxedema
Hypoalbuminemia
Fontan procedure
Cerebrospinal fluid leaks to pleura
Sarcoidosis

EXUDATIVE PLEURAL EFFUSIONS

Neoplastic diseases
Metastatic disease
Mesothelioma

Pyothorax-associated lymphoma

Bacterial infections

Tuberculosis

Fungal infections

Parasitic infections

Viral infections

Pulmonary embolization

Gastrointestinal disease

Heart diseases

Obstetric and gynecologic diseases

Collagen vascular diseases

Drug-induced pleural disease

Asbestos exposure

Sarcoidosis

Hemothorax

Chylothorax
NEEDLE BIOPSY OF THE PLEURA

ABRAM’S NEEDLE

The Abram’s needle consists of three parts: a large outer trocar, an inner cutting cannula, and an inner solid stylet. The end of outer trocar is blunt so that the instrument requires one to make a small scalpel incision in the anesthetized skin and subcutaneous tissue to permit insertion of the biopsy needle without undue force. This incision should be made along the lines of cleavage to minimize postoperative scarring. The inner cutting cannula fits tightly in the outer trocar and can be locked in one of two positions: (a) a closed position, in which the inner cannula obstructs the notch on the outer trocar to make the needle airtight, and (b) an open position, in which the inner cannula is slightly withdrawn so that the notch on the outer trocar is not occluded. An indicator knob in the hexagonal grip of the larger outer trocar indicates the position of the notch in the distal end of the trocar.
INDICATIONS

A needle biopsy of the pleura is currently recommended when tuberculous pleuritis is suspected and the pleural fluid ADA or interferon-gamma levels are not suspected but the pleural fluid cytology is negative and thoracoscopy is not readily available.

With a needle biopsy of the pleura, a small piece of the parietal pleura is obtained for microscopic or microbiologic evaluation. The main diagnoses established with a needle biopsy of the pleura are tuberculous pleuritis and malignancy of the pleura. Currently, needle biopsy of the pleura is used less than in the past because the diagnosis of tuberculous pleuritis can be made by measuring the adenosine deaminase (ADA) or interferon-gamma level in the pleural fluid, and the diagnosis of pleural malignancy is usually established by pleural fluid cytology or thoracoscopy (4).
CONTRAINDICATIONS

The main contraindication to a pleural biopsy is a bleeding diathesis.

Another contraindication to needle biopsies is the presence of an empyema (5). Other contraindications include an uncooperative patient and local cutaneous lesions such as pyoderma or herpes zoster infection.

A pleural biopsy should not be performed in patients who are taking anticoagulants or whose bleeding parameters are prolonged. If the platelet count is below 50,000/mm³, platelet transfusion should be given before the procedure is attempted.

If the patient has borderline respiratory failure, one should hesitate to perform a pleural biopsy because the production of a pneumothorax could precipitate respiratory failure.
TECHNIQUE

When there is a moderate or larger pleural effusion, the biopsy is usually done without image guidance. If the effusion is small or loculated, then either ultrasound or computed tomography (CT) can accurately identify the location of the fluid. Ultrasound is the preferred technique for guiding biopsy because it offers the advantage of a real-time approach to the biopsy and has the added advantages of the absence of ionizing radiation, portability, ready availability and low expense. Because the patient can be imaged in the erect position, the depth of the fluid is maximized, thereby minimizing complications (6).

The patient is positioned, and the site is selected as for diagnostic thoracentesis. The skin is cleaned, and the local anesthetic is administered as for diagnostic thoracentesis. Liberal amounts of lidocaine should be injected once the rib is passed to ensure adequate anesthesia of the parietal pleura. In general, if no fluid is obtained with the local anesthetic, biopsy should not be attempted. When pleural fluid has been obtained with the lidocaine syringe and needle, a pleural biopsy can be performed with an Abram’s needle. A biopsy is sometimes attempted without free pleural fluid. If there is no fluid, the procedure should be performed with ultrasonic or CT guidance.
COMPLICATIONS

Pleural biopsy has the same complications as diagnostic thoracentesis. One might expect pneumothorax to be more common with pleural biopsy than with thoracentesis for two reasons. First, the atmosphere has much more opportunity to be in communication with the pleural space with the biopsy. Second, when the biopsy specimen is obtained, the visceral pleura may be inadvertently incised, leaving a small bronchopleural fistula that can lead to a large pneumothorax. However, the incidence of pneumothorax and the requirement for tube thoracostomy are comparable after thoracentesis and pleural biopsy (7). This is probably because more experienced individuals usually perform the pleural biopsy.

