Original Article

Utility of semi-rigid thoracoscopy in undiagnosed exudative pleural effusion

Loganathan Nattusamy, Karan Madan, Anant Mohan, Vijay Hadda, Deepali Jain[1], Neha Kawatra Madan[1], Sudheer Arava[1], Gopi C Khilnani, Randeep Guleria

Departments of Pulmonary Medicine and Sleep Disorders and [1]Pathology, All India Institute of Medical Sciences, New Delhi, India

ABSTRACT

Background: Semi-rigid thoracoscopy is a safe and efficacious procedure in patients with undiagnosed pleural effusion. Literature on its utility from developing countries is limited. We herein describe our initial experience on the utility of semi-rigid thoracoscopy from a tertiary care teaching and referral center in north India. We also perform a systematic review of studies reporting the utility of semi-rigid thoracoscopy from India. **Patients and Methods:** The primary objective was to evaluate the diagnostic utility of semi-rigid thoracoscopy in patients with undiagnosed exudative pleural effusion. Semi-rigid thoracoscopy was performed under local anesthesia and conscious sedation in the bronchoscopy suite. **Results:** A total of 48 patients underwent semi-rigid thoracoscopy between August 2012 and December 2013 for undiagnosed pleural effusion. Mean age was 50.9 ± 14.1 years (range: 17–78 years). Pre-procedure clinico-radiological diagnoses were malignant pleural effusion [36 patients (75%)], tuberculosis (TB) [10 (20.83%) patients], and empyema [2 patients (4.17%)]. Patients with empyema underwent the procedure for pleural biopsy, optimal placement of intercostal tube and adhesiolysis. Thoracoscopic pleural biopsy diagnosed pleural malignancy in 30 (62.5%) patients and TB in 2 (4.17%) patients. Fourteen (29.17%) patients were diagnosed with non-specific pleuritis and normal pleura was diagnosed on a pleural biopsy in 2 (4.17%) patients. Overall, a definitive diagnosis of either pleural malignancy or TB was obtained in 32 (66.7%) patients. Combined overall sensitivity, specificity, positive predictive value and negative predictive value of thoracoscopic pleural biopsy for malignant pleural effusion were 96.77%, 100%, 100% and 66.67%, respectively. There was no procedure-related mortality. On performing a systematic review of literature, four studies on semi-rigid thoracoscopy from India were identified. **Conclusion:** Semi-rigid thoracoscopy is a safe and efficacious procedure in patients with undiagnosed exudative pleural effusions.

KEY WORDS: Malignant pleural effusion, pleural biopsy, pleural effusion, semi-rigid thoracoscopy, tuberculosis

Address for correspondence: Dr. Karan Madan, Department of Pulmonary Medicine and Sleep Disorders, All India Institute of Medical Sciences, Ansari Nagar, New Delhi - 110 029, India. E-mail: drkaranmadan@gmail.com

INTRODUCTION

Pleural effusion is a common clinical problem with diverse etiologies accounting for around 4% patients in pulmonary practice.[1,2] Pleural effusion results from an abnormal collection of fluid due to excessive production or decreased pleural fluid absorption and can be transudative or exudative depending on the fluid composition. For a definitive etiological diagnosis in pleural effusions which remain undiagnosed after diagnostic thoracentesis, pleural biopsy is usually required for diagnostic evaluation.[2-4] Medical thoracoscopy/pleuroscopy is a minimally invasive procedure that allows complete visualization of the pleural space using a combination of viewing and working instruments enabling the diagnostic and the therapeutic procedures, like pleural biopsy and talc insufflation for pleurodesis to be performed safely.[5] The procedure which can be performed using either rigid or semi-rigid instruments provides minimally invasive access to the pleural space, mediastinum and the lungs.[6] Rigid thoracoscope has been the most widely utilized modality for medical thoracoscopy. Development of the technique of semi-rigid thoracoscopy provided an alternate method

Access this article online

Quick Response Code:

Website: www.lungindia.com

DOI: 10.4103/0970-2113.152618

to access the pleura using a scope which essentially resembles the flexible bronchoscope. Over the past decade, the use of semi-rigid thoracoscope for pleuroscopy has been increasingly evaluated.[7-9] The aim of our study was to evaluate the diagnostic utility and safety of semi-rigid thoracoscopy in patients with undiagnosed exudative pleural effusions presenting to our center.

PATIENTS AND METHODS

The study was conducted in the Department of Pulmonary Medicine and Sleep Disorders at the All India Institute of Medical Sciences (AIIMS), New Delhi, India. Medical thoracoscopy (semi-rigid thoracoscopy) procedures were performed as part of the routine clinical protocol. Informed and written consent for the procedure was obtained from all the patients. Facility of rigid thoracoscopy was not available in the department during the study period. The study was approved by the local institute ethical committee.

