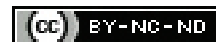


# Diagnostic Value of Medical Thoracoscopy- A Retrospective Analysis

BINU KRISHNAN<sup>1</sup>, SONISH KRISHNAN<sup>2</sup>, PRIYA SHANMUGHARAJ<sup>3</sup>

## ABSTRACT

**Introduction:** Clinical and radiological parameters might not be sufficient to diagnose the aetiology of exudative pleural effusions accurately. Often, thoracoscopy serve as an important added tool in the correct diagnosis.

**Aim:** To analyse the diagnostic accuracy of initial diagnosis (clinical and radiological) compared with thoracoscopic biopsy.

**Materials and Methods:** This was the retrospective study done on all the consecutive medical thoracoscopic procedures conducted in tertiary care centre (pulmonology wing), Trivandrum, India from May 2010 to April 2016. All thoracoscopic procedures were conducted in adult patients above the age of 18 years. Kappa statistics was performed to find the diagnostic accuracy.

**Results:** During this period, 94 diagnostic medical thoracoscopic procedures were performed. Majority of them were males (68.1%) and mean age was 54.8±13.53 years. Main diagnostic indications were undiagnosed exudative effusions (85.4%) and emphysema (7.1%). Tuberculosis was the most common

initial diagnosis prior to the procedure (70.2%). Histopathology reports showed tuberculosis as the most common final diagnosis (45.7%), followed by malignancy (38%) and chronic inflammation (6.4%). Four patients who were not biopsied were excluded from diagnostic accuracy analysis. When thoracoscopic biopsy was taken as the gold standard, sensitivity was found to be 67.4% for initial diagnosis of tuberculosis and only 13.9% for malignancy. But specificity was found to be more for malignancy (81.5%) than tuberculosis (27.7%). Overall diagnostic accuracy of initial diagnosis was found to be 46.7% for tuberculosis and 54.4% for malignancy. There was minimal or no correlation ( $R=-0.173$ ) between the diagnostic outcome and type of anaesthesia (local or general anaesthesia). There was no significant difference in occurrence of complications between local and general anaesthesia ( $p$ -value=0.717).

**Conclusion:** Medical thoracoscopy had an important additional diagnostic value in management of pleural diseases as evidenced by slight agreement between initial and final diagnosis.

**Keywords:** Malignancy, Pleural effusion, Pneumothorax, Tuberculosis

## INTRODUCTION

Medical thoracoscopy is a widely accepted procedure in the management of exudative pleural effusion. It serves as an important tool for obtaining the correct aetiology in effusions. The procedure is used as an important parameter to distinguish between benign and malignant conditions. Also, it is used to subclassify malignancies [1]. In India, there are only a few centres performing this procedure as part of evaluation of pleural and peripheral lung pathologies. Hence, reliable data regarding the aetiology of exudative pleural effusion is lacking [1-3].

Due to limited availability of thoracoscopy, diagnosis is often based on clinical and radiological profile of the patients. Almost all the currently available parameters have poor sensitivity and specificity in detecting the correct aetiology. Clinicians find it difficult to proceed further after the routine initial analysis is complete. The diagnostic dilemma of tuberculosis versus malignancy is a common crisis in day to day practice [1].

Many a time, it has been practice to start empirical anti-tuberculosis therapy in undiagnosed pleural effusions. This practice in itself has no scientific back-up. Often, these exudative effusions may turn out to be malignancy at a later stage. Such patients run the risk of late diagnosis and may have limited treatment options at that time [2,4-6]. Also, the unwanted toxicity due to various anti-tuberculosis medications is yet another preventable mishap. If there was a provision for doing thoracoscopic biopsy in such scenario, it would definitely have added more value in finding the appropriate aetiology. So, author had found that there exist a clear gap between the current actual practice and correct diagnosis.

In order to address these shortcomings, we tried to retrospectively analyse the diagnostic accuracy of current practice (clinical and

radiologic diagnosis) when compared with thoracoscopic biopsy as the gold standard. Thus, we would be able to identify the probable additional value of including thoracoscopic biopsy into our diagnostic algorithm.