The second major complication of pleural biopsy is bleeding. If an intercostals artery or vein is inadvertently biopsied, a hemothorax can result (8,9). There is one case report of an arteriovenous fistula from an intercostals artery to an intercostals vein developing after pleural biopsy (10).
FIBEROPTIC BRONCHOSCOPY

Since its introduction in 1966 by Ikeda, the flexible bronchoscope has been widely applied to investigate a variety of bronchopulmonary disorders.

The role of fiberoptic bronchoscopy in the investigation of patients who present with a pleural effusion is not well defined. Although the inclusion of bronchoscopy as a part of routine evaluation of all such patients is frequently advocated, evidence to support this is sparse.

Fiberoptic bronchoscopy seems justified in managing unknown pleural effusions based on following reasons:

- Bronchogenic carcinoma is the most common neoplasm that causes a pleural effusion (11,12,13).
Diagnostic yield of pleural fluid cytologic findings or closed pleural biopsy is often unsatisfactory (14,15,16,17).

Before planning of effective management in patients with massive pleural effusions caused by malignancy, bronchogenic carcinoma of a central bronchus, should be excluded first.

INDICATIONS

DIAGNOSTIC

- Malignancy
  
  Diagnosis of bronchogenic carcinoma
  
  Staging of bronchogenic carcinoma
  
  Abnormal sputum cytology
  
  Follow up after treatment of carcinoma

- Mediastinal mass

- Infection
  
  Recurrent or unresolved pneumonia
  
  Infiltrate in immunocompromised patient
  
  Cavitary lesion
• Unexplained lung collapse
• Interstitial lung disease
• Unexplained pleural effusion
• Unexplained chronic cough
• Hemoptysis
• Endotracheal intubation
• Tracheo bronchial stricture and stenosis

**THERAPEUTIC**

• Pulmonary toilet
• Removal foreign bodies
• Insertion of endotrachael tube
• Tamponade for bleeding
• Drainage of abscess
• Stent placement
• Bronchoalveolar lavage
• Aspiration of mediastinal and bronchogenic cysts

• Lobar collapse

CONTRAINDICATIONS

• Un cooperative patient

• Refractory hypoxemia

• Unstable cardiac status

• Bleeding diathesis

• Poorly controlled asthma

• Uremia

• Hypercarbia

COMPLICATIONS

Intraoperative hypoxemia is the most common complication of fiberoptic bronchoscopy. It results from partial airway obstruction from a bronchoscope that is too large, atelectasis due to continuous suctioning from the side port of bronchoscope. Arrhythmias are often associated with severe hypoxemia. The two most important complications of
transbronchial lung biopsy are hemorrhage and pneumothorax. Other complications include laryngospasm, vomiting with associated pulmonary aspiration.

**TUBERCULOUS PLEURAL EFFUSION**

When a tuberculous pleural effusion occurs in the absence of radiologically apparent TB, it may be the sequel to a primary infection 6 to 12 weeks previously or it may represent reactivation TB (18). In industrialized countries, more pleural effusions may be due to reactivation than are due to post primary infection (18). However, in a recent study from San Francisco, pleural TB cases were approximately two times more likely to be clustered than were pulmonary TB and three times more likely to be clustered than non respiratory TB cases (19).

The tuberculous pleural effusion is thought to result from rupture of a subpleural caseous focus in the lung into pleural space (20). Supporting evidence comes from the operative findings of Stead et al (21), who reported that they could demonstrate a caseous tuberculous focus in the lung contiguous with the diseased pleura in 12 to 15 patients with tuberculous pleuritis. The remaining three patients in this series
were found to have parenchymal TB, although these patients did not have caseous foci adjacent the pleura.

It appears that delayed hypersensitivity plays a large role in the pathogenesis of tuberculous pleural effusion. The hypersensitivity reaction is initiated when tuberculous protein gains access to the pleural space.

It is probable that delayed hypersensitivity also plays a large role in the development of tuberculous pleural effusions in humans. The mycobacterial cultures of the pleural fluid from most patients with tuberculous pleural effusions are negative (22,23).

Although delayed hypersensitivity to tuberculous protein is probably responsible for most clinical manifestations of tuberculous pleuritis, many patients when first evaluated have a negative PPD skin test. The explanation for this paradox may be a combination of two factors. First, in some (24), but not in all (25) patients with tuberculous pleuritis, a circulating mononuclear adherent cell suppresses the specifically sensitized circulating T lymphocytes in the peripheral blood. Second, there may be a sequestration of PPD-reactive T lymphocytes in
the pleural space involving both Leu-2(suppressor/cytotoxic) and Leu-3(helper) positive T cells (25).

**MALIGNANT PLEURAL EFFUSION**

Carcinomas of the lung and breast and lymphomas account for approximately 75% of malignant plural effusions. Lung cancer is the leading cause of malignant pleural effusion (26). When patients with lung cancer are first evaluated, approximately 15% have a pleural effusion (27).

