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Original Research Article

Comparison of diagnostic yield and complications of bronchoscopy, closed pleural biopsy and medical thoracoscopic pleural biopsies in undiagnosed pleural effusions

Kizhakkepeedika Davis Rennis*, Jaboy Bibin, Vadakkan Thomas, Easwaramangalath Venugopal Krishnakumar

Department of Pulmonology, Amala Institute of Medical Sciences, Amala Nagar, Thrissur-680555, Kerala, India

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***Correspondence:**
Dr. Kizhakkepeedika Davis Rennis,
E-mail: rennis@rediffmail.com

ABSTRACT

Background: Undiagnosed exudative pleural effusion is a commonly encountered clinical scenario, which requires further evaluation. This study was aimed to analyze the diagnostic yield and complications of three procedures- Bronchoscopy, closed (Abram's) pleural biopsy and medical thoracoscopy. Further, this study assessed whether combining closed pleural biopsy with bronchoscopy can be a substitute for medical thoracoscopy.
Methods: An observational study was conducted among people with undiagnosed exudative pleural effusion. Initially, closed pleural biopsies were performed with Abrams needle and multiple tissue fragments were taken through the incision and the samples were sent in formalin to the laboratory for histopathology examination. For thoracoscopy, a cannula of 10 mm diameter with blunt trocar was inserted into the pleural cavity and semi rigid thoracoscope was introduced through the trocar. Bronchoscopy was performed 48 hours after thoracoscopy. Sensitivity, specificity and positive and negative predictive values were calculated and compared.
Results: Out of 25 people, 14 were diagnosed to have malignancy and 7 were diagnosed tuberculosis. The overall sensitivity of the three procedures were 28.5% for closed pleural biopsy, 14.2% for bronchoscopy, 95.2% for medical thoracoscopy, 42.8% for the combined pleural biopsy and bronchoscopy. The complication rate was lowest for bronchoscopy (4%), followed by medical thoracoscopy (8%) and closed pleural biopsy (16%).
Conclusions: Medical thoracoscopy is a comparatively safe procedure which has got the highest sensitivity for the diagnosis of undiagnosed exudative pleural effusions. Bronchoscopy combined with closed pleural biopsy, the diagnostic yield was increased (than that of individual yield), but cannot be a substitute for medical thoracoscopy.

Keywords: Abram's needle, Bronchoscopy, Closed pleural biopsy, Exudative pleural effusion, Malignancy, Medical thoracoscopy, Tuberculosis

INTRODUCTION

Pleural effusion is the abnormal accumulation of fluid in the pleural space. It can be transudate or exudates and Light's criteria help to differentiate them.[1] Exudative pleural effusion is a commonly encountered clinical scenario among both respiratory and non-respiratory specialists. In humans, approximately 75% of the cells in the pleural fluid are macrophages, 25% are lymphocytes and mesothelial cells, neutrophils and eosinophils accounting for less than 2% each.[2] The precise pathophysiology of fluid accumulation vary based upon

underlying etiologies. There are more than 50 recognized causes for effusion which include pleural or parenchymal lung diseases, systemic diseases, organ dysfunction and drugs.[3]

As the differential diagnosis for pleural effusion is wide, a systematic approach for evaluation is needed. The initial evaluation of pleural fluid by biochemical, microbiological and cytological methods may not reveal the cause for the pleural effusion. The diagnostic yield of cytology from sending more than two specimens which had taken on different occasions was found to be very low.[4] Hence biopsy, thoracoscopy and bronchoscopy were recommended for the diagnosis of undiagnosed exudative pleural effusion.

Fibre-Optic Bronchoscopy (FOB) was found to be limited role in the evaluation of undiagnosed pleural effusion as its diagnostic yield is very low in addition to the complication rate of between <0.1 to 11%.[5-8] Because of advanced instruments and simpler anesthetic agents it can be done as a day-care procedure, medical thoracoscopy has received great interest among pulmonologists.[9] But it is an expensive procedure and requires great expertise. In centers, where medical thoracoscopy is not available, bronchoscopy can be performed in addition to the closed pleural biopsy. Traditionally, it was done using Abram's needle/cutting needle.[10, 11]

Though it is a simple, inexpensive procedure; the diagnostic yield is very low compared to thoracoscopy. The common complications of pleural biopsy with Abram's needle include pain (1-15%), pneumothorax (3-15%), vasovagal reaction (1-5%), haemothorax (<2%), site haematoma (<1%), transient fever (<1%) and, rarely death.[9] This study was aimed to know if closed pleural biopsy combined with bronchoscopy may improve the diagnostic yield of undiagnosed exudative pleural effusions; and if they can be a substitute for medical thoracoscopy.

