

# Diagnostic Yield of Medical Thoracoscopy in Undiagnosed Pleural Effusion

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## INTRODUCTION

Pleuroscopy is a complicated technique that aids in the diagnosis of 25% of pleural effusions (1) that remain undiagnosed despite primary tests such as biochemical tests, thoracocentesis and biopsy. Pleuroscopy is an accepted procedure in Europe and in the United States; however, in Asia, it is