Because pleural effusions of unknown origin are frequently caused by malignant tumor, especially bronchogenic carcinoma, fiberoptic bronchoscopy is of value in the diagnostic work-up of a pleural effusion of unknown origin and can be performed to make a diagnosis of malignancy or other entities particularly in those patients who have hemoptysis or concurrent parenchymal infiltrates in the chest x-ray films (28).
Adenocarcinoma of the lung is a form of non-small cell lung cancer. Eighty percent of lung cancers are non-small cell cancers, and of these, about 50% are adenocarcinomas. Adenocarcinoma of the lung begins in the outer parts of the lung, and it can be present for a long time before it is diagnosed. It is the type of lung cancer most commonly seen in women and is often seen in non-smokers. The most common type of
lung cancer in lifelong non-smokers is the adenocarcinoma. This cancer usually is seen peripherally in the lungs, as opposed to small cell lung cancer and squamous cell lung cancer, which both tend to be more centrally located. The adenocarcinoma has an increased incidence in smokers, but is also the most common type of lung cancer seen in non-smokers.

Adenocarcinoma of the lung tends to stain mucin positive as it is derived from the mucus producing glands of the lungs. Similar to other adenocarcinoma, if the tumor is well differentiated (low grading) it will resemble the normal glandular structure. Poorly differentiated adenocarcinoma will not resemble the normal glands (high grade) and will be detected by seeing that they stain positive for mucin (which the glands produce).
SQUAMOUS CELL CARCINOMA

Squamous cell lung cancer is a form of non-small cell lung cancer. Squamous cell lung cancers usually begin in the bronchial tubes (large airways) in the central part of the lungs.

Squamous cell carcinoma cells are large, flattened and stratified with a high cytoplasm to nucleus ratio. Key diagnostic features include the presence of intracytoplasmic keratin which may be linked to the presence of intercellular bridges and squamous pearl formation. Most
squamous cell carcinomas arise centrally within the main, lobar, segmental or subsegmental bronchi but some occur more peripherally. The tumor mass generally extends into the lumen of the airway with invasion into the underlying wall.

SMALL CELL LUNG CARCINOMA

Small cell lung cancer (SCLC) is a tumor of extremes. Untreated, it is one of the most highly virulent malignancies known, with a life expectancy best measured in days to weeks. On the other hand, it displays exquisite chemosensitivity, resulting in partial or complete responses in vast majority of cases. Unfortunately, although many patients can be rendered free of clinical evidence of disease, most quickly relapse and die from this malignancy.

Like all other lung cancers, SCLC is linked to a variety of environmental risk factors. By for the strongest association is with the use of tobacco: Up to 98% of SCLC patients have a history of smoking. Occupational risks for SCLC include exposure to bischloromethyl ethers, nickel, vinyl chloride, asbestos, cadmium, and radon daughters (in uranium miners). Other types of radiation exposure also appear to be
significant risk factors, with an increased incidence of SCLC in atomic bomb survivors and patients (typically those with breast cancer or Hodgkin’s lymphoma) exposed to therapeutic irradiation.

OTHER RELATED STUDIES

The study done by Shi-Chuan Chang, MD, Reury-Perng Perng, MD, PhD on “The Role of Fiberoptic Bronchoscopy in Evaluating the Causes of Pleural Effusions” says, Fiberoptic bronchoscopy is seemed to be justified in the diagnostic work-up of pleural effusions of
unknown origin, since neoplasm is frequently the cause of a pleural effusion that remains undiagnosed after analysis of pleural fluid and closed pleural biopsy (1,2,3). On conclusion of this study, For patients with unknown pleural effusions, Fiberoptic bronchoscopy was more likely to yield a diagnosis than thoracentesis with closed pleural biopsy in those who had hemoptysis or pulmonary abnormality on chest x-ray films, whereas the reverse applied when these features were absent. (Arch Intern Med 1989;Vol-149;855-857).

The study done by R H Poe, P C Levy, R H Israel, C R Ortiz and M C Kallay on “Use of fiberoptic bronchoscopy in the diagnosis of bronchogenic carcinoma. A study in patients with idiopathic pleural effusions.” says Fiberoptic bronchoscopy is justified in patients with malignant effusion and no obvious primary tumor, since up to one third of malignant pleural disease is due to bronchogenic carcinoma (29). They concluded that Fiberoptic bronchoscopy is likely to be helpful and should be done when an isolated effusion is large, in which case the yield approaches that found for patients who presents with hemoptysis or who have infiltrates on chest x-ray films. (CHEST 1994;VOL-105;1663-1667).
The study done by Kim CH, Son JW, Kim GY, Kim JS, Chae SC, Hee J, Kim YJ, Park JY, Jung TH on **“The Role of Bronchoscopy in Determining the Etiology of Pleural Effusion”** had the following results. In 25 cases with unknown etiology after pleural biopsy, additional diagnostic yield by bronchoscopy was 36%(4/11) in patients with associated features and only 7%(1/14) with lone effusion, and, as the sole mean for diagnosis in all patients with pleural effusion, was only 4.5%(5/12). They concluded that, in a region of high prevalence of TB as a cause of pleural effusion, pleural biopsy is more effective method when invasive method is required for confirmative diagnosis of unexplained exudative pleural effusion, and bronchoscopy is unlikely to aid in the diagnosis of lone pleural effusion. *(Tuberc Respir Dis 1998 Apr 45(2):397-403.)*