METHODS

Patients' selection and design of the study

Patients of age between 15 and 80 who were admitted with undiagnosed exudative pleural effusions in Pulmonology department, of our hospital during the period of January 2014 to September 2015 were included in this observational study. Patients with transudative effusions, respiratory failure, those already on empirical treatment for effusion and showing clinicoradiological improvement, bleeding disorders or too sick to undergo medical thoracoscopy were excluded from the study.

The study design was approved by Institutional research and ethics committee, Amala Institute of Medical Sciences, Amala Nagar, Thrissur, Kerala, India for conducting study in humans. The sample size of 25 cases of undiagnosed pleural effusion was calculated using the formula, n = 4pq/d2, where p=diagnostic yield, q=1-p, d=20% of p (p =80%).

Procedure

After taking informed consent, all admitted cases of pleural effusion initially underwent diagnostic pleural fluid aspiration under local anesthesia using 2% lignocaine. The pleural fluid was sent for investigations – total count, differential count, cytology, protein, albumin, sugar, Adenosine deaminase, Lactate dehydrogenase, bacterial culture and sensitivity, acid fast bacillus (AFB) smear and fungal smear. Based on Light's criteria, transudative effusions were excluded from the study. Those patients, in whom initial fluid analysis was inconclusive, were taken as 'undiagnosed exudative pleural effusion' and they were selected for medical thoracoscopy.

Patients were placed in the lateral decubitus position with the involved side up. Under local anesthesia (with 2% lignocaine), and conscious sedation (using intravenous midazolam, pentazocin and promethazine), a small incision of 8-10mm was made in mid-axillary line of 5th, 6th or 7th intercostal space. The Abram's needle was inserted at 90° to the ribs, just above the lower rib of the intercostal space chosen, into the pleural cavity. Rotating the cutting trocar then opens the needle. Fluid was aspirated to confirm that the needle is within the pleural cavity. The needle was then angled either inferiorly or horizontally within the intercostal space, placing the cutting groove up against the pleura. The cutting trocar was then rotated to the closed position, cutting the biopsy. Multiple tissue fragments were taken through the same incision and the samples were sent in formalin to the laboratory for histopathology examination.

After closed pleural biopsy, blunt dissection of subcutaneous tissue and the intercostal muscles with curved artery forceps was done. A cannula of 10 mm diameter with blunt trocar was inserted into the pleural cavity and semi rigid thoracoscope was introduced through the trocar. Pleural fluid was suctioned to enable clear visualization of entire pleural surface. Continuous monitoring of electrocardiogram, blood pressure and oxygen saturation were done. Whole parietal and visceral pleura were visualized and multiple biopsies were taken from suspicious lesions, if present any. The procedure was followed by placing of a 24F Inter costal Drainage tube, which was kept under water seal. Bronchoscopy was performed 48 hours after thoracoscopy. Bronchial wash, brush and biopsy were taken from the suspicious areas and were sent for microbiological as well as histopathological examination. Minor and major complications, if any, were routinely recorded. Major complications are defined as those requiring active medical management and minor complications, those requiring medical supervision only. Histopathology was considered as gold standard for confirming the diagnosis

of malignancy. The reports were collected and the diagnostic results of three procedures- closed Abram's pleural biopsy, medical thoracoscopy guided pleural biopsy and bronchoscopies were compared.

RESULTS

This observational study included 25 people with undiagnosed exudative pleural effusion. The age of the study population was 57±17.28 (68% were males and 32% females) with maximum number of cases were seen in the age group 50-60 (32%) (Figure 1).

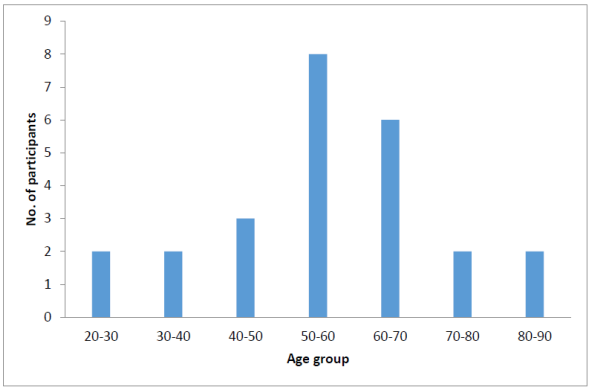

Figure 1: Distribution of age.

The commonest symptoms were cough (96%), dyspnoea (84%) and loss of appetite (68%) (Figure 2).