### Objectives:

- To determine the diagnostic accuracy of initial diagnosis (clinical and radiological) when thoracoscopic biopsy is considered as the gold standard.
- To identify the difference in diagnostic outcome between thoracoscopy done under local and general anaesthesia.
- To identify the difference in complications between local and general anaesthesia procedures.

## MATERIALS AND METHODS

Retrospective analysis of all consecutive medical thoracoscopic procedures was conducted in tertiary care centre (pulmonology wing) of PRS Hospital, Trivandrum, Kerala, India from May 2010 to April 2016. Medical Thoracoscopy programme was started in May 2010 in the institution. This human study was approved by Institutional Ethics Committee- PRS Hospital (PRSH/IEC/2020/DR/BK-54) and informed consent was taken from the participants.

The medical records of all consecutive medical thoracoscopies during January 2021 were analysed in detail. All thoracoscopic procedures were conducted with rigid thoracoscope (Karl Storz). Thoracoscopy is a procedure used to visualise the space inside the chest wall. In present study, this is done with a rigid thoracoscope with light source and camera and was visualised on a screen. The tube was inserted into the intercostal space through a small nick given after appropriate anaesthesia. Ninety-four thoracoscopic

procedures were performed in adult patients above the age of eighteen years.

**Inclusion criteria:** Adult patients above the age of 18 years and in which diagnostic thoracoscopic procedures were done were included. Patients, whose specific biopsy medical records were present were included.

**Exclusion criteria:** Patients with therapeutic procedures (namely pleurodesis) were excluded from the study. Transudative pleural effusions patients were also excluded.

## Parameters

**Body Mass Index (BMI)** of more than 30 was considered as obese (according to World Health Organisation (WHO) general population BMI classification) [7].

**Dyspnoea** was classified according to Modified Medical Research Council grading system with grade 2 indicating that the person walked at a slow pace than contemporaries on a level ground [8].

**Initial Diagnosis** is the diagnosis recorded before performing medical thoracoscopy. This diagnosis was obtained after considering both clinical and radiological profile of all patients. If more than one diagnosis were recorded as differentials, then the first mentioned one was considered as the initial clinical diagnosis (assuming that they were mentioned in the order of descending probability).

**Diagnostic Indications** included recurrent exudative effusion, emphysema, recurrent pneumothorax, interstitial lung disease, chronic liver disease, chronic kidney disease and peripheral lung lesion. Recurrent effusion was defined as those which were aspirated on more than two occasions. Pleural fluid Acid Fast Bacilli (AFB) smear and Polymerase Chain Reaction (PCR) for Mycobacterium tuberculosis were negative in all these samples. Pleural fluid cytology for malignant cells was inconclusive for at least two occasions. Exudative effusion was defined as per Modified Lights criteria [9].

**Final Diagnosis** is the diagnosis obtained after thoracoscopic procedure. Final diagnosis which were mentioned as acute inflammation, chronic inflammation or not biopsied were excluded from 'specific biopsy result' category.

**Complications** mentioned in the medical records during the course of hospital stay were pain, bleeding, subcutaneous emphysema, anaemia.

**Anaesthesia** Wherever possible, local anaesthesia was the preferred option due to lower length of hospital stay. Common indications for general anaesthesia included were patients already mechanically ventilated prior to the procedure and those who preferred for general anaesthesia.

## STATISTICAL ANALYSIS

Categorical and quantitative variables were expressed as frequency (percentage) and mean±SD, respectively. Diagnostic test evaluation such as sensitivity, specificity, positive and negative predictive values and accuracy were used to find the diagnostic accuracy of initial diagnosis. Kappa statistics was performed to find the diagnostic accuracy of initial diagnosis and biopsy. Chi-square test was used to determine association between categorical variables. For all statistical interpretations, p<0.05 was considered the threshold for statistical significance. The data were entered into Microsoft Excel 2013 and statistical analyses were performed by using Statistical Package for Social Sciences (SPSS) version 20.0.