The study done by Heaton RW, Roberts CM on **“The Role of Fiberoptic bronchoscopy in the investigation of Pleural effusion”** reviewed the case records of 32 patients who had bronchoscopy for undiagnosed pleural effusion, in only 6 patients FOB yielded a diagnosis and in 4 of these the diagnosis was also established by less invasive means. The other 2 had radiographic abnormalities suggestive of bronchial neoplasm. In conclusion of the study, FOB
should be performed only in those patients who have independent clinical evidence suggestive of a bronchial carcinoma. 

(Postgrad Med J 1988;Vol-64:581-2.[IV]).

The review article by, Marios E.Froudarakis on **Diagnostic Work-up of Pleural Effusions** says, when an endotracheal and/or endobronchial lesion is suspected, FOB is indicated (30). After initial work up, pleural effusion of unknown origin is associated with bronchogenic carcinoma in more than 30% of the cases(30,31,32). Also FOB is useful in assessing the extent of the disease in tracheobronchial tree, which is important for treatment and prognosis. (30)
MATERIALS AND METHODS

STUDY DESIGN

This is a Prospective (Observational) study designed to evaluate the role of Fiberoptic bronchoscopy in evaluating causes of undiagnosed pleural effusion.

STUDY CENTER

The study was done at the Department of Thoracic Medicine - Rajiv Gandhi Government General Hospital, Chennai.

STUDY DURATION

January 2011 to September 2011

STUDY POPULATION

Patients with diagnosis of pleural effusion in more than 14 years of age.

Proforma was designed and ethical clearance was obtained. A written informed consent was obtained from all the patients included in the study after explaining in detail the nature and purpose of the study.
INCLUSION CRITERIA

Individuals of more than 14 years of age with diagnosis of pleural effusion.

EXCLUSION CRITERIA

- Refractory hypoxemia
- Bleeding diathesis
- Un co-operative patients
- Patients not willing for scopy
- Cardiac, Renal, and Liver diseases

STUDY PROCEDURE

Patients with the diagnosis of pleural effusion, fulfilling inclusion criteria were admitted in Thoracic Medicine Ward at Rajiv Gandhi Government General Hospital.

Routine blood investigations, Chest skiagram, Sputum for Acid Fast Bacillus, Mantoux test and Pleural fluid analysis were done for all patients.
Pleural fluid was sent for biochemical, microbiological, and cytological analysis.

Informed and written consents were obtained from the patient.

For patients with exudative Pleural effusion to whom initial investigations were inconclusive, pleural biopsy and Fiberoptic bronchoscopy were done under strict aseptic precaution under local anaesthesia and specimen were sent for biochemical, microbiological, cytological and histopathological analysis.

**METHOD OF FIBEROPTIC BRONCHOSCOPY**

Having determined the indication for bronchoscopy, patient was advised to be in nil oral for 4-6 hours on the day of procedure. Patient’s consent was obtained and premedicated with intramuscular Glycopyrrolate injection to reduce the secretions in the airways and to diminish the chance of vasovagal phenomena such as bronchoconstriction and bradycardia. About 30 minutes after premedication the patient was transferred to a couch, made flat, and supported by two pillows only. Topical anaesthesia was given by three methods. First, 4% lidocaine solution was sprayed directly into the
patient’s mouth in the direction of the fauces. Second, To further anaesthetize the cords and upper respiratory tract with about 5 mL of 4% lidocaine solution given by transcutaneous cricothyroid injection. Third, nasal mucosa was anaesthetized with 2% lidocaine gel containing 20mg/mL, 5mL was applied directly from the tube into each nostril.

Having anaesthetized the upper respiratory tract, the shaft of the bronchoscope was well lubricated with 2% lidocaine gel and was advanced into a nostril under direct vision. FOB was passed along the floor of the nose. When the nasal approach was too narrow to permit the bronchoscope to pass, patient was asked to hold a bite block between the teeth or gums and the scope was introduced through oropharynx. As the bronchoscope was advanced, the tip was flexed downwards and epiglottis and larynx came into view. The position and movement of the vocal cords with respiration was noted and vocal cord paralysis confirmed or excluded.

