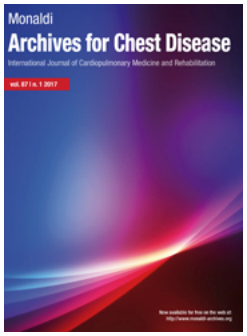

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Comparative study between ultrasound-guided closed pleural biopsy and thoracoscopic pleural biopsy in undiagnosed exudative pleural effusions

Sreyas Sharma, Nitesh Gupta, Pranav Ish, Rajnish Kaushik,
Neeraj Kumar Gupta, Tanmaya Talukdar, Rohit Kumar

Department of Pulmonary Medicine, Critical Care and Sleep Medicine, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India

Correspondence: Rohit Kumar, Department of Pulmonary Medicine, Critical Care and Sleep Medicine,Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India. Tel.: 9911218081. E-mail: dr.rohitkumar@gmail.com

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Abstract

Pleural biopsies are often required to establish a diagnosis in exudative pleural effusions, which remain undiagnosed after initial pleural fluid analysis. Medical thoracoscopy offers a high diagnostic yield but has limited availability in resource-constrained settings. This prospective comparative study evaluated the diagnostic yield between ultrasound-guided closed pleural biopsy and medical thoracoscopy among patients with undiagnosed exudative pleural effusions with pleural-based lesions at least 10 mm in size. Both groups achieved an equal diagnostic yield of 92% despite fewer biopsy specimens being taken in the ultrasound-guided biopsy group (4.52±0.65) compared to the thoracoscopic group (7.8±1) ($p<0.0001$). In conclusion, ultrasound-guided closed pleural biopsy is a suitable alternative to medical thoracoscopy in patients with undiagnosed exudative pleural effusion having pleural thickening or nodularity of at least 10 mm in size in terms of having similar diagnostic yield as compared to medical thoracoscopy.

Key words: ultrasound-guided pleural biopsy, image-guided pleural biopsy, closed pleural biopsy, medical thoracoscopy, exudative pleural effusion.

Abbreviations

CPB, closed pleural biopsy; CT, computed tomography; USG, ultrasound; MT, medical thoracoscopy; ICDT, intercostal drainage tube; BTS, British Thoracic Society.

Introduction

Pleural effusions are commonly encountered in medical practice. Understanding the underlying cause is vital for appropriate management, as treatment strategies can vary and are sometimes mutually exclusive. Pleural fluid is labelled as exudative if it meets any one of the light's criteria. Initial pleural fluid analysis, which includes tests for biochemical markers, microbiological tests and cytological examination, can pinpoint the cause in 60-80% of cases. Despite these measures, 20-40% of cases remain undiagnosed after the initial fluid analysis, often leading to a pleural biopsy to confirm the diagnosis [1-3].

A parietal pleural biopsy can be performed through invasive methods [medical or surgical thoracoscopy] or semi-invasive methods [closed pleural biopsy (CPB), which may or may not be assisted by radiological imaging]. CPB can be conducted with guidance from computed tomography (CT) and ultrasound (USG) or performed blindly [4,5].

Medical thoracoscopy (MT) allows direct visualization and biopsy of the pleura, offers a higher diagnostic yield than blind CPB and thoracocentesis. Specifically, it achieves 91–95% diagnostic accuracy rates for malignant diseases and can reach up to 100% for diagnosing pleural tuberculosis [6]. Nevertheless, the availability of MT can be limited, especially in resource-constrained settings, and not all patients may be suitable for the procedure due to underlying medical conditions [1]. When MT is not feasible, USG-guided CPB is a viable alternative, offering a substantial diagnostic yield with fewer complications. The present study aims to compare the diagnostic yield of USG-guided CPB and MT pleural biopsy in patients with undiagnosed exudative pleural effusion.

Materials and Methods

This prospective comparative study received approval from the institute ethical committee and all enrolled patients signed the written informed consent. This study investigated the diagnostic efficacy between USG-guided CPB and MT in patients with undiagnosed exudative pleural effusions. Eligible patients were selected (based on Light's criteria) and those with specific comorbidities or contraindications (such as patients > 80 years or less than 18 years of age, Bleeding diathesis/ coagulopathy, recent myocardial infarction within four weeks, acute or chronic renal failure, uncontrolled diabetes mellitus and hemodynamic instability) were excluded.