Patient preparation

Patients were asked to report fasting (for solids and liquids) for at least 8 hours prior to the thoracoscopy procedure. History of systemic hypertension, diabetes mellitus, cardiac disease, bleeding disorders, previous anesthetic complications and any medication history including anti-platelet/anticoagulant therapy were obtained. Patients with systemic hypertension were advised to take their morning dose of anti-hypertensive medications at 5 A.M. on the day of procedure with a sip of water. In known diabetic patients, morning dose of anti-diabetic medications were skipped. A recent CT scan of the thorax was available for all the patients. Hemoglobin, platelet counts, ECG and prothrombin time values were available for all patients. All patients had undergone diagnostic thoracentesis [total and differential cell count, protein, glucose, ADA (adenosine deaminase), acid fast stain, Gram stain and bacterial cultures and three pleural fluid cytology examinations (whole amount of pleural fluid)], prior to the pleuroscopy procedure. Closed pleural biopsy (not a routine practice at our center) prior to thoracoscopy had been performed in two patients and had been non-contributory. Pre-procedure thoracic ultrasound examination (to assess the amount of pleural fluid, loculations and for optimum site of entry) was performed for all patients before the procedure. Other relevant investigations as appropriate for the underlying clinical condition were performed in all patients.

Premedication and anesthesia

The procedures were performed in the bronchoscopy suite. Peripheral venous access was secured on forearm on the side of pleural effusion and low-flow oxygen was administered via nasal cannula. Intravenous promethazine was used for premedication. Intravenous anesthesia for conscious sedation comprised a combination of short-acting benzodiazepine (midazolam) and an opioid (pentazocine/fentanyl) administered by the bronchoscopy nurse under supervision of the operating team. Atropine or glycopyrrolate were not administered. Heart rate, blood pressure, continuous electrocardiographic monitoring and pulse oximetric saturation measurement were observed throughout the procedure and in the post-procedure period for 2 hours. After the procedure, patients were observed for recovery from anesthesia and were discharged from the hospital (usually on the same day) and were followed up in the outpatient clinic.

Semi-rigid thoracoscopy procedure

The operating team usually comprised of one/two teaching faculty, one pulmonary fellow (resident doctor) and two nurses (one to administer the intravenous medications and other to assist with the procedure proper). Site of thoracoscope entry (port) was selected based on the pre-procedure chest ultrasound examination. The usual site was in either one of the 4th to 7th intercostal space in the mid axillary line. A lower intercostal space was usually chosen in patients with smaller sized effusions or where, CT thorax indicated a basal predominance of pleural abnormality/nodules. Patient was positioned on the operating table in lateral decubitus position with the side of pleural effusion upward and the normal side being dependent. The ipsilateral arm was placed over the head to widen out the intercostal spaces. The incision site was exposed, marked and prepared aseptically covering the area from the shoulder level till the iliac crest using 10% povidone iodine. Pneumothorax creation prior to trocar introduction was not routinely performed. Local anesthetic [2% lignocaine (21.6 mg/ml), usually maximum of 10 ml and taking into consideration the body weight] was infiltrated into the selected intercostal space from the skin level to the parietal pleura. A linear incision, approximately 1 cm in size (usual site being in the mid axillary line or slightly anteriorly) was given and blunt dissection was performed to gain entry to the pleural space. A 10 mm size plastic trocar was inserted into the port of entry.

Semi-rigid thoracoscopy was performed using the Olympus, LTF-Type 160 semi-rigid thoracoscope. The scope essentially resembles a flexible bronchoscope and is compatible with the light source and video processor used for the flexible video-bronchoscope of corresponding make. The scope has a 22 cm rigid insertion shaft with a 5 cm flexible tip and has a 2.8 mm internal working channel for introduction of forceps and other accessories. The high resolution video imaging system provides sharp clear images. The angulation range of flexible tip is Up 160°/Down 130°.

After entry of the scope into the pleural space, pleural fluid was aspirated slowly so as to allow maximum possible visualization of pleural cavity. Suction was intermittently stopped so to allow air to enter into the pleural cavity to replace the pleural fluid and to facilitate the lung collapse in order to minimize the likelihood of development of re-expansion pulmonary edema. The

entire pleural space was then systematically inspected and visualized abnormalities were noted such as pleural adhesions (thick, thin or both), pleural nodules and distribution and pleural infiltration (visceral/parietal). Multiple pleural biopsies (about 10 to 12 biopsy samples) were taken from the visualized abnormal areas and the samples were collected in formalin (for histopathological examination) and in saline (for mycobacterial cultures), if TB was clinically suspected. In those patients with no visualized pleural abnormality on inspection findings, biopsies were taken from the parietal pleura and sent for histopathological examination. In patients with a clinical diagnosis of lung cancer and thoracoscopic appearance suggestive of malignant pleural involvement, samples were also additionally obtained for epidermal growth factor receptor/anaplastic lymphoma kinase (EGFR/ALK) mutation analysis. In those patients with proven lung cancer or a high likelihood of extensive malignant pleural infiltration, pleurodesis was performed either as intraprocedural talc insufflation (4 grams of graded large particle size talc, [STERITALC, Novatech, France]) or iodopovidone pleurodesis (20 cc of 10% iodopovidone) later. After the procedure, intercostal tube (size 28 F or 30 F) was inserted and secured using non-absorbable silk suture. Patients were monitored in the post-procedural period for reversal of sedation. A post procedure chest radiograph was obtained in all the patients. Intercostal tube was removed on the day following the procedure, or usually within 3–4 days time if there was increasing fluid drainage initially.

Pleural biopsies were subjected to detailed histopathological analysis/immunohistochemistry and interpreted by experienced pathologists. Adhesiolysis if required was performed using the 2 mm biopsy forceps inserted through the working channel of the semi-rigid thoracoscope. Due to inherent limitations of the small forceps size, adhesiolysis was partial in most of the cases.