The tip of the bronchoscope was centered with regard to the vocal cords and quickly advanced through the opening during inspiration. Additional 2.5mL aliquots of 2% lidocaine instilled down the suction channel of the bronchoscope, using boluses from 5 mL syringes made up to volume with air in order to allow for the bronchoscope and to
rapidly empty all the local anaesthetic from its channel. After passing through the vocal cords further lidocaine was given through the suction channel as 2% solution. The local anaesthetic action of lidocaine is about 20 minutes and allowance of a safety margin of 1 hour after bronchoscopy is quite long enough, for advising patient to have liquids initially.

Once the carina reached, 2% lidocaine solution was given before entering the major bronchi. Both bronchial tree were thoroughly examined, when intraluminal lesion was found, bronchial wash and bronchoscopic lung biopsy was done whichever was required. Bronchoscopic lung biopsy was preferably done as the last procedure to minimize the cough after biopsy by avoiding subsequent instrumentation that frequently results in cough, thereby reducing the risk of pneumothorax resulting from cough-induced barotrauma.

While taking biopsy, bronchoscope was advanced as far distally as possible, with repeated application of topical anaesthetic as needed to suppress cough. The bronchoscope was then maintained in the wedged position while the biopsy forceps was inserted into the working channel of the scope. After the distal end of the biopsy forceps exited the distal end of the scope, the forceps was further advanced distally until its tip
was beyond bronchoscopic visualization. The biopsy forceps was opened 5-6 mm proximal to the area to be biopsied, advanced to the lesion and then closed. At this point, the patient was asked if any pain was experienced. If the patient indicated pain, the forceps was opened and withdrawn without obtaining biopsy. The biopsy was then attempted in another area.

During withdrawal of the forceps, the bronchoscope was maintained in the wedged position (33,34). Two advantages of this “wedge” technique: one, it maintains the tip of bronchoscope in the optimal position so that more biopsies can be obtained without having to withdraw the bronchoscope to clean the objective lens. Second, if post biopsy bleeding occurs, the wedged position of the bronchoscope limits the bleeding to the biopsied segment or subsegment of the lung.

After the biopsy was completed and the lack of bleeding was confirmed, the bronchoscope was withdrawn proximally and the patient was instructed to cough gently to see if this induces further bleeding. When no further bleeding was observed, the bronchoscopy was fully withdrawn from the airways to terminate the procedure. The obtained biopsy specimen was sent for microbiological and histopathological examination.
RESULTS

We included 110 pleural effusion patients in our study. With initial work up, diagnosis was made in 43 (39.09%) patients. In the remaining 67 patients, 3 patients were not willing for bronchoscopy. Bronchoscopy and Pleural biopsy were done in 64 patients. Out of 64 patients whose diagnosis was not made by initial work up, FOB was useful in making diagnosis in 18 (28.1%) cases. Pleural biopsy helped in diagnosing 26 (40.62%) cases. The results from bronchoscopy and pleural biopsy were analyzed and the results of which were as follows.
AGE & SEX DISTRIBUTION

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</table>

During the study period of 9 months, Pleural biopsy and Fiberoptic bronchoscopy were done in 64 patients [38 males, 26 females] in whom initial diagnostic work up was inconclusive. There was clear male predominance with the incidence more in elder age group, relatively lower in middle age and very low incidence in younger age group.
DIAGNOSIS FROM INITIAL WORK UP

After initial work up [chest skiagram, sputum for AFB, mantoux test, pleural fluid analysis] of pleural effusion in 110 patients, diagnosis was able to make up in 43 patients. Transudative effusion was most commonly diagnosed in 20 patients, followed by tuberculosis (sputum AFB +ve) in 10 patients. Cytology positive for malignant cells and parapneumonic effusion each seen in 5 patients. Pancreatitis was diagnosed in 2 patients and Lymphoma in one patient. Out of 110 patients, initial work up (Chest skiagram, Sputum AFB, Mantoux test, Pleural fluid analysis) itself was able to diagnose in 43 (39.09%) patients.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transudative effusion</td>
<td>20</td>
</tr>
<tr>
<td>Sputum AFB +ve</td>
<td>10</td>
</tr>
<tr>
<td>Cytology +ve for malignant cells</td>
<td>5</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>1</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>2</td>
</tr>
<tr>
<td>Parapneumonic effusion</td>
<td>5</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>43 (39.09%)</strong></td>
</tr>
</tbody>
</table>
**DIAGNOSIS FROM INITIAL WORK UP**

This Pie chart shows the distribution of diagnosis made after initial work up. Most common diagnosis made was Transudative pleural effusion followed by Pulmonary Tuberculosis and then by Malignancy and Parapneumonic effusion.
Total Study population in our study was 110 patients. With Initial work up, diagnosis was made in 43 (39.09%) patients. In the remaining 67 patients, 3 patients were not willing for bronchoscopy. Bronchoscopy was done in 64 patients, where as Pleural Biopsy was done in 54 patients. Pleural Biopsy was not done in 10 patients in whom initial work up was inconclusive, because of minimal plural effusion.