Details of USG-guided pleural biopsy and medical thoracoscopy

USG-guided pleural biopsy

Localization of the site for CPB was done by USG chest (phased-array probe, 5-1 MHz). Areas of pleural thickening more than 10 mm were preferred for biopsy (Figure 1 a and b). Utmost care was taken to pursue a site of entry at least 6 cm away from the vertebra's spinous process and on the lower rib's upper border. A maximum of two sites for closed pleural biopsy were chosen. Two percent of lignocaine was infiltrated into the skin, subcutaneous tissues, rib, periosteum, and parietal pleura. Under real-time USG guidance, manually operated 18- gauge Tru-cut biopsy needle was advanced till the parietal pleura was reached. At this point, the biopsy needle was actuated to launch the specimen notch forward. USG and color doppler of the biopsy site(s) were performed after the procedure to exclude any pneumothorax or bleeding. Complications were treated according to standard protocol.

Medical thoracoscopy

MT was performed utilizing the Olympus LTF-Type 160 semi-rigid thoracoscope. The scope has a 22 cm proximal rigid insertion shaft with a 5 cm flexible tip and a 2.8 mm internal working channel to introduce forceps and other accessories. While the patient was lying in lateral decubitus position with the affected side up, the site of entry was marked with USG. All the patients were monitored using a pulse oximeter, blood pressure monitor, and nasal prongs were applied at a flow rate sufficient to maintain saturation above 95%. Two percent lignocaine was infiltrated into the skin, subcutaneous tissues, rib, periosteum, and parietal pleura. 1.5 to 2 cm skin incision parallel to the rib was made under aseptic conditions at the marked site. After that, blunt dissection of the subcutaneous tissue was done with straight artery forceps till the pleura was punctured. At this point, the trocar and cannula were inserted. The trocar was removed, and the pleural fluid was drained using a 16-French suction catheter. After drainage of the pleural fluid, thoracoscope was introduced, and an inspection of the pleura, along with a video recording, was done. Afterward, biopsy forceps were introduced, and biopsy pieces were obtained from areas of pleural irregularity. A 24-French intercostal drainage tube (ICDT) was inserted and insertion site was covered aseptically with gauze pieces and a sticky bandage. Complications were treated according to standard protocol.

Statistical analysis

The categorical variables were presented in the form of numbers and percentages. On the other hand, the quantitative data were presented as the means ± SD and median with 25th and 75th percentiles (interquartile range). The data normality was checked by using the Shapiro-Wilk test. In the cases in which the data was not normal, we used nonparametric tests. The following statistical tests were applied to the results:

1. The comparison of the quantitative and not normally distributed variables was analyzed using the Mann-Whitney Test, and quantitative and normally distributed variables were analyzed using the Independent t-test. The association of pleural nodularity/Pleural thickening(cm) with the final diagnosis was analyzed using ANOVA.
2. The comparison of the qualitative variables was analyzed using the Chi-Square test. If any cell had an expected value of less than 5, Fisher's exact test was used.

The final analysis was done using Statistical Package for Social Sciences (SPSS) software, developed by IBM in Chicago, USA, and version 25.0. For statistical significance, a p-value of less than 0.05 was considered statistically significant.

Results

A total of 136 patients with exudative pleural effusions were screened for inclusion in the study. After applying inclusion and exclusion criteria, 50 patients aged ≥18 years with undiagnosed exudative pleural effusion (as per Light's criteria) were included in the study. Twenty-five patients underwent USG-guided CPB, and 25 underwent MT. In our study, the mean age was 57.56 ± 11.54 years for the USG-CPB group and 57.32 ± 14.16 years for the MT group. There was a male preponderance (66%). Table 1 shows the baseline demographic characteristics of the study population.

No significant differences were observed in the distribution of CT chest findings between patients undergoing USG-guided CPB and those undergoing MT (Table 2). No significant difference was observed in the mean ± standard deviation of pleural nodularity or thickening between patients undergoing USG-guided CPB and those undergoing MT (Figure 2).

No significant differences were observed in pleural fluid investigations between patients undergoing USG-guided CPB and those undergoing MT. Both the USG-guided pleural biopsy and MT groups achieved a diagnostic yield of 92%, despite fewer biopsy specimens being taken in the ultrasound-guided CPB group (4.52 ± 0.65) compared to the MT group (7.8 ± 1) ($p < 0.0001$).