In case of failure of lung expansion (hydropneumothorax) or air leak, it was planned to keep the intercostal drain (ICD) *in situ* for a longer duration. In most of the patients, the ICD was removed on the next day following the procedure.

Data analysis

Semi-rigid thoracoscopy procedure was considered diagnostic, if the pleural biopsy showed definitive features such as malignancy or granulomatous inflammation suggestive of TB or positive microbiological investigations. Procedure was considered non-diagnostic, if pleural biopsy showed features of non-specific pleuritis or normal pleura. Patients with clinico-radiological features suggestive of TB and pleural biopsy suggestive of non-specific pleuritis were started on anti-tuberculosis therapy and were followed up.

STATA statistical analysis software was used for statistical analysis and descriptive analysis was performed. Categorical variables were expressed as frequency (percentages) and quantitative variables were expressed as mean (SD) or median (IQR). Sensitivity, specificity, positive and negative predictive values were calculated using standard formulas.

Systematic review

We searched the PubMed and EMBASE databases for studies and systematic reviews in order to identify the Indian studies reporting the diagnostic efficacy of semi-rigid thoracoscopy. We excluded case reports and series with <10 patients.

RESULTS

Forty-eight patients with undiagnosed pleural effusion underwent semi-rigid thoracoscopy during the period August 2012 to December 2013, at our center. The mean age of the patients was 50.9 ± 14.1 years (range 17–78 years). There were 31 males (64.58%) and 17 females (35.42%). 36 (75%) patients were clinically suspected to have malignant pleural effusion and in 10 (20.83%) patients, a clinical possibility of pleural TB had been considered. Pre-procedure diagnostic possibility was based on the clinical, radiological and pleural fluid analysis profile according to the treating physician. Two (4.17%) patients with empyema underwent semi-rigid medical thoracoscopy for pleural biopsy, optimal placement of intercostal tube and adhesiolysis. Twenty-five (52.08%) patients had right-sided pleural effusion and 23 (47.92%) had left-sided pleural effusion. Small, moderate, large pleural effusion were present in 23 (47.92%), 18 (37.50%), 7 (14.58%) patients, respectively. Eighteen (37.5%) patients had associated co-morbidities [Table 1]. Thoracic CT examination showed following features: Pleural nodularity – 14 (29.79%) patients, lung mass – 18 (38.30%) patients, mediastinal lymphadenopathy –11 (23.40%) patients and pleural fluid loculations – 13 (27.66%) patients. All patients had exudative pleural effusion with mean pleural fluid protein of 4.58 ± 0.74 (Mean ± SD) g%. Three pleural fluid cytological examinations were negative in all the patients before thoracoscopy. Pleural fluid AFB stain was positive in one patient. Baseline clinico-radiological and pleural fluid characteristics of the study group are shown in Table 1.

Findings observed during pleural visualization included adhesions (thick and/or thin adhesions) in 35 (72.92%) patients; pleural nodularity and pleural infiltration in 29 (60.42%) patients each; diaphragmatic nodules in 13 (27.08%) patients and visceral pleural infiltration in 19 (39.58%) patients. These observations are summarized in Table 2.

Performance characteristics of semi-rigid thoracoscopy procedures in our study in undiagnosed exudative pleural effusions are depicted in Table 2. A definitive diagnosis with a thoracoscopic pleural biopsy was obtained in 32 (66.67%) out of 48 patients. Malignant pleural involvement was diagnosed in 30 (62.5%) patients, non-specific pleuritis in 14 (29.17%) patients and TB and normal pleura were diagnosed in 2 (4.17%) patients each.

Table 1: Baseline characteristics of patients with undiagnosed pleural effusion undergoing semi-rigid thoracoscopy

Total number of patients, *n*	48
Age (mean±SD), (years)	50.9±4.1
Sex (%)	
Male	31 (64.5)
Female	17 (35.42)
Side of pleural effusion (%)	
Right	25 (52.08)
Left	23 (47.92)
Size of pleural effusion (%)	
Small pleural effusion	23 (47.92)
Moderate pleural effusion	18 (37.50)
Large pleural effusion	7 (14.58)
Associated co-morbid illness (%)	
Coronary artery disease	4 (8.33)
Diabetes mellitus and systemic hypertension	4 (8.33)
Rheumatoid arthritis	1 (2.08)
Carcinoma breast	3 (6.25)
Sphenoid mass with granulomatous hepatitis	1 (2.08)
Mediastinal mass with right atrial mass	1 (2.08)
Pancreatitis	2 (4.16)
Acute lymphoblastic leukemia	1 (2.08)
Coronary artery disease with heart failure	1 (2.08)
Clinico-radiological diagnosis (%)	
Malignant pleural effusion	36 (75)
Tuberculosis	10 (20.83)
Empyema	2 (4.17)
CT thorax findings (%)	
Pleural nodularity	14 (29.79)
Lung mass	18 (38.30)
Mediastinal lymphadenopathy	11 (23.40)
Pleural fluid loculations	13 (27.66)
Closed pleural biopsy prior to thoracoscopic procedure	2 (4.17)
Pleural fluid characteristics	
Appearance (%)	
Straw colored	25 (52.08)
Hemorrhagic	21 (43.75)
Purulent	02 (4.17)
Total count (/mm^3)	1109.91 (1433.09)
Lymphocyte predominant effusions (%)	40 (83.33)
Protein (g%)	4.58 (0.74)
Glucose (mg%)	77.9 (58.1)
ADA	24.79 (16.85)

The results are depicted as mean±SD or No (%), SD: Standard deviation

Out of the two patients with empyema who underwent the procedure, one patient had normal pleura and the other patient had non-specific pleuritis.