**PLEURAL BIOPSY**

Out of 67 patients in whom initial work up was inconclusive, Pleural biopsy was done in 54 patients after obtaining informed written consent. Pleural biopsy was not done in rest of patients because of minimal pleural effusion. Pleural biopsy was diagnostic in 26 (40.62%) patients. Most common diagnosis made was Tuberculosis in 18 patients followed by Adenocarcinoma in 5 patients, and then by Metastatic carcinoma, Squamous cell carcinoma, and Small cell carcinoma each in one patient.
### PLEURAL BIOPSY

<table>
<thead>
<tr>
<th>DIAGNOSIS</th>
<th>NUMBER</th>
</tr>
</thead>
<tbody>
<tr>
<td>TUBERCULOSIS</td>
<td>18</td>
</tr>
<tr>
<td>METASTATIC CARCINOMA</td>
<td>1</td>
</tr>
<tr>
<td>ADENOCARCINOMA</td>
<td>5</td>
</tr>
<tr>
<td>SQUAMOUS CELL CARCINOMA</td>
<td>1</td>
</tr>
<tr>
<td>SMALL CELL CARCINOMA</td>
<td>1</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>26 (40.62%)</strong></td>
</tr>
</tbody>
</table>

#### Results of Pneural Biopsy

![Bar chart showing the distribution of diagnoses](chart.png)

- **Tuberculosis**: 18 cases
- **Metastatic carcinoma**: 1 case
- **Adenocarcinoma**: 5 cases
- **Squamous cell carcinoma**: 1 case
- **Small cell carcinoma**: 1 case
FOB OBSERVATIONS AND RESULTS

Out of 67 patients in whom initial work up was inconclusive, 3 patients were not willing for Bronchoscopy. FOB was done in rest of 64 patients after obtaining informed written consent. Findings observed in bronchoscopy were Erythema, Nodularity/Sessile lesion, Polypoidal lesion, External compression. FOB was normal in 25 patients. Erythema was seen in 5 patients, but none of them showed positive results. Nodularity/Sessile lesion was seen in 16 patients, out of them 10 patients showed positive results. In those 10 patients, 9 were diagnosed as Malignancy and 1 as Endobronchial Tuberculosis. Polypoidal lesion was seen in 5 patients, all of them showed positive results as Malignancy. External compression was seen in 13 patients, out of them 3 patients showed positive results as Endobronchial Tuberculosis. Totally, FOB was able to diagnose 18 cases (28.1%) out of 64 patients in whom initial work up was inconclusive.
## FOB OBSERVATIONS AND RESULTS

<table>
<thead>
<tr>
<th>Findings</th>
<th>Number</th>
<th>Positive results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td>Erythema</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Nodularity/sessile lesion</td>
<td>16</td>
<td>10</td>
</tr>
<tr>
<td>Polyoidal growth</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>External compression</td>
<td>13</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>64</td>
<td>18 (28.1%)</td>
</tr>
</tbody>
</table>

### No. of Patients

![Bar chart showing FOB findings and their counts](chart.png)

- **No of cases**
- **Positive results**
SUBTYPES OF MALIGNANCY

Out of 18 cases that were diagnosed from FOB, 14 cases diagnosed as Malignancy and 4 cases as Endobronchial Tuberculosis. In Malignancy, Squamous cell carcinoma was most commonly diagnosed in 6 cases, followed by Small cell carcinoma in 5 cases, and then by Adenocarcinoma in 3 cases.

<table>
<thead>
<tr>
<th>Type</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squamous cell Carcinoma</td>
<td>6</td>
</tr>
<tr>
<td>Small cell carcinoma</td>
<td>5</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>14</strong></td>
</tr>
</tbody>
</table>

![Graph showing the distribution of subtype of malignancy]
RESULTS BRONCHOSCOPY AS PER AGE DISTRIBUTION

We analyzed the bronchoscopy results based on age distribution in our study. In patients of more than 50 years age group, bronchoscopy is diagnostic in 13 patients out of 43 patients. Out of them 12 patients were diagnosed as malignancy and one patient as Tuberculosis. In patients of below 50 years age group, bronchoscopy is diagnostic in 5 patients out of 18 patients. Out of them 2 patients were diagnosed as malignancy and 3 patients as Tuberculosis.