## RESULTS

During the six year period, 94 diagnostic thoracoscopic procedures were performed using the rigid scope. Males constituted the majority. Sixty four (68.1%) of them were males and 30 (31.9%) being females. Mean age was 54.8±13.53 (Range: 22-80 years). Maximum number of patients (32, 34%) were in the 51-60 years age group category. Chronic Obstructive Pulmonary Disease (COPD) (8.5%), Coronary

artery disease (9.6%), diabetes mellitus (16%) and hypertension (13.8%) were the important co-morbidities [Table/Fig-1].

Characteristics	Frequency (N)	Percentages (%)
<b>Age range (in years)</b>		
21-30	5	5.31
31-40	9	9.57
41-50	18	19.14
51-60	32	34.04
61-70	19	20.21
71-80	11	11.70
Gender (Male)	64	68.1
Smoker	51	54.3
<b>Body mass index</b>		
>30	12	12.8
<30	82	87.2
<b>Co-morbidities</b>		
Dyspnoea mMRC grade (>2)	16	17.0
Diabetes mellitus	15	16.0
Hypertension	13	13.8
Chronic Obstructive Pulmonary Disease (COPD)	8	8.5
Coronary artery disease	9	9.6
Chronic liver disease	2	2.1
Chronic kidney disease	1	1.1

[Table/Fig-1]: Baseline characteristics (N=94).

**Diagnostic indications:** The major diagnostic indication was recurrent exudative effusion (85.1%) [Table/Fig-2]. The other common indication was evaluation of empyema which constituted 7.4%. Two patients with recurrent pneumothorax were subjected to thoracoscopy as part of their diagnostic work-up. One patient with interstitial lung disease was subjected to this procedure because of peripheral predominance of lesions on high resolution CT scan of thorax. Two patients with chronic liver disease and one patient with chronic kidney disease were evaluated for any associated tuberculosis aetiology.

Indications	Frequency (N)	Percentages (%)
Effusion	80	85.1
Emphysema	7	7.4
Pneumothorax	2	2.1
Peripheral lesion	1	1.1
Chronic kidney disease	1	1.1
Chronic liver disease	2	2.1
Interstitial lung diseases	1	1.1

[Table/Fig-2]: Percentage distribution of the sample according to indications.

**Initial diagnosis:** Most of the patients (70.2%) had a provisional diagnosis of tuberculosis prior to the procedure. Malignancy was thought to be the probable diagnosis in only 16% of patients. Other bacterial infections were supposed to be in 12.8% and interstitial lung disease in one of the patients [Table/Fig-3].

Initial diagnosis	Frequency (N)	Percentages (%)
Tuberculosis	66	70.2
Malignancy	15	16.0
Other bacterial	12	12.8
Interstitial lung diseases	1	1.1

[Table/Fig-3]: Percentage distribution of the sample according to initial diagnosis.

**Biopsy results:** Of all patients subjected to diagnostic work-up, four patients were not biopsied. These included two patients with chronic liver disease, one with chronic kidney disease and one

case of recurrent pneumothorax. This was because no obvious anomalies were detected in pleura and lung during the thoracoscopic procedure. So, they were excluded from the biopsy analysis.

Histopathology results showed that tuberculosis was the most common diagnosis. Of the 94 diagnostic procedures, 43 (45.7%) of them turned out to be of tuberculosis aetiology. This was closely followed by malignancy in 36 (38.3%) cases. Out of seven cases with empyema, biopsy was reported as necrotising lesion in three of them. Biopsy result in one case of unilateral recurrent haemothorax came as cavernous haemangioma of the lung which is a very rare entity. Six patients had a diagnosis of chronic inflammation. Out of these six patients, three of them had initial diagnosis of other bacterial infection, two as tuberculosis and one with provisional diagnosis of interstitial lung disease. Biopsy report of one patient came as acute inflammation. This patient presented with recurrent exudative effusion and bacterial infection was thought to be the clinical diagnosis [Table/Fig-4].