Adenocarcinoma (lung) was the most common histological pleural malignancy seen in our study group (18 patients) followed by small-cell lung carcinoma and metastatic carcinoma breast in three (6.25%) patients each. Squamous cell lung carcinoma, metastatic papillary thyroid carcinoma, poorly differentiated malignant tumor, germ cell tumor, leiomyosarcoma and adenocarcinoma with unknown primary were seen in one patient each [Table 2]. There were no patients with mesothelioma. Representative images of the radiological and thoracoscopic pleural abnormalities in patients with malignant pleural effusion are shown in Figure 1.

Table 2: Performance characteristics of semi-rigid thoracoscopy in undiagnosed exudative pleural effusions

Thoracoscopic procedure details	
Lignocaine volume used (mg)	214.79 (33.96)
Incision length (cm)	1.27 (0.25)
Midazolam dose (mg)	2.06 (0.63)
Pentazocine dose (mg)	27.29 (9.26)
Procedure duration (minutes)	45.52 (13.99)
Thoracoscopic pleural appearance (%)	
Adhesions (thick and/or thin adhesions)	35 (72.92)
Pleural nodularity	29 (60.42)
Diaphragmatic nodules	13 (27.08)
Pleural infiltration	29 (60.42)
Visceral pleural infiltration	19 (39.58)
Histopathological diagnosis (%)	
Malignant Pleural effusion	30 (62.5)
Non-specific pleuritis	14 (29.17)
Tubercular pleural Effusion	2 (4.17)
Normal pleura	2 (4.17)
Pathological subtypes of MPE (%)	
Lung cancer	
Adenocarcinoma lung	18 (35.42)
Small cell carcinoma lung	03 (6.25)
Metastatic carcinoma breast	03 (6.25)
Squamous cell carcinoma lung	01 (2.08)
Others	
Poorly differentiated malignant tumor	01 (2.08)
Germ cell tumor	01 (2.08)
Leiomyosarcoma	01 (2.08)
Adenocarcinoma with unknown primary	01 (2.08)
Metastatic papillary thyroid carcinoma	01 (2.08)
Pleurodesis (%)	
Talc insufflation	4 (8.33)
Betadine pleurodesis	25 (52.08)
Procedural complications (%)	
Localized subcutaneous emphysema	8 (16.67)
Mild bleeding	2 (4.17)
Minor visceral pleural injury	1 (2.08)

The results are depicted as mean±SD or No (%)

Sixteen (33.33%) patients remained undiagnosed after thoracoscopic pleural biopsy [pathological findings of non-specific pleuritis (14) or normal pleura (2)]. Among 14 patients with non-specific pleuritis, 5 patients were started on anti-tuberculosis therapy (ATT) based on a clinical possibility of underlying TB. Two patients had complete response (resolution of effusion) with ATT, one patient is currently on ATT (under follow-up and showing improvement) and one patient was lost follow-up. The remaining fifth patient, who was initially started on ATT, was later diagnosed to have adenocarcinoma lung on follow-up. Six patients expired on follow-up in the non-specific pleuritis group. The remaining three patients with non-specific pleuritis were lost to follow-up. Pleural biopsy samples were sent for mycobacterial cultures in 19 (40.43%) patients and all were negative. The representative appearances of non-specific pleuritis and TB are shown in Figures 2 and 3, respectively.

EGFR mutations were positive in 6 (12.50%) out of 19 patients with adenocarcinoma. Pleurodesis using iodopovidone and talc were performed in 25 (52.08%) and 4 (8.33%) patients, respectively.