<table>
<thead>
<tr>
<th>Age [in yrs]</th>
<th>Bronchoscopy</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-diagnostic</td>
<td>Diagnostic</td>
</tr>
<tr>
<td>&lt; or = 25</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>26-50</td>
<td>13</td>
<td>5</td>
</tr>
<tr>
<td>&gt;50</td>
<td>30</td>
<td>13</td>
</tr>
<tr>
<td>Total</td>
<td>46</td>
<td>18</td>
</tr>
</tbody>
</table>
RESULTS OF FIBEROPTIC BRONCHOSCOPY AS PER AGE DISTRIBUTION

RESULTS OF BRONCHOSCOPY AND PLEURAL FLUID EXAMINATION IN PATIENTS CLASSIFIED BY HEMOPTYSIS

We analyzed the study patients in whom initial work up was inconclusive, based on clinical history of hemoptysis. Hemoptysis was present in 26 patients and absent in 38 patients. The yield from Bronchoscopy was more in patients with hemoptysis. The yield from Pleural fluid examination was more in patients who had no hemoptysis.
RESULTS OF BRONCHOSCOPY AND PLEURAL FLUID EXAMINATION IN PATIENTS CLASSIFIED BY HEMOPTYSIS.

<table>
<thead>
<tr>
<th>Hemoptysis</th>
<th>No</th>
<th>Br. Wash (or) Biospy</th>
<th>Pleural fluid examination</th>
<th>P- Value</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>26</td>
<td>13</td>
<td>8</td>
<td>0.000&lt;0.05</td>
<td>Student t test</td>
</tr>
<tr>
<td>Absent</td>
<td>38</td>
<td>5</td>
<td>18</td>
<td>0.000 &lt; 0.05</td>
<td></td>
</tr>
</tbody>
</table>

![Bar chart showing the number of patients with hemoptysis present and absent, and the results of bronchoscopy and pleural fluid examination.](image)
RESULTS OF BRONCHOSCOPY AND PLEURAL FLUID EXAMINATION IN PATIENTS CLASSIFIED BY RADIOLOGIC PATTERN

Apart from hemoptysis we also analyzed the study patients based on radiologic pattern, as those who presented only with pleural effusion in 42 patients, and those with pleural effusion and parenchymal abnormality in 22 patients. The yield from Bronchoscopy was more in patients who presented with both Pleural effusion and Parenchymal abnormality. The yield from Pleural fluid examination was more in patients who presented only with Pleural effusion.
RESULTS OF BRONCHOSCOPY AND PLEURAL FLUID EXAMINATION IN PATIENTS CLASSIFIED BY RADIOLOGIC PATTERN

<table>
<thead>
<tr>
<th>Radiologic Pattern</th>
<th>No</th>
<th>Br. Wash (or) Biopsy</th>
<th>Pleural fluid examination</th>
<th>P- Value</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Only Pleural effusion</td>
<td>42</td>
<td>4</td>
<td>19</td>
<td>0.000&lt;0.05</td>
<td>Student t test</td>
</tr>
<tr>
<td>Pleural Effusion + Parenchymal Abnormality</td>
<td>22</td>
<td>14</td>
<td>7</td>
<td>0.000 &lt; 0.05</td>
<td></td>
</tr>
</tbody>
</table>
DISCUSSION

In 19 to 25% of patients, the cause of pleural effusion remains unexplained after pleural fluid analysis and pleural biopsy (35,36). Fiberoptic Bronchoscopy is a useful tool in these patients of unexplained pleural effusion.

Chang et al (28) performed Bronchoscopy, Thoracentesis and Pleural biopsy on 140 consecutive patients with pleural effusion. In the patient group with an isolated pleural effusion, with no hemoptysis or pulmonary abnormality on the chest radiograph, the yield from bronchoscopy was 16% whereas pleural investigation yielded a positive diagnosis in 61%. In the patient group of pleural effusion with hemoptysis or pulmonary abnormality, the yield from bronchoscopy was more than 70% whereas the yield from pleural investigation was less than 35%.

Williams et al (37) evaluated the role of FOB in 28 patients with pleural effusion of undetermined etiology. In this group, 4 patients had a diagnostic FOB, 3 for malignancy and one for tuberculosis. They concluded that FOB was of value in the evaluation of patients with undiagnosed pleural effusion.
In our study, Out of 64 patients whose diagnosis was not made by initial work up, FOB was useful in making diagnosis in 18 (28.1%) cases (p value- 0.000<0.005). Pleural biopsy helped in diagnosing 26 (40.62%) cases (p value- 0.000<0.005).

Pleural biopsy is particularly important for diagnosing tuberculosis but will also slightly increase the yield for malignancy (38,39,40).

