

The role of medical thoracoscopy in the diagnosis of exudative pleural effusion at the Chest Department of Zagazig University Hospitals

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Background Thoracoscopy is a minimally invasive procedure that allows visualization of the pleural space and intrathoracic structures. It enables taking pleural biopsies under direct vision, therapeutic drainage of effusions, and pleurodesis in one sitting. Persistent and recurrent exudative pleural effusions become common and thoracentesis and blind pleural biopsy procedures do not give a definitive diagnosis in many patients. Therefore, thoracoscopy today remains the gold standard for these cases. In tuberculous pleuritis, the combined yield of histology and culture for rigid thoracoscopy was nearly 100%.

Objective The aim of the present study was to examine the diagnostic yield of medical thoracoscopy in patients with undiagnosed exudative pleural effusion.

Patients and methods This study was carried out at the chest department of Zagazig University Hospitals in the period from October 2014 to October 2015. It included 36 patients with undiagnosed pleural effusion. All participants signed a written informed consent. The included patients were subjected to full history taking, clinical examination, plain chest radiograph, ultrasonography, computed tomography of the chest, and tuberculosis assessment. Diagnostic aspiration of pleural fluid was performed by using chemical, cytological, and bacteriological analyses. Closed pleural biopsy was carried out in patients with unhelpful pleural fluid analysis. Lastly, if the etiology remained unknown, thoracoscopy was carried out.

Results The present study included 18 men and 18 women patients, with a mean age of 54.4 ± 16.1 years. Dyspnea was

Introduction

Thoracoscopy is a minimally invasive procedure that allows visualization of the pleural space and intrathoracic structures. It enables taking pleural biopsies under direct vision, therapeutic drainage of effusions, and pleurodesis in one sitting [1]. In recent years, 'medical thoracoscopy' performed by interventional pulmonologists needs a room equipped with a cardiac monitor, a pulse oximeter, a blood pressure cuff, intravenous lines, sedation, and some medications. According to the literature, medical thoracoscopy uses rigid instruments or semiflexible ones. Pulmonologists use trocars, camera, and biopsy forceps. Thoracoscopy is safely performed between the 4th and the seventh intercostal space in the mid to anterior axillary line [2].

Nearly, 25% of the exudative pleural effusions remain undiagnosed after thoracentesis and closed pleural biopsy maneuvers. For patients with tuberculous

the most common presenting symptom among the studied patients. Sixteen (72.2%) patients had moderate right-sided pleural effusion. The diagnostic yield of medical thoracoscopy among the studied patients was 80.6%. The histopathological yield of thoracoscopic pleural biopsies was as follows: 25 (69.4%) malignant cases, two (5.6%) patients with tuberculous pleuritis, one (2.8%) patient diagnosed with empyema, and another one (2.8%) with collagenic disease. There were seven (19.4%) patients who were not diagnosed. The post-thoracoscopic complications in this study occurred only in nine (25%) patients, which were minor complications in the form of surgical emphysema and prolonged air leak, wound infection, dislodged drain, trapped lung, and pain during the procedure.

Conclusion Medical thoracoscopy is a good diagnostic procedure for pulmonologists to evaluate undiagnosed pleural effusions.

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pleuritis, the combined yield of histology and culture for rigid thoracoscopy has been reported to be nearly 100% [3]. In early studies, rigid thoracoscopy achieved a high diagnostic yield of 95% for malignant pleural diseases [4]. The aim of this study was to assess the diagnostic yield of medical thoracoscopy in patients with undiagnosed exudative pleural effusion.

Patients and methods

This prospective, uncontrolled clinical trial study was conducted at the Chest Department of Zagazig University Hospitals in the period from October 2014 to October 2015. The study was carried out on

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36 patients with undiagnosed exudative pleural effusion after failure to reach a definitive diagnosis by using thoracentesis and closed pleural biopsy.

Patients

Accessible patients of exudative pleural effusion were included in the study.