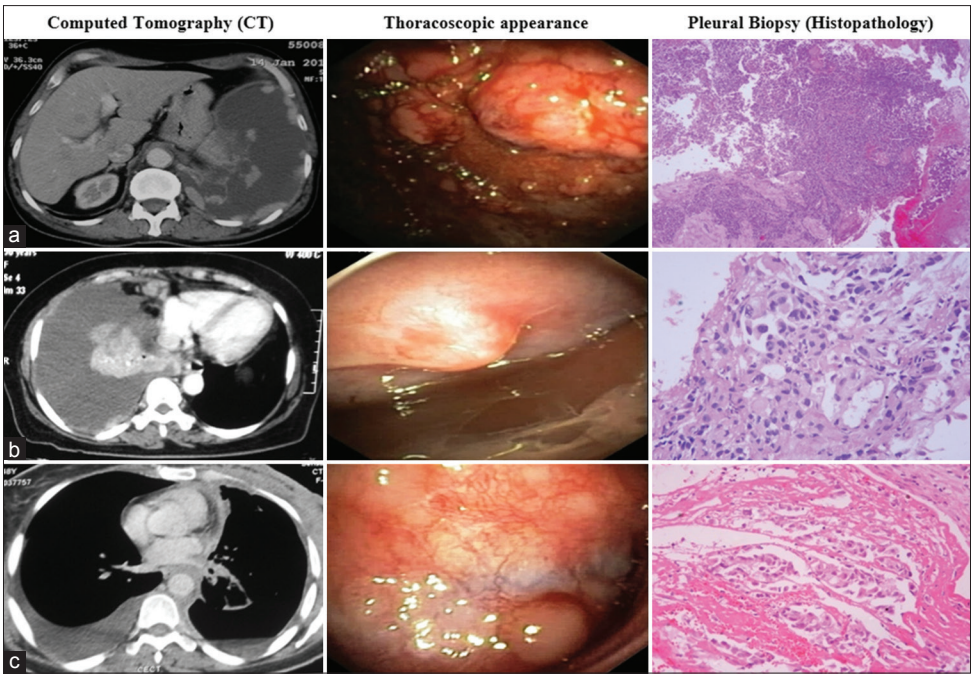

Figure 1: Radiological (CT), thoracoscopy and histopathological appearance of patients with malignant pleural effusion (a) Small Cell Carcinoma - CT - Large left pleural effusion with extensive areas of pleural nodularity and pleural thickening seen. Thoracoscopy - Extensive multiple variable sized pleural nodules seen over the parietal pleura. Histopathological examination - Photomicrograph showing sheets of small round cells with scant cytoplasm and hyper chromatic nuclei infiltrating in between fibrocollagenous tissue. Tumor cells are showing smudging of nuclear chromatin at places. (H and E, ×100) (b) Metastatic papillary thyroid carcinoma - CT - Large right pleural effusion with few areas of pleural nodularity seen over the posterior and basal aspects. Thoracoscopy - A large sized discrete area of parietal pleural nodularity. Histopathological examination - Tumor cells showing cytoplasmic positivity for thyroglobulin. (IHC, ×400) (c) Metastatic Breast Carcinoma - CT - Bilateral pleural effusion is seen right > left without any obvious areas of pleural thickening. Thoracoscopy - Extensive areas of pleural infiltration and increased vascularity are observed. In addition, few large sized glistening parietal pleural nodules are also seen. Histopathological examination - Photomicrograph showing breast carcinoma cells infiltrating the fibrocollagenous tissue in small nests and singly. (H and E, ×400)

Minor procedure-related complications included localized subcutaneous emphysema (8 patients), mild bleeding (2 patients) and minor visceral pleural injury (1 patient). The patient with visceral pleural injury had forced expiratory air leak which resolved with autologous blood patch. Other complications improved with conservative management. There was no procedure-related mortality. Combined overall sensitivity, specificity, positive predictive value and negative predictive value of thoracoscopic pleural biopsy for malignant pleural effusion were 96.77%, 100%, 100% and 66.67%, respectively.

Systematic review

On performing the systematic review, four studies reporting the utility of semi-rigid thoracoscopy from India were identified which met the inclusion criteria. The results of these four studies are summarized in Table 3.

DISCUSSION

Traditionally, medical thoracoscopy has been performed using rigid instruments and the same continued to be the case till the introduction of the semi-rigid thoracoscope. The near complete similarity of the semi-rigid thoracoscope with the flexible bronchoscope has made its adoption easy for the pulmonologists familiar with performance

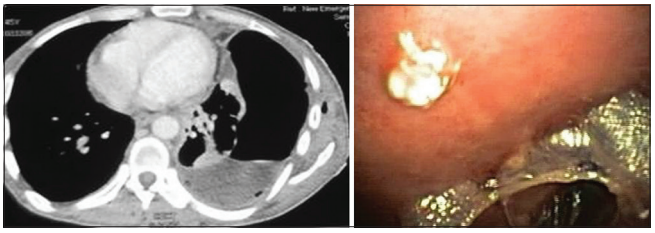

Figure 2: Left panel - CECT examination of the thorax demonstrating moderate left pleural effusion. No obvious pleural thickening or loculations are noted. Right panel: Thoracoscopic appearance of a discrete whitish appearing nodule over the parietal pleura. Histopathological examination of pleural biopsy from the nodule demonstrated granulomatous inflammation compatible with Tuberculosis

of flexible bronchoscopy. The efficacy, safety and high diagnostic yield of semi-rigid thoracoscopy has been reported in multiple reports and this had led to the development of this technique into a useful adjunctive diagnostic modality in patients with undiagnosed pleural effusion.[10] The distal flexible tip (5 cm) of the instrument and the better maneuverability makes easy to obtain multiple pleural biopsy samples from all accessible pleural aspects. In addition, it allows removal of thin pleural adhesions and can also guide the correct positioning of the intercostal drains.