For patients with exudative effusion still undiagnosed after pleural fluid examination and with parenchymal abnormalities on chest radiograph or with hemoptysis, Fiberoptic bronchoscopy is a useful next step (28).

When combining Initial work up, Pleural biopsy, and Fiberoptic Bronchoscopy in our study, 87 patients (79.09%) were diagnosed out of 110 patients.
CONCLUSION

1. Pleural effusion of unknown origin both hemorrhagic and non-hemorrhagic, are frequently encountered in tertiary care centre even after completion of exhaustive work-up.

2. Fiberoptic bronchoscopy is useful in the diagnosis of pleural effusion, where at the end of usual diagnostic work-up, no etiological diagnosis was arrived at.

3. In pleural effusion of unknown origin especially in the more than 50 years age group, the contribution of Fiberoptic bronchoscopy in reaching a diagnosis of malignancy is significant.

4. In below 50 years age group with undiagnosed pleural effusion, the contribution of Fiberoptic bronchoscopy in diagnosing non malignant causes like Tuberculosis is significant.

5. Hence, In patients with exudative pleural effusion still undiagnosed after pleural fluid cytology and with parenchymal abnormalities on chest skiagram or with history of hemoptysis, Fiberoptic bronchoscopy is a useful procedure for arriving at a diagnosis.
BIBLIOGRAPHY


CERTIFICATE OF APPROVAL

To

Dr. K. Anbananthan
PG in MD TB&RD
Madras Medical College, Chennai -3.

Dear Dr. K. Anbananthan

The Institutional Ethics Committee of Madras Medical College reviewed and discussed your application for approval of the proposal entitled “The Role of Fiberoptic bronchoscopy in evaluating the causes of undiagnosed pleural effusion” No. 36022011.

The following members of Ethics Committee were present in the meeting held on 17.02.2011 conducted at Madras Medical College, Chennai -3.

1. Prof. S.K. Rajan, MD
2. Prof. A. Sundaram, MD
   Dean i/c, Madras Medical College, Chennai -3
3. Prof R. Sathianathan
   Director, Institute of Psychiatry, MMC,Ch-3
4. Prof R. Nandhini, MD
   Director, Institute of Pharmacology, MMC, Ch-3
5. Prof. Pregna B. Dolia MD
   Director, Institute of Biochemistry, MMC, Ch-3
6. Prof. C. Rajendiran ,MD
   Director, Institute of Internal Medicine, MMC, Ch-3
7. Prof. Geetha Subramanian, MD,DM
   Prof. & Head , Dept. of Cardiology, MMC, Ch-3
8. Thiru. A. Ulaganathan
   Administrative Officer, MMC, Chennai -3
9. Thiru. S. Govindasamy . BA,BL
10. Tmt. Arnold Souling

We approve the proposal to be conducted in its presented form.

Sd /s. Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee
INFORMATION SHEET

► We are conducting a prospective study of “The Role of Fiberoptic bronchoscopy in evaluating the causes of undiagnosed pleural effusion” at Department of Thoracic Medicine, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai.

► The purpose of the study is to evaluate the diagnostic merit of fiberoptic bronchoscopy in evaluating the causes of pleural effusion.

► The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

► Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

► The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of investigator  Signature of participant

Date:
PATIENT CONSENT FORM

Study Details   :   "The Role of Fiberoptic bronchoscopy in evaluating the causes of undiagnosed pleural effusion” at Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai

Study Centre   :   Department of Thoracic Medicine, Madras Medical College, Chennai.

Patient may check (✓) these boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction.

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms.

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological tests.

I hereby consent to participate in this study.

Signature/ Thumb Impression:

Patient Name and Address:       Place     Date

Signature of Investigator

Study Investigator's Name:       Place     Date
PROFORMA

Name of the Patient :

Age : Sex : Date :

Presenting Complaints :

Cough with Expectoration
Chest Pain
Breathlessness
Fever
Loss of Weight
Loss of Appetite
Difficulty in Swallowing
Hoarseness of Voice

Past H/O

H/o Prior ATT / Contact with TB
H/o DM / Hypertension / CAD

Personal H/O

H/O Smoking
H/O Alcoholism

Investigations :

i. Chest x ray findings

ii. Mantoux Test
iii. Sputum AFB results
iv. Complete Blood Count
v. Renal Function tests
vi. Liver Function tests

**Pleural Fluid Analysis:**

i. Sugar
   Protein
   LDH
ii. AFB
iii. Cytology
iv. Cell Count
v. NT C/S

**Pleural Biopsy**

**Bronchoscopy Findings:**

**Bronchial Wash:**

i. Cytology
ii. AFB
iii. NT C/S
iv. Cell Count
v. Fungal Smear

**Bronchial Biopsy:**