The patients who had any of the following criteria were excluded [5]:

- (1) Initial pleural fluid examination by using thoracentesis reaching a definitive diagnosis.
- (2) Not fit for performing thoracoscopy, as in the following cases:
 - (a) Patients with severe chronic obstructive pulmonary disease and consequent respiratory insufficiency, with hypoxemia ($\text{PaO}_2 < 60 \text{ mmHg}$) and hypercapnia ($\text{PaCO}_2 > 50 \text{ mmHg}$), who will not tolerate induction of a pneumothorax.
 - (b) When there is a contralateral lung or pleural involvement, thoracoscopy is not advisable, as patients cannot not withstand the lateral decubitus for a period long enough to undergo the procedure.
 - (c) Patients with unstable cardiovascular or hemodynamic status.
 - (d) Patients with coagulation defects. At least, the prothrombin activity should be greater than 60% and the platelet count should be greater than $60\,000/\text{mm}^3$.
 - (e) Patients with significant comorbidities such as coronary artery disease, uncontrolled diabetes mellitus, and uncontrolled systemic hypertension.
- (3) Recent history of chest trauma or proved hemothorax.
- (4) Absolute contraindications, as in the following conditions:
 - (a) Patients in whom the pleural space has been judged to be inaccessible, those who had their pleural space obliterated by the fibrous tissue, or those who were suspected of having multiloculated effusions.
 - (b) Patients with much thickened pleural, as demonstrated by computed tomography scanning, as it can impair the expansion of the underlying lung following the procedure.
 - (c) Patients with honey comb lung, as, after induction of pneumothorax, it can be difficult to re-expand the lung due to the loss of elasticity of the pulmonary tissue.

Methods

An informed and written consent was obtained from the patients.

Included patients were subjected to the following: full medical history, full clinical examination (general and local chest examination), plain chest radiograph (posteroanterior and lateral views), routine hematologic investigations [complete blood picture, erythrocyte sedimentation rate, liver function, kidney function, prothrombin time and activity and partial thromboplastin time, fasting and 2 h post-prandial blood glucose, and simultaneous measurement of pleural fluid glucose level, serum lactate dehydrogenase simultaneous with measurement of pleural fluid value of lactate dehydrogenase, serological analysis, which includes serum rheumatoid factor, and serum antinuclear antibody], pleural fluid aspiration (pleural fluid was aspirated from the patients and sent for full chemical, bacteriological, and cytological analysis), tuberculin skin test by using Mantoux maneuvers, sputum examination (Ziehl-Neelsen stain for acid fast bacilli), pelviabdominal ultrasound, chest ultrasonography, conventional contrast enhanced computed tomography, closed pleural biopsy, and thoracoscopic examination of the pleural space.

Technique

The standard equipment for thoracoscopy consists of a blind tip trocar, an obturator, an optical telescope, a light source, biopsy forceps (either optical or not), and a suction catheter [6]. The rigid thoracoscope used in this study was TEKNO (Tuttlingen, Germany). The length of the thoracoscope was 200 cm, outer diameter 7.5 mm, inner one 3.5 mm, and its working channel size was 4 mm. The procedures were carried out in our endoscopy unit using the full aseptic techniques with the patient under conscious sedation, which was achieved by intravenous midazolam (Midathetic ampoule; Amoun, Egypt, First industrial zone, Elobour city, Qalubia) with a loading dose of 0.01–0.05 mg/kg with or without fentanyl (fentanyl ampoule; Amoun) with an infusion rate of 0.7–10 $\mu\text{g}/\text{kg}/\text{h}$. Blood pressure, pulse rate, and transcutaneous oxygen saturation were monitored continuously throughout the whole procedure, and all patients received supplemental oxygen through the nasal cannulae. During the procedure, the patients were kept in the lateral decubitus position with the affected side upwards. The portal of the entry was usually at the mid-axillary line, between fourth and sixth intercostal spaces. Local anesthesia (2% lignocaine) was administered to the skin, subcutaneous tissue, muscle, and parietal pleura. Skin incision about 1–2⁰cm was

made with a scalpel, which was followed by blunt dissection of the intercostal muscles until the pleural space was reached. A rigid trocar 8 mm in size and its length 100 mm was inserted through the chest wall. Pleural fluid was then aspirated while air was allowed to enter the pleural space. A thorough examination of the pleural cavity was then undertaken by inserting the scope through the trocar. Pleural biopsy samples were obtained from the parietal pleura with biopsy forceps, particularly where it appeared abnormal. At least six biopsies were taken from each patient. Chest tube was introduced through the entry site at the end of the procedure. A chest radiograph was subsequently taken to monitor the re-expansion of the lung and check the position of chest tube, which was removed as soon as full lung expansion was achieved and the amount of pleural fluid drained less than 100 ml/day [7].