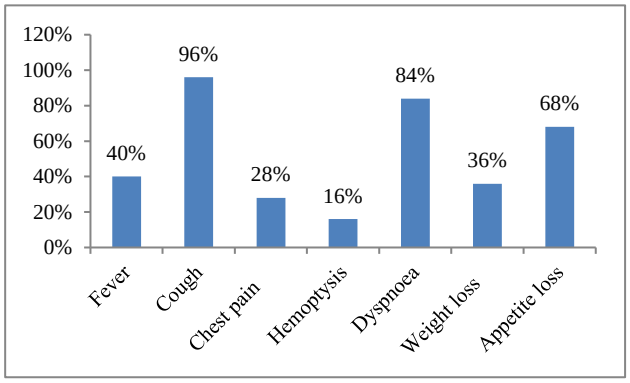

Figure 2: Distribution of the commonest symptoms.

Table 1: Diagnostic yield of closed pleural biopsy (CPB).

CPB (diagnosis)	Final diagnosis		Total
	Yes	No	
Yes	6	0	6
No	15	4	19
Total	21	4	25

Diagnostic yield of closed pleural biopsy is given in Table 1. Out of 21 diagnosed cases, 6 were diagnosed by closed pleural biopsy. Sensitivity, specificity, positive predictive value, negative predictive value were 28.5%, 100%, 100% and 16.6%, respectively. Among 14 cases of malignancy, 3 cases of malignancy were diagnosed by closed pleural biopsy with sensitivity of 35.7%, specificity of 100%, and positive predictive value of 100% and negative predictive value of 55%. Out of 7 tubercular (TB) cases, closed pleural biopsy could diagnose 3 cases with sensitivity, specificity; positive predictive value and negative predictive value were 42.8%, 100%, 100% and 81.8%, respectively. The overall complications rate was 16%. Two patients (8%) had bleeding from the biopsy site which was treated conservatively and 2 patients (8%) had severe pain requiring analgesics.

Table 2: Diagnostic yield of bronchoscopy.

Bronchoscopy (diagnosis)	Final diagnosis		Total
	Yes	No	
Yes	3	0	3
No	18	4	22
Total	21	4	25

Diagnostic yield of bronchoscopy is given in Table 2. Bronchoscopy could aid in making a diagnosis in 3 out of 21 cases with specificity of 100%, sensitivity of 14.2%, positive predictive value of 100% and negative predictive value of 18.1%. Only 1 TB case was diagnosed by bronchoscopy among 7 TB cases, while it could diagnose only 2 cases out of 14 malignancies presenting as exudative pleural effusion. Among the 25 patients who underwent bronchoscopy, 1 patient (4%) had hypoxia during the procedure. No other complications were recorded.

Table 3: Diagnostic yield of thoracoscopy.

Thoracoscopy (diagnosis)	Final diagnosis		Total
	Yes	No	
Yes	20	0	20
No	1	4	5
Total	21	4	25

Diagnostic yield of Thoracoscopy was given in Table 3. Thoracoscopy had highest sensitivity. It could diagnose 20 cases out of 21 diagnosed cases. Sensitivity, specificity, positive predictive value and negative predictive value were 95.2%, 100%, 100% and 80% respectively.

It had 100% sensitivity and specificity in diagnosing TB pleural effusions. While the diagnostic yield for malignant effusion was slightly low when compared to yield for TB effusions (Sensitivity= 92.8%, specificity= 100%, positive predictive value= 100%, negative predictive value= 91.6%), the overall complications rate was 8%. 1 patient (4%) had severe pain requiring analgesics and 1 patient (4%) had hypoxia during the procedure.

Diagnostic yield of combined closed pleural biopsy and bronchoscopy is given in Table 4. It could diagnose 8/25 cases (Sensitivity=38.1%, Specificity=100%, Positive predictive value=100%, Negative predictive value=23%). The diagnostic yield of combined closed pleural biopsy and bronchoscopy for TB was 3/25 and that for malignancy was 5/25.

Table 4: Diagnostic yield of closed pleural biopsy (CPB) and bronchoscopy.

CPB or bronchoscopy (diagnosis)	Final diagnosis		Total
	Yes	No	
Yes	8	0	8
No	13	4	17
Total	21	4	25

DISCUSSION

The overall sensitivity of closed pleural biopsy in our study was 28.5%. The sensitivity in cases of TB was found to be 42.8% and 35.7% for malignancy cases. Our result is consistent with that of Verma et al.[12] in which a diagnostic yield of 21.7% was obtained.A randomized control study by Haridas et al reported an overall diagnostic yield of 62.1%. Maskell et al.[13,14] conducted Abram's closed biopsy in 25 patients, which diagnosed malignancy in eight of 17 patients with sensitivity of 47%, specificity of 100%, negative predictive value 44% and positive predictive value 100%.