Discussion

While image-guided or assisted needle biopsies and MT have significantly enhanced the diagnostic accuracy for pleural diseases, the primary challenge now is to improve the success rate of the initial procedure. This would help minimize costs, complications, and hospital burden, as well as enhance patient comfort. The key lies in identifying the most appropriate method for each patient. In other words, a strategy that recommends the sequence and preference of needle biopsy or MT based on the patient's specific pleural pathology would be beneficial.

The mean age of participants in our study was similar across both groups, with a male predominance observed, consistent with findings from previous studies by Maturu et al. and Durgesheswar et al [7,8]. In terms of smoking status, our study found a higher proportion of reformed smokers compared to the study by Durgesheswar et al [8].

Consensus in the literature exists that MT is the most effective procedure for the invasive diagnosis of pleural disease. In MT, the samples are obtained under direct visual observation. Therefore, the diagnostic sensitivity is notably high, about 95%, and the procedure has a very low complication rate; the major complication rate is < 3% [9-12]. The British Thoracic Society (BTS) guidelines on pleural disease (2023) state that diagnostic accuracy appears to be higher with MT pleural biopsy when compared with image-guided CPB. However this statement was based on a low quality of evidence. So BTS guidelines recommend that thoracoscopic or image-guided pleural biopsy may be used depending on the clinical indication and local availability of techniques [13]. MT also presents the advantage of facilitating a potentially definitive therapeutic intervention (i.e., talc poudrage pleurodesis) for patients with recurrent symptomatic effusion simultaneously. However, the cost is slightly higher, and the procedure time is longer than that of needle biopsy [14]. Studies have shown that diagnostic sensitivity of image-guided or image-assisted pleural biopsy is higher for pleural thickening, pleural nodular lesions, and pleural based masses [15-20]. In a study by Zhang et al. [21], a pleural thickness of ≥3 mm independently predicted diagnostic accuracy, 85.2% vs 61.0%. The authors pointed out that it is important to detect focal thickening or pleural nodule or mass with imaging examination before biopsy to increase the accuracy of diagnosis. Similar results also were found in a prospective randomized study [16]. In patients with only pleural effusion, the diagnostic sensitivity of pleural biopsies performed with either a cutting needle or an Abrams needle was significantly lower than in patients with pleural thickening or a lesion accompanying pleural effusion (56.5% vs 93.7% for Abrams needle; 42.9% vs 80% for cutting

needle) [16]. In prospective, randomized study by Metintas M et.al, the sensitivity of needle biopsy was 82% in patients with a pleural thickening of < 1 cm compared with 95% in patients with a pleural thickening of ≥ 1 cm [10]. In another study by Metintas M et.al, in which the method of sampling was decided by examining the CT scan findings of the patients considering that it could increase the success of the methods, the diagnostic accuracy of MT was found to be 95.2%. The same rate was 90.2% for a needle biopsy. The sensitivity of the entire workup was 92.4% [22]. In the work of Niu et al. [5], all patients demonstrated a pleural thickness of > 5 mm, and the diagnostic accuracy of pleural needle biopsy using CT scan guidance was 89.2%. In their study, Bugalho et al. concluded that image-assisted needle biopsy is more likely to be diagnostic in pleural thickening of > 10 mm [23]. In the prospective randomized study by Metintas et al. [24], the sensitivity of Image assisted- Abram needle pleural biopsy (69.7%) was significantly lower than that of MT (96.9%) in patients with only pleural effusion on CT imaging. However, no difference was found between needle biopsy and MT in terms of sensitivity (88.1% vs 95.4%) in the group with pleural thickening or lesion in addition to pleural effusion.

In our study, 88% of participants in the USG-guided CPB group were diagnosed with malignant pleural effusion, compared to 72% in the MT group. The overall diagnostic yield was 92% for both methods (Table 3), which is consistent with results from Durgeshwar et al. and Chang et al. [8,25]. The high diagnostic yield in our study can be credited to the benefits of USG guidance, which enables real-time imaging and the precise identification of biopsy sites.

According to the results of our study and the other studies described herein, we suggest that thorax CT imaging of patients with undiagnosed pleural effusion should be examined carefully before biopsy. Image guided pleural biopsy should be performed if pleural thickening or a localized lesion is present on the pleura accompanied by effusion on CT imaging and within reach of the needle. MT should be performed in patients with only an effusion or with a lesion that the needle cannot reach on CT imaging. Also, MT can be used as the second procedure in patients who remain undiagnosed after Image guided pleural biopsy. This approach can save time, can reduce hospital workload, and can be cost-effective.