Statistical analysis

All data were collected, tabulated, and reformed for statistical analysis using the statistical package for the social sciences (SPSS version 19; SPSS Inc., Chicago, Illinois, USA). The results of this study were analyzed and presented as numbers and percentage or mean \pm SD. Student's *t*-test, analysis of variance, and the χ^2 -test (or Fisher's exact test) were used for comparisons between different groups. A *P*-value of less than 0.05 was considered significant and a *P*-value of less than 0.001 was considered highly significant [8].

Results

The study was conducted on 36 undiagnosed exudative pleural effusion patients – 18 males and 18 females, with a mean age of 54.4 ± 16.1 years. Overall, 52.8% of these patients were smokers, 61.1% were urban resident, and 63.9% were employers (Table 1).

Dyspnea was the most common symptom encountered among the studied patients (100%), followed by chest pain (91.7%) and cough (72.2%) (Table 2).

As regards different gross pictures at thoracoscopy, nodules were found in 27 (75%) patients, plaques in six (16.7%) patients, adhesions in eight (22.2%) patients, masses in five (13.9%) patients, and violaceous lesions in three (8.3%) patients (Table 3).

The histopathological yield of thoracoscopic pleural biopsies was as follows: 25 (69.4%) malignant cases, two (5.6%) patients with tuberculous pleuritis, one (2.8%) patient diagnosed with empyema, and another one (2.8%) with rheumatoid arthritis; and there were seven (19.4%) patients with nonspecific inflammation (Table 4).

The most common type of malignancy obtained by using thoracoscopic pleural biopsy in the studied group was malignant adenocarcinoma (25%), followed by malignant mesothelioma (16.7%) (Table 5).

Table 1 Sociodemographic criteria of the studied group

	Age (mean \pm SD) (years)		Sex		Smoking		Employment		Residence	
	Male	Female	Male	Female	Smoker	Nonsmoker	Employer	Nonemployer	Urban	Rural
<i>N</i>	56.8 \pm 16.4	52.0 \pm 16	18	18	19	17 (47.2)	23 (63.9)	13 (36.1)	18	18
(%)	(20–81)	(19–75)	(50.0)	(50.0)	(52.8)				(50)	(50)
Total	54.4 \pm 16.1	36 (100%)								
	(19–81)									

Table 2 Clinical data among studied patients

	Clinical symptoms					
	Dyspnea	Chest pain	Cough	Expectoration	Fever	Loss of weight
<i>N</i> (%)	36 (100)	33 (91.7)	26 (72.2)	11 (30.6)	2 (5.6)	5 (13.9)

Table 3 Different gross thoracoscopic findings of studied patients

	Gross findings				
	Nodules	Adhesions	Mass	Violaceous lesion	plaques
<i>N</i> (%)	27 (75)	8 (22.2)	5 (13.9)	3 (8.3)	6 (16.7)

Table 4 Histopathological results of different pleural biopsies of studied patients

	Histopathological results					
	Malignancy	TB	Rheumatoid arthritis	Empyema	Nonspecific pleurisy	Total
<i>N</i> (%)	25 (69.4)	2 (5.6)	1 (2.8)	1 (2.8)	7 (19.4)	36 (100)

TB, tuberculosis.

In the studied group, there were different histopathological presentations under the nodular gross picture where adenocarcinoma (100%) and mesothelioma (83.3%) were the most common (Table 6). On the other hand, the histopathology of mass lesions included squamous cell carcinoma (50%) and small cell carcinoma (33.3%) (Table 7).

The post-thoracoscopic complications in the studied group were surgical emphysema and prolonged air leak in three (8.3%) patients, pain during procedure in two (5.6%) patients, wound infection in two (5.6%) patients, and dislodged tube in two (5.6%) patients (the size of the chest tube was 24) (Table 8).

Discussion

Even after extensive diagnostic evaluation of a patient with pleural effusion, the etiology may remain unknown. Pleural fluid studies and blind pleural biopsy have their own limitations. Cytological examination is diagnostic in only 60–80% of the

patients with metastatic pleural involvement and in 20% of the patients with mesothelioma [9].

An additional closed pleural biopsy can increase the diagnostic yield in malignancy by only about 10%, because pleural metastases often locate at sites that are inaccessible [7].

Thoracoscopy is a valuable tool for the diagnosis of undiagnosed pleural effusions, particularly for patients with high probability of malignancy. Overall cost effectiveness of thoracoscopy is better in view of its better yield and lesser duration of hospital stay [10].

Thus, thoracoscopy becomes an important tool as the pleural surface can be visualized and representative sample can easily be picked. The concept of medical thoracoscopy is a simplification of video-assisted thoracoscopic surgery, as it is performed under conscious sedation through a single port by chest physicians at a bronchoscopy unit [2].