Biopsy diagnosis	Frequency (N)	Percentages (%)
Tuberculosis	43	45.7
Malignancy	36	38.3
Others	11	
Necrotising lesion	3	3.2
Chronic inflammation	6	6.4
Acute inflammation	1	1.1
Cavernous haemangioma	1	1.1
Not biopsy	4	4.3

[Table/Fig-4]: Percentage distribution of the sample according to biopsy diagnosis.

Of those 36 malignancies, 29 (80.5%) were reported as adenocarcinoma followed by metastasis in 6 (16.7%) cases. One patient was diagnosed to have malignant mesothelioma.

For the purpose of accurate analysis of initial diagnosis, all patients who underwent biopsy were included. Hence, four patients were excluded from that analysis. Apart from tuberculosis and malignancy, all other diagnosis was considered under the subgroup others. Sensitivity was found to be 67.4% for initial diagnosis of tuberculosis and only 13.9% for malignancy. But specificity was found to be more for malignancy (81.5%) than tuberculosis (27.7%). Overall diagnostic accuracy of initial diagnosis (clinical and radiological) was found to be 46.7% for tuberculosis and 54.4% for malignancy [Table/Fig-5,6].

Clinical diagnosis	Biopsy diagnosis			
	TB	Malignancy	Others	Total
Tuberculosis	29	31	3	63
Malignancy	10	5	0	15
Others	4	0	8	12
Total	43	36	11	90

[Table/Fig-5]: Diagnosis accuracy of clinical diagnosis when biopsy diagnosis is gold standard.

Kappa: 0.08; p-value=0.236; Slight agreement

Variables	Tuberculosis (%)	Malignancy (%)
Sensitivity	67.4	13.9
Specificity	27.7	81.5
False negative	32.6	86.1
False positive	72.3	18.5
Positive predictive value	46.0	33.3
Negative predictive value	48.1	58.7
Positive likelihood ratio	0.93	0.75
Negative likelihood ratio	1.18	1.06
Accuracy	46.7	54.4

[Table/Fig-6]: Measures of diagnostic accuracy of initial diagnosis.

**Local versus general anaesthesia:** Majority of procedures were done under local anaesthesia. A total of 73 procedures (77.7%) were done with local anaesthesia. The remaining 21 patients (22.3%) were subjected to general anaesthesia. Correlation has been calculated between the final diagnosis and type of anaesthesia. This was done to identify whether general or local anaesthesia was better in determining the diagnosis after thoracoscopy. Results in the [Table/Fig-7,8] showed that Pearson's correlation coefficient is -0.17, indicating that there was minimal or no correlation between the diagnostic outcome and type of anaesthesia.

Biopsy diagnosis		Anaesthesia	
		Local	General
TB	Frequency (n)	33	10
	Percentages (%)	76.7	23.3
Malignancy	Frequency (n)	25	11
	Percentages (%)	69.4	30.6
Necrotising lesion	Frequency (n)	3	0
	Percentages (%)	100	0
Chronic inflammation	Frequency (n)	6	0
	Percentages (%)	100	0
Acute inflammation	Frequency (n)	1	0
	Percentages (%)	100	0
Cavernous haemangioma	Frequency (n)	1	0
	Percentages (%)	100	0
Not Biopsy	Frequency (n)	4	0
	Percentages (%)	100	0
Total	Frequency (n)	73	21
	Percentages (%)	77.7	22.3

[Table/Fig-7]: Biopsy diagnosis and type of anaesthesia.

Symmetric measures					
Parameters		Value	Asymp. std. error <sup>a</sup>	Approx. T <sup>b</sup>	Approx. Sig.
Interval by interval	Pearson's R	-0.173	0.050	-1.688	0.095 <sup>c</sup>
Ordinal by ordinal	Spearman correlation	-0.103	0.089	-0.996	0.322 <sup>c</sup>
N of valid cases		94			

a. Not assuming the null hypothesis.

b. Using the asymptotic standard error assuming the null hypothesis.

c. Based on normal approximation.

[Table/Fig-8]: Correlation between biopsy diagnosis and type of anaesthesia.