Strengths of our study include pragmatic study design. Our study also looked into the relation between the diagnostic yield and the number of biopsy specimens obtained. This study brings important points into notice as there is scarcity of comparative studies between USG-guided pleural biopsy and MT in India.

Limitations of our study are small sample size, single centre study, lack of blinding due to the nature of the interventions. The pleural nodularity or thickness cut-off taken in this study was set at 10 mm; further studies are needed to evaluate the utility of both biopsy methods with a lower cut-off.

Our findings suggest that USG-guided CPB is a suitable alternative to MT in diagnosing undiagnosed exudative pleural effusion, especially in patients with pleural thickening or nodularity exceeding 10 mm on radiological imaging. Despite fewer biopsy samples being taken in the USG-guided CPB group, the diagnostic yield remained similar in both groups. This approach can streamline diagnosis and treatment, ultimately improving patient outcomes. Further studies, particularly randomized controlled trials with a lower cut-off for pleural nodularity or thickening, are needed to comprehensively evaluate diagnostic yield.

Conclusions

USG-guided CPB is a suitable alternative to MT in diagnosing undiagnosed exudative pleural effusion, especially in patients with pleural thickening or nodularity exceeding 10 mm on radiological imaging. More studies, particularly randomized controlled trials with a lower cut-off for pleural nodularity or thickening, are needed to comprehensively evaluate diagnostic yield.

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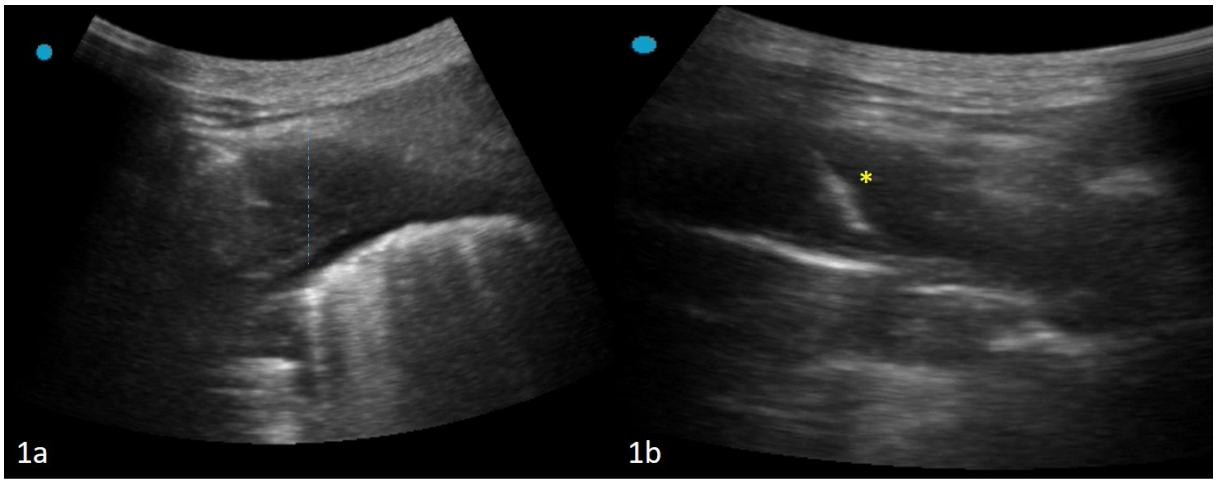

Figure 1. a) Localization of the pleural based lesion (blue dashed line represents the pleural thickness); b) USG guided pleural biopsy (yellow asterisk represents the biopsy needle).