Table 5 Different pathological subtypes of malignant pleural effusion patients

	Malignant type						Total
	Metastatic adenocarcinoma	Mesothelioma	Small cell carcinoma	Squamous cell carcinoma	Undifferentiated carcinoma	Lymphoma	
N (%)	9 (25)	6 (16.7)	3 (8.3)	2 (5.6)	3 (8.3)	2 (5.6)	25 (69.4)

Table 6 Different pathological subtypes of gross nodular picture among studied patients

Nodules	Diagnosis							
	Metastatic adenocarcinoma	Mesothelioma	Undifferentiated carcinoma	Squamous cell carcinoma	Small cell carcinoma	Lymphoma	TB	Collagen
N (%)	9 (100)	5 (83.3)	2 (66.7)	2 (100)	2 (66.7)	2 (100)	1 (50)	1 (100)

TB, tuberculosis.

Table 7 Different pathological subtypes of gross mass picture among studied patients

Mass	Diagnosis			
	metastatic adenocarcinoma	Mesothelioma	Squamous cell carcinoma	Small cell carcinoma
N (%)	2 (22.2)	1 (16.7)	1 (50)	1 (33.3)

Table 8 Different complications of medical thoracoscopy among studied patients

Complications	N (%)
Shock	1 (2.8)
Bleeding	1 (2.8)
Pulmonary embolism	1 (2.8)
Pain during procedure	2 (5.6)
Surgical emphysema	3 (8.3)
Prolonged air leak	3 (8.3)
Trapped lung	2 (5.6)
Wound infection	2 (5.6)
Dislodged drain	2 (5.6)

Therefore, the aim of the present study was to assess the diagnostic yield of medical thoracoscopy in patients with undiagnosed exudative pleural effusion.

This study was conducted on 36 undiagnosed pleural effusion patients who were not diagnosed by either thoracentesis or closed pleural biopsy (18 men and 18 women patients). The mean age of the patients was 54.4 ± 16.1 years, with a range between 19 and 81 years.

In this study, dyspnea was by far the most common symptom among the studied patients (100%), followed by chest pain (91.7%), cough (72.2%), expectoration (30.6%), loss of weight (13.9%), and fever (5.6%). This was in agreement with the findings of a study by Law *et al.*[7] and Prabhu and Narasimhan [11], who reported that dyspnea was the main complaint of their studied pleural effusion patients.

Regarding the gross thoroscopic picture in the studied group, there were various types of macroscopic features such as nodules, adhesions, and masses in the pleura. Nodules were the most common gross lesion, as they were encountered in 27 (75%), whereas adhesions were encountered in eight (22.2%) patients, plaques in six (16.7%) patients, masses in five (13.9%) patients, and violaceous appearances in three (8.3%) patients. This may be attributed to a higher number of cases of metastatic adenocarcinoma that are mainly presented as nodules. A compelling support to our results was given by those of a study the Prabhu and Narasimhan [11] and Mohamed *et al.*[12] who reported similar findings, where nodules were the most common finding (48.5 and 82.5%, respectively), followed by adhesions (38.2 and 42.5%, respectively).

In our study, the most common yield of histopathological results of diagnosed patients was malignancy, found in 25/36 (69.4%) patients, followed by two (5.6%) tuberculous pleuritis cases, one (2.8%) patient diagnosed with rheumatoid arthritis, and other one (2.8%) diagnosed with empyema, but nonspecific pleurisy were found in seven (19.4%) patients. These results were in agreement with the results obtained in several studies, in which malignancy was the final diagnosis of most of the studied patients with undiagnosed pleural effusion, such as in respective studies by Mootha *et al.* [13], Helala *et al.*[14], Mohamed and Shaban [15], and Ali *et al.*[16], where malignant pleural effusion cases were 73, 70, 74.4, and 83.9%, respectively.

While our results regarding definite diagnosis were not consistent with other results which were very higher in other studies than our findings. This can be attributed to some obstacles we faced during some procedures, such as severe pain, which may be due to ineffective anesthesia and hard manipulation.

Among patients with malignant pleural effusion, metastatic adenocarcinoma was the most common pleural malignancy, encountered in nine (25%) patients, followed by mesothelioma in six (16.7%) patients, undifferentiated carcinoma in three (8.3%) patients, small cell carcinoma in three (8.3%) patients, squamous cell carcinoma in two (5.6%) patients, and lymphoma in two (5.6%) patients.