Mungall et al have reported diagnostic rates of 72% for malignant effusions and 88% for tuberculous effusions, which is the highest diagnostic yield for closed pleural biopsy seen in studies.[15] The low yield in our study is probably due to not sending specimens for AFB smear or culture for *Mycobacterium tuberculosis*. In present study, repeated pleural biopsy was not done. Data from various studies indicates that repeated pleural biopsy will increase the diagnostic yield. Kirsch et al found a direct correlation between the yield of closed pleural biopsy and the number of biopsy samples given.[16]

The low sample size of the study also can be a reason for the low sensitivity of the test. The high yield for TB when compared to malignancy is because of the pleural distribution of the lesions. In TB, nodules/inflammation will be diffuse, whereas in malignancy the nodules will be very few and discrete. The complications of bleeding at the site of entry were managed by applying pressure, and no other surgical interventions were required. No other complications were encountered during closed pleural biopsy. Haridas et al reported a complication rate of 17.2% for closed pleural biopsy whereas study by Mungall et al reported the complication rate of 10.9%. The non-occurrence of major complications may be because of less number (<5) of biopsies.[13,15]

The sensitivity obtained for FOB was 3 out of 21 cases (14.2%) but the specificity was 100%. Very few studies were available for bronchoscopy in pleural effusion cases. Heaton et al performed bronchoscopy in 32 cases of pleural effusion. In 6 cases FOB was diagnostic.[17]

Williams et al carried out bronchoscopy in undiagnosed pleural effusion and obtained a diagnosis in only 4 of 28 patients.[18] Of these, three were found to have a bronchial carcinoma. Bronchoscopy is a safe procedure. Various published data regarding complications of FOB shows complication rate of between <0.1 to 11%, with mortality generally reported between 0 and 0.1%.[19-22] The main complications reported in various studies were Pneumothorax, hemorrhage, hypoxemia, arrhythmias, bronchospasm, and post-bronchoscopy fever. The complications rate in present study is 4%. Only 1 patient (4%) had oxygen desaturation during the procedure, which was managed by oxygen support. No other complications were observed.

In this study, 1 case which was undiagnosed with medical thoracoscopy was diagnosed later by CT guided biopsy and 1 case was reported as non-specific chronic inflammation. No opinion could be possible in 3 cases. The sensitivity of diagnostic thoracoscopy in our study was 92.8%, signifying a high diagnostic yield of medical thoracoscope. The specificity obtained for thoracoscopic pleural biopsy was 100%. The diagnostic sensitivity in previous thoracoscopic studies varied from 66% to 100%.[13,23,24] The sensitivity of thoracoscopic pleural biopsy for malignancy in present study was 92.8% and for TB was 100%. This result is comparable with the study by Sakuraba et al who studied 138 patients and reported a diagnostic efficacy of 92.6% in the cases of carcinoma, and in tuberculosis it was 93.8%.[26]

Previous study had demonstrated a sensitivity of 100% in diagnosing tuberculosis in TB pleurisy by medical thoracoscopy.[26] In present study 1 out of 25 cases was diagnosed with non-specific chronic inflammation (pleurisy). There are various studies showing the probability of getting this diagnosis in undiagnosed pleural effusions.[27] We could take biopsies from all 25 cases. On analyzing the complications of medical thoracoscopy, our study population had overall complication rate of 8%. 1 patient (4%) had severe pain which required analgesics and 1 patient (4%) had hypoxia during the procedure, which was corrected by oxygen inhalation. There were neither major complications nor mortality. Studies show complications following thoracoscopy varying from 1.8%, up to 40.3%.[28, 29]

The diagnostic sensitivity of combined closed pleural biopsy and bronchoscopy is found to be 38.1%. The specificity and positive predictive value are 100%. There are no other studies comparing the yield of combined closed biopsy and bronchoscopy with the yield of medical thoracoscopy in pleural effusions. Even though there is increased sensitivity than individual tests, combined closed pleural biopsy and bronchoscopy was still having a low yield than medical thoracoscopy.

CONCLUSION

Result of this study concluded that medical thoracoscopy has the highest diagnostic yield for undiagnosed exudative pleural effusion than the bronchoscopy and closed pleural biopsy. A combined closed pleural biopsy with bronchoscopy cannot be a substitute for medical thoracoscopy. Small sample size is a limitation of our study. Therefore, studies with greater sample size are warranted to assess the issue further.

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