Forty-eight patients with undiagnosed exudative pleural effusion underwent single port semi-rigid thoracoscopy procedure under local anesthesia and conscious sedation

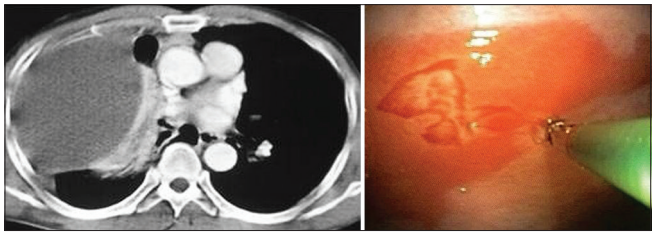

Figure 3: Left panel - CECT examination of the thorax in a patient with rheumatoid arthritis demonstrating a large loculated right pleural effusion. Right panel: Thoracoscopic appearance of a large area of plaque like erythema over the visualized parietal pleura from which pleural biopsy is being obtained. Histopathological examination of pleural biosy demonstrated non specific chronic inflammation

in our study. CT thorax demonstrated pleural nodularity in 14 (29.79%) patients. All patients who had pleural nodularity on CT chest were detected to have pleural nodules during the thoracoscopy procedures and were positive for malignancy on histopathological examination of the pleural biopsy. A flexible bronchoscopy examination was usually performed prior to thoracoscopy in patients with suspected malignant pleural effusion with possibility of endobronchial obstruction. In none of the patients with a contralateral mediastinal shift (8 (17.02%) patients) seen on CT/Chest X ray did fiber optic flexible bronchoscopy demonstrate any endobronchial lesion. As has been described in the literature, contralateral shift of the mediastinum in a patient with pleural effusion essentially rules out the presence of significant ipsilateral major bronchial obstruction.

Table 3: Systematic review of studies from India reporting experience with semi-rigid thoracoscopy

Author	Year	Number of patients	Inclusion criteria	Type of anesthesia	Diagnostic yield (%)	Thoracoscopic diagnosis	Significant procedural complications
Thangakunam, *et al*.[12]	2010	21	Undiagnosed Pleural effusion-18 Thoracoscopy as an initial modality for pleural samples-2 Pleurodesis in pneumothorax-1	Local anesthesia and conscious sedation	12/18 (66.7)	Malignancy-8 Adenocarcinoma-6 Non-Hodgkin's Lymphoma-1 Mesothelioma-1 Tuberculosis-3 Inflammatory Pseudotumor-1	None reported
Mehta, *et al*.[13]	2010	25	Undiagnosed pleural effusion-20 Thoracoscopy for talc poudrage-5	Local anesthesia and conscious sedation	16/20 (80)	Malignancy-9 Adenocarcinoma-5 Brochoalveolar carcinoma-1 Poorly differentiated carcinoma-3 Chronic pleuritis-7 Tuberculosis-2 Empyema-1 Endometriosis-1	None reported
Prabhu, *et al*.[14]	2012	68	Undiagnosed unilateral exudative pleural effusion	General Anesthesia-65 Local anesthesia and conscious sedation– 3	97	Malignancy-24 Metastatic adenocarcinoma-15 Mesothelioma-3 Undifferentiated carcinoma-3 Lymphoma-1 Metastatic clear cell carcinoma-1 Metastatic squamous cell carcinoma-1 Non-specific inflammation-22 Tuberculosis-16 Empyema-2 Sarcoidosis-1 Normal pleura-1 Non Diagnostic-2	Subcutaneous Emphysema-3 Prolonged Air leak-1
Dhooria, *et al*.[15]	2014	45	Undiagnosed pleural effusion	Local anesthesia and conscious sedation	73.3	Malignancy-7 Tuberculosis-9 Non-specific pleuritis-17 Aspergillosis-1 Rheumatoid nodule-1	Major complications Empyema-1 air leak (>3 days) -1 Re-expansion pulmonary edema-1 Minor complications Subcutaneous Emphysema-3 Operative site Infection-1 Minor hemorrhage-1 Non-infective fever-1

In patients with malignant pleural effusion, closed pleural biopsy has been reported to be diagnostic in 44%, pleural fluid cytology in 62%, and yield is 74% when both these modalities are combined.[11] As a standalone modality, medical thoracoscopy is diagnostic in 95% cases and 97% when all these three modalities are combined.[11] Overall sensitivity and specificity of semi-rigid thoracoscopy for malignant pleural effusion in our study were 96.8% and 100%, respectively. Pleural fluid cytology examination was performed three times prior to pleuroscopy in all our patients. Cytopathological examination of the pleural fluid was inconclusive for malignancy in all the patients.

Out of the 36 patients who were initially suspected to have malignant pleural effusion on clinico-radiological basis, malignant pleural involvement was confirmed on histopathology in 30 patients. Non-specific pleuritis was diagnosed in five patients and normal pleura in one patient. No patients were diagnosed with TB in this group. Out of the 10 patients with clinico-radiological suspicion of TB, 2 patients had histopathologically confirmed TB and remaining 8 patients had non-specific pleuritis. Of the two patients with empyema who underwent semi-rigid thoracoscopy, one patient had normal pleura and the other had non-specific pleuritis on pleural biopsy. Both these patients had remarkable improvement after thoracoscopic adhesiolysis and guided chest drain placement.