These results were in agreement with those of Mootha *et al.*[13] and Prabhu and Narasimhan [11], who reported that the most common pleural malignancy among studied patients was adenocarcinoma (20 and 22%). On the other hand, this was not consistent with the findings of Ali *et al.*[16] and Mohamed and Shaban [15], who reported that most cases of malignant pleural effusion were diagnosed as mesothelioma (54.9 and 47%, respectively), followed by adenocarcinoma (14.1 and 22.2%, respectively).

This could be attributed to the fact that the most common cause of malignant pleural effusion is metastatic adenocarcinoma of the lung, breast, and ovaries [17].

In this study, nodules were the gross picture of different histopathological subtypes of diagnosed cases of pleural effusion after medical thoracoscopy. It was the most common gross finding in patients who were diagnosed with metastatic adenocarcinoma (100% of cases); this higher percentage of metastatic adenocarcinoma, which proved to be in thoroscopic nodules, could be explained by the implantation theory of pleural metastasis and hematogenous dissemination [15]. Metastatic adenocarcinoma were followed by five (83.3%) patients with mesothelioma, two squamous cell carcinoma cases, two lymphoma cases, and one collagen vascular patient. Near similar results were reported by Mohamed and Shaban [15], who reported 25 patients from a total of 26 patients with nodular gross appearance who were diagnosed with adenocarcinoma, and other 18 patients from a total of 55 patients who were diagnosed with mesothelioma.

In our study, pleural mass lesion was also commonly detected in patients who were diagnosed with squamous cell carcinoma (50%), followed by patients

who were diagnosed with adenocarcinoma (22.2%); one (33.3%) patient was diagnosed with small cell carcinoma and one (16.7%) patient with mesothelioma. This was in contrast to the findings of Mohamed and Shaban [15], who reported that pleural mass lesion most commonly presented in patients with mesothelioma (22 patients), followed by patients with adenocarcinoma (one patient) among 25 patients who presented with pleural mass.

Serious complications following thoracoscopy are rare. In the present study, there was no reported mortality among the studied patients. The most common complications that were reported in our study were minor complications. The post-thoracoscopic complications occurred in nine cases (25% of the studied patients). Surgical emphysema and prolonged air leak occurred in three (8.3%) patients. Pain during procedure and wound infection occurred in two (5.6%) patients. The results of several studies were in agreement with the above-mentioned results. In their study, Mohamed and Shaban [15] reported no mortality and no major complications; however, minor complications reported by them included subcutaneous emphysema (two patients), prolonged air leak (one patient), wound infection (11 patients) and empyema (11 patients).

Three major complications were reported in this study in the form of shock, which was reported in only one patient who was neurogenic in type due to high irritability of the patient and improper sedation, but was controlled within few minutes. In addition, massive bleeding during the procedure was reported in one patient, with discontinuation of procedure; the bleeding was controlled within few minutes but the cause of bleeding remained unknown. Pulmonary embolism was also reported in one patient after 10 days of procedure; this patient was diagnosed as malignant, which explained the hypercoagulable state. This was in agreement with the findings of Brims *et al.*[18], who reported major complications during their study in the form of hypotension, which was reported in four (7%) patients. Moreover, Mootha *et al.*[13] reported hemorrhage (0.3–0.4%) and shock (0.2%) as major complications in their study.

Shawgo [19] reported that the main risks of thoracoscopy are those associated with early complications after the procedure, such as pulmonary edema and excessive bleeding and/or hemorrhage, which may need a thoracotomy to stop it. In their retrospective study, Blanc *et al.*[20] classified thoracoscopic complications detected into major

complications, which included death, severe sepsis, pulmonary embolism, and hypercapnic coma; these were of equal incidence of percentage (0.6%), whereas empyema was detected in 3.6% of the cases. On the other hand, minor complications included residual pneumothorax (8.3%), subcutaneous emphysema (5.3%), and fever (3.6%); furthermore, opiates were prescribed in 1.2% of the cases to control the post-procedure chest pain.

Conclusion

Medical thoracoscopy is a good diagnostic procedure for pulmonologists to evaluate undiagnosed pleural effusions after thoracentesis and closed pleural biopsy. This procedure is safe and well-tolerated under local and conscious sedation. Proper case selection and accumulation of experience will improve the diagnostic and therapeutic utility of the procedure.

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Conflicts of interest

There are no conflicts of interest.

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