**Complications:** Main complication was post procedure pain which occurred in 16 (17%) patients and subsided with oral or parenteral pain relievers. Bleeding alone was noted in 3 (3.2%) of procedures and bleeding followed by anaemia was present in 3 (3.2%) [Table/Fig-9]. Subcutaneous emphysema was noted in two patients upon removal of intercostal drainage tube. These patients were managed in intensive care with reinsertion of intercostal drainage tube. Subsequently, high resolution CT scan was done before removing the tube again, to ensure complete absence of air leakage. For both local as well as general anaesthesia, it was found that there was no significant difference in the number of complications (p-value=0.717) [Table/Fig-10].

Complications	Frequency (n)	Percentages (%)
Pain	16	17
Bleeding	3	3.2
Subcutaneous emphysema	2	2.1
Bleeding+Anaemia	3	3.2
Total	24	25

[Table/Fig-9]: Complications of thoracoscopy.

Complications	Local		General		Chi-square ( $\chi^2$ )	p-value
	Frequency (n)	Percentages (%)	Frequency (n)	Percentages (%)		
Absent	55	75.3	15	71.4	0.13	0.717
Present	18	24.7	6	28.6		

[Table/Fig -10]: Comparison of complications based on anaesthesia.

## DISCUSSION

To the best of our knowledge, this is one of the premier studies from India estimating the relation between initial diagnosis and final definitive diagnosis after rigid thoracoscopy. Even though retrospective in nature, we were able to analyse the data of 94 patients who underwent thoracoscopy in our institution.

In their retrospective study, Kho SS et al., analysed the diagnostic yield of medical thoracoscopy in exudative pleural effusions in regions where tuberculosis burden was high [10]. They concluded that medical thoracoscopy had a sensitivity of 89.1%, specificity of 100% and Positive Predictive Value (PPV) of 100% and Negative Predictive Value (NPV) of 92.1% in the diagnosis of malignant pleural effusions. With regards to tuberculosis, medical thoracoscopy had a sensitivity of 90.5%, specificity of 100%, PPV of 100% and NPV of 93.9%. Overall complication rate for the procedure was 3.3%. They concluded that thoracoscopy had excellent sensitivity and specificity in the diagnosis of exudative pleural effusion in that region. Further, it reduced the need for empirical therapy by providing histological evidence of disease when initial non invasive investigations were inconclusive. In the present study, the sensitivity of initial diagnosis was only 67.4% and 13.9% for tuberculosis and malignancy respectively, while specificity was 27.7% and 81.5% for the same.

Murthy V et al., reviewed the role of medical thoracoscopy and its evolving role in the diagnosis and treatment of pleural disease [3]. They suggested that the excellent yield and favourable safety profile of medical thoracoscopy had led to it replacing closed pleural biopsy for many indications, particularly in the management of suspected malignant pleural effusions. There was an increased appreciation for its important role alongside percutaneous and surgical approaches in the diagnosis of pleural diseases.

Males constituted a significant majority in the present study- 70% vs 30%. This is in tune with the prevalence of tuberculosis and lung and pleural malignancy which is more common among males in India [2]. A retrospective study was conducted by Gong L et al., regarding the usefulness of medical thoracoscopy in the management of exudative pleural effusions [11]. They concluded that medical thoracoscopy had high feasibility and accuracy in the diagnosis of exudative pleural effusion and should be routinely recommended in clinical management of exudative pleural effusion. The main indication for diagnostic thoracoscopy in the present study was undiagnosed recurrent exudative pleural effusion which is consistent with available international literature [1,12]. Interstitial lung disease was also subjected to diagnostic evaluation. It signified that in future, this modality could be useful in the work-up of interstitial lung diseases especially while dealing with a peripheral distribution pattern. Also, peripheral lung lesions could be assessed with medical thoracoscopy when other methods turned out to be inconclusive.