The overall diagnostic yield of thoracoscopic pleural biopsy in our study was 66.7%. The results of previously reported studies from India describing the utility of semi-rigid thoracoscopy have been summarized in the Table 3.[12-15] Studies have reported diagnostic yield of thoracoscopy procedures ranging from 66% to 97%.[12,13,16-18] A surprisingly low incidence of TB on a thoracoscopic pleural biopsy was found in our study (4.17%). This is in contrast to high incidence of TB reported by other studies with thoracoscopic pleural biopsy in TB endemic populations such as by Kannan, *et al*. (52.4%)[19] and Mootha, *et al*.(22.8%).[17] The low incidence of TB on a thoracoscopic pleural biopsy in our study can be explained by referral bias. Our institution is a tertiary care referral centre in a TB endemic population. Most of the patients with a clinical diagnosis of pleural effusion are often started on anti-tuberculous medications (often without a pleural fluid examination also). Therefore, many patients who present to us for evaluation of undiagnosed pleural effusion have often received some combination of anti-TB medications. Therefore, patients with tuberculous pleural effusion, most of whom improve with anti-TB drugs are less likely to be referred to us. Also, the sensitivity and specificity of pleural fluid ADA for tubercular pleural effusions in high prevalence populations is good and most the patients in our setting receive successful treatment for TB without a pleural biopsy. Notwithstanding, the diagnostic utility of thoracoscopic pleural biopsy for pleural tuberculosis has been reported to be excellent.

Though we observed diaphragmatic nodules in 13 patients, they were not biopsied in most of the patients as adequate pleural biopsies could be obtained from other sites of parietal pleural abnormalities.

Out of the 30 pleural biopsies confirmatory of malignancy, lung adenocarcinoma was the most common histology seen in our group (18 patients) as has been reported in other studies also. Non-specific pleuritis was seen in 14 (29.17%) patients in our study group. In a retrospective study of 142 patients undergoing thoracoscopic pleural biopsy, Davies, *et al*. reported non-specific pleuritis in 44 (31%) patients.[20] All patients with the diagnosis of non-specific pleuritis were kept under close clinical follow-up in our study. Out of these, five patients were started on ATT based on the clinical and radiological suspicion and out of them, two patients completely responded to the therapy, one patient improved (on treatment till the time of writing the manuscript) and one patient was lost on follow-up. The last remaining patient was later diagnosed with adenocarcinoma lung on follow-up after 5 months of ATT. It has been proposed that deep pleural biopsies should be obtained in patients where mesothelioma is suspected. We attempted to obtain deep pleural biopsies in all the patients but there are inherent limitations in obtaining deep pleural biopsies using the 2 mm flexible forceps.

Six patients expired on follow-up in the non-specific pleuritis group. The causes of death in these patients were likely related to their associated co-morbidities and not with pleural effusion *per se*. Venekamp, *et al*. followed 75 patients with non-specific pleuritis and among these, 8.3% eventually developed a malignancy during the follow-up period and in the remaining patients (91.7%), the clinical evolution followed a benign course. In the same study, true idiopathic pleuritis was seen in 25% of patients with the histological diagnosis of non-specific pleuritis.[21]

The procedure-related complications were minor in our study and there was no procedure-related mortality in our study population. All our patients tolerated the procedure well. No procedure was prematurely terminated because of any procedural complications. On follow-up, no patients had malignant infiltration of the thoracoscopic port site. This may be due to absence of any mesothelioma in our study group in which tumor seedling of the tract is more common. None of the patients developed re-expansion pulmonary edema. No patient underwent a repeat thoracoscopic procedure.

Medical thoracoscopy is an extremely useful diagnostic modality that can often contribute crucially to accurate clinical decision-making in patients with undiagnosed pleural effusion.[22,23] In patient where a successful biopsy can be obtained, the yield of medical thoracoscopy performed by either rigid or semi-rigid thoracoscopy instruments has been reported to be similar in a randomized comparison between the two techniques.[14] In a prospective randomized study comparing the size, quality and diagnostic adequacy of biopsy specimens obtained by

semi-rigid and rigid thoracoscope, it was demonstrated that there were no differences in the quality and interpretability of the specimens obtained by both the procedures.[24] The diagnostic accuracy was 100% for the rigid thoracoscope and 97.6% for the semi-rigid thoracoscope. Although the specimens obtained by semi-rigid thoracoscope were smaller, they were still of adequate quality and the diagnostic accuracy was comparable with that of rigid thoracoscopy in the evaluation of pleural effusion of undiagnosed etiology. Rigid thoracoscope allows obtaining pleural biopsies of larger size and deep pleural biopsies which possibly may be of added utility in mesothelioma. It is definitely superior compared with the semi-rigid thoracoscope when performing adhesiolysis is the aim.[25] In cases where an aggressive adhesiolysis is not the aim, semi-rigid thoracoscope offers particular advantages in terms of the procedure being less painful, lesser requirements of analgesic drugs and a smaller scar size.[14] The greatest advantage, however, is the ease of adoption of the semi-rigid thoracoscope by bronchoscopist as the handling of the instrument essentially resembles that of a flexible bronchoscope.

CONCLUSION

Medical thoracoscopy should be considered in all patients with undiagnosed exudative pleural effusions. Semi-rigid thoracoscopy is a safe procedure with high diagnostic yield in undiagnosed pleural effusion. Rigid thoracoscope is preferable when performing adhesiolysis is the aim and for obtaining deep pleural biopsies in suspected mesothelioma. Patients with non-specific pleuritis require close clinical follow-up and other ancillary investigations to ascertain the underlying cause for pleural effusion.