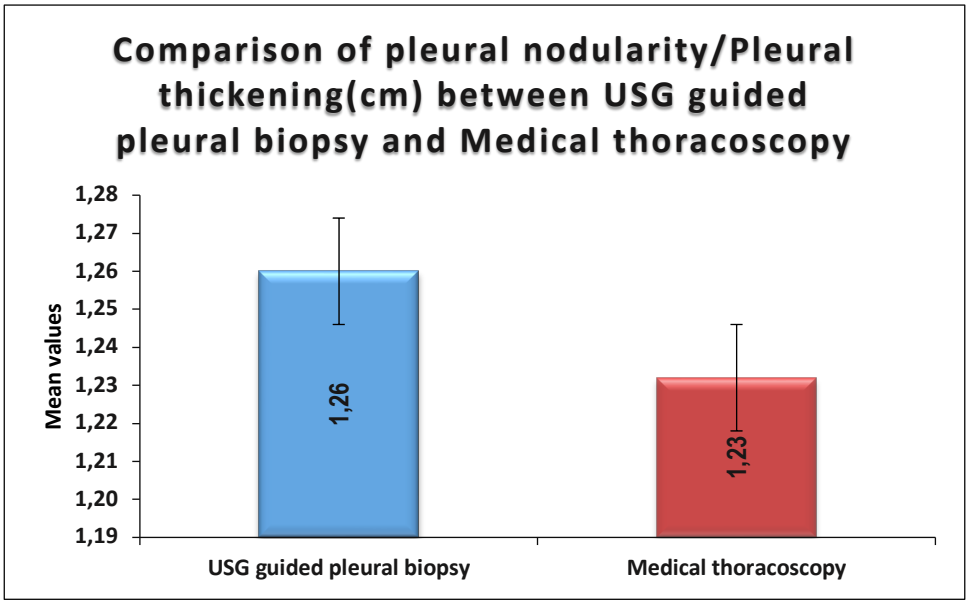

Figure 2. Comparison of pleural nodularity/pleural thickening(cm) between USG guided pleural biopsy group and Medical thoracoscopy group. No significant difference was observed in the mean ± standard deviation of pleural nodularity or thickening between patients undergoing USG-guided CPB and those undergoing MT.

Table 1. Comparison of demographic parameters between the Ultrasound (USG) guided closed pleural biopsy (CPB) group and Medical thoracoscopy (MT) group.

Parameters	USG guided pleural biopsy(n=25)	Medical thoracoscopy(n=25)	p
Age [Median in years]	60 (Range- 49-65 year)	56 (53-66 year)	0.948
Age [Mean ± SD]	57.56 ± 11.54	57.32 ± 14.16	
Age [Range]	19-75	19-85	
Gender (Male)	18 (72%)	15 (60%)	0.37
Gender (Female)	7 (28%)	10 (40%)	
Non smoker	8 (32%)	14 (56%)	0.253
Reformed smoker	12 (48%)	8 (32%)	
Current smoker	5 (20%)	3 (12%)	
No co-morbidities	19 (76%)	18 (72%)	0.747†
Systemic hypertension	3 (12%)	4 (16%)	1*
Coronary artery disease	1 (4%)	1 (4%)	1*
COPD	4 (16%)	2 (8%)	0.667*
Diabetes mellitus	1 (4%)	2 (8%)	1*

Table 2. Comparison of CT chest between Ultrasound (USG) guided closed pleural biopsy (CPB) group and Medical thoracoscopy (MT) group.

CT chest	USG guided pleural biopsy(n=25)	Medical thoracoscopy(n=25)	Total	p
Bilateral pleural effusion with pleural based nodules	8 (32%)	5 (20%)	13 (26%)	0.514*
Left pleural effusion with plerual based nodules	5 (20%)	5 (20%)	10 (20%)	
Right pleural effusion with pleural nodules	11 (44%)	15 (60%)	26 (52%)	
Right pleural effusion with pleural thickening	1 (4%)	0 (0%)	1 (2%)	
Total	25 (100%)	25 (100%)	50 (100%)	

Table 3. Summary of all the diagnosis in the Ultrasound (USG) guided closed pleural biopsy (CPB) group and Medical thoracoscopy (MT) group.

Final diagnosis	USG guided pleural biopsy(n=25)	Medical thoracoscopy(n=25)	Total	p
Acute inflammation	0 (0%)	1 (4%)	1 (2%)	
Adenocarcinoma	5 (20%)	8 (32%)	13 (26%)	
Ewing's sarcoma	1 (4%)	0 (0%)	1 (2%)	
Moderately differentiated keratinizing squamous cell carcinoma	1 (4%)	0 (0%)	1 (2%)	
Non-small cell carcinoma	8 (32%)	5 (20%)	13 (26%)	
Non-specific inflammation	2 (8%)	1 (4%)	3 (6%)	
Poorly differentiated keratinizing squamous cell carcinoma	1 (4%)	0 (0%)	1 (2%)	0.383*
Poorly differentiated non-keratinizing squamous cell carcinoma	2 (8%)	1 (4%)	3 (6%)	
Small cell carcinoma	1 (4%)	3 (12%)	4 (8%)	
Tuberculosis	1 (4%)	5 (20%)	6 (12%)	
Undifferentiated carcinoma	3 (12%)	1 (4%)	4 (8%)	
Total	25 (100%)	25 (100%)	50 (100%)	