According to Jany B and Welte T, pleural effusion had a wide differential diagnosis ranging from congestive heart failure, cancer, pneumonia, and pulmonary embolism [2]. A delayed etiological diagnosis could be associated with markedly higher morbidity and mortality. The present study pointed out that the major cause of recurrent exudative effusion in India is tuberculosis. This is in sharp contrast to the available western literature which depicts malignancy as the primary aetiology [2]. Given that tuberculosis is endemic in India, the result may not be surprising at all. Malignancy came out to be the second common cause.

When biopsy was considered as the gold standard, diagnostic accuracy of initial diagnosis was found to be 46.7% for tuberculosis and 54.4% for malignancy. Also, sensitivity of clinical diagnosis was very low for malignancy. The study showed that there is only minimal correlation between initial clinical diagnosis and the final biopsy results. This conclusion has important clinical ramifications. Because of the endemic nature of tuberculosis, it is a common practice to start anti tuberculosis treatment in undiagnosed pleural effusion. By this unscientific practice, author may be subjecting many potential malignancies to delayed diagnosis and subsequent limited treatment options [13]. Also, the toxic effects of anti tuberculosis medications may add on to the misery. These results further strengthen the inference that treatment should be initiated only after biopsy confirmation in recurrent exudative effusions. According to Casalini AG et al., thorascopic biopsy greatly increased the diagnostic accuracy in pleural tuberculosis [14]. In their retrospective analysis of 52 patients, they found that the diagnostic yield of the microbiological tests on pleural fluid was only 17.3%. Without pleural biopsy, a diagnosis would have been reached in only 15 out of 52 patients (28.6%). They concluded that in the majority of patients, a diagnosis could be reached only with pleural biopsy.

No difference in diagnostic outcome was observed between thoracoscopy done under local and general anaesthesia. So, it is evident that medical thoracoscopy can be done even under local anaesthesia wherever feasible. This in turn reduces the resource utilisation in terms of manpower, machinery and cost.

Eighty two patients were analysed in a retrospective study by Gong L et al., [11]. They reported that five cases (6.09%) had pain, three cases (3.65%) had subcutaneous emphysema, and one case (1.21%) had bleeding as side-effects during the procedure [11]. In another study by Wan YY et al., it was reported that pain (38.9%) and fever (20.8%) were the most common complications during medical thoracoscopy [15]. They inferred that medical thoracoscopy was generally a safe and effective method in the diagnosis of undiagnosed pleural effusions and management of pleural diseases. In the present study, out of the 25% patients who experienced some forms of complications, no life threatening events were noted. Postoperative pain was the most common complication and could be managed conservatively. Occurrence of subcutaneous emphysema in two patients after removal of intercostal tube signifies the importance of adequate set up for proper monitoring. There was also no difference in rate of occurrence of complications between the two types of anaesthesia. So, it could be inferred that medical thoracoscopy is a relatively safe procedure regardless of the type of anaesthesia used [16-18].

## Limitation(s)

The drawback of this study was the limited sample size for the purpose of diagnostic analysis. Another drawback was the retrospective nature of this study. Also, a multicentre study should be done to compare the results.

## CONCLUSION(S)

There was slight agreement between initial and final diagnosis signifying that medical thoracoscopy has got an important additional diagnostic value in the management of pleural diseases. It was rather a safe procedure with minimal complications and could be done under local anaesthesia in most cases. Improper diagnosis was common when only clinical and radiological features were relied upon. Lack of adequate diagnostic facilities might lead on to more and more misdiagnosis. In order to avoid such instances, more thorascopic programmes should be started in all countries including India.

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**PARTICULARS OF CONTRIBUTORS:**

1. Senior Consultant Pulmonologist, Department of Pulmonary and Sleep Medicine, PRS Hospital, Trivandrum, India.
2. Consultant, Department of Anaesthesia, PRS Hospital, Trivandrum, India.
3. Registrar, Department of Pulmonary and Sleep Medicine, PRS Hospital, Trivandrum, India.

**NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:**

Dr. Binu Krishnan,  
Senior Consultant Pulmonologist, Trivandrum, Kerala, India.  
E-mail: binukrishnanck@hotmail.com

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