REFERENCES

1. Ansari T, Idell S. Management of undiagnosed persistent pleural effusions. Clin Chest Med 1998;19:407-17.
2. Dev D, Basran GS. Pleural effusion: A clinical review. Monaldi Arch Chest Dis 1994;49:25-35.
3. Cantó A, Blasco E, Casillas M, Zarza AG, Padilla J, Pastor J, *et al*. Thoracoscopy in the diagnosis of pleural effusion. Thorax1977;32:550-4.
4. Hirsch A, Ruffie P, Nebut M, Bignon J, Chrétien J. Pleural effusion: Laboratory tests in 300 cases. Thorax1979;34:106-12.
5. Ernst A, Silvestri GA, Johnstone D; American College of Chest Physicians. Interventional pulmonary procedures: Guidelines from the American College of Chest Physicians. Chest 2003;123:1693-717.
6. Colt HG. Therapeutic thoracoscopy. Clin Chest Med 1998;19:383-94.
7. Agarwal R, Aggarwal AN, Gupta D. Diagnostic accuracy and safety of semirigid thoracoscopy in exudative pleural effusions: A meta-analysis. Chest 2013;144:1857-67.
8. Mohan A, Naik S, Naseer R, Boon C, Mills J, Pandey RM, *et al*. Performance characteristics of semirigid thoracoscopy in pleural effusions of undetermined etiology. J Bronchology Interv Pulmonol 2010;17:289-94.
9. Mohan A, Chandra S, Agarwal D, Naik S, Munavvar M. Utility of semirigid thoracoscopy in the diagnosis of pleural effusions: A systematic review. J Bronchology Interv Pulmonol 2010;17:195-201.
10. Hooper C, Lee YC, Maskell N; BTS Pleural Guideline Group. Investigation of a unilateral pleural effusion in adults: British Thoracic Society Pleural Disease Guideline 2010. Thorax 2010;65 Suppl 2:ii4-17.
11. Loddenkemper R, Schönfeld N. Medical thoracoscopy. Curr Opin Pulm Med 1998;4:235-8.
12. Thangakunam B, Christopher DJ, James P, Gupta R. Semi-rigid thoracoscopy: Initial experience from a tertiary care hospital. Indian J Chest Dis Allied Sci 2010;52:25-7.
13. Mehta A, Rajesh V, Vishwam D, Sethu B, Varun P, Lakshmanan H, *et al*. Value of semirigid thoracoscopy in pleural effusion. Pulmon 2010;12:43-5.
14. Prabhu VG, Narasimhan R. The role of pleuroscopy in undiagnosed exudative pleural effusion. Lung India 2012;29:128-30.
15. Dhooria S, Singh N, Aggarwal AN, Gupta D, Agarwal R. A randomized trial comparing the diagnostic yield of rigid and semirigid thoracoscopy in undiagnosed pleural effusions. Respir Care 2014;59:756-64.
16. Wang Z, Tong ZH, Li HJ, Zhao TT, Li XY, Xu LL, *et al*. Semi-rigid thoracoscopy for undiagnosed exudative pleural effusions: A comparative study. Chin Med J (Engl) 2008;121:1384-9.
17. Mootha VK, Agarwal R, Singh N, Aggarwal AN, Gupta D, Jindal SK. Medical thoracoscopy for undiagnosed pleural effusions: Experience from a tertiary care hospital in north India. Indian J Chest Dis Allied Sci 2011;53:21-4.
18. Kendall SW, Bryan AJ, Large SR, Wells FC. Pleural effusions: Is thoracoscopy a reliable investigation? A retrospective review. Respir Med 1992;86:437-40.
19. Kannan SK, Lin WJ, Teck TS, Azizi AR. Pleuroscopy: Early experience in an East Malaysian state with high tuberculosis prevalence. J Bronchology Interv Pulmonol 2009;16:250-3.
20. Davies HE, Nicholson JE, Rahman NM, Wilkinson EM, Davies RJ, Lee YC. Outcome of patients with nonspecific pleuritis/fibrosis on thoracoscopic pleural biopsies. Eur J Cardiothorac Surg 2010;38:472-7.
21. Venekamp LN, Velkeniers B, Noppen M. Does 'idiopathic pleuritis' exist? Natural history of non-specific pleuritis diagnosed after thoracoscopy. Respiration 2005;72:74-8.
22. Madan K, Singh N, Das A, Behera D. Pleural tuberculosis following lung cancer chemotherapy: A report of two cases proven pathologically by pleural biopsy. BMJ Case Rep 2013;2013. pii: bcr2012008196.
23. Madan K, Bal A, Agarwal R. Pleural effusion in a patient with allergic bronchopulmonary aspergillosis. Respir Care 2012;57:1509-13.
24. Rozman A, Camlek L, Marc-Malovrh M, Triller N, Kern I. Rigid versus semi-rigid thoracoscopy for the diagnosis of pleural disease: A randomized pilot study. Respirology 2013;18:704-10.
25. Khan MA, Ambalavanan S, Thomson D, Miles J, Munavvar M. A comparison of the diagnostic yield of rigid and semirigid thoracoscopes. J Bronchology Interv Pulmonol 2012;19:98-101.

How to cite this article: Nattusamy L, Madan K, Mohan A, Hadda V, Jain D, Madan NK, *et al*. Utility of semi-rigid thoracoscopy in undiagnosed exudative pleural effusion. Lung India 2015;32:119-26.

Source of Support: Nil, **Conflict of Interest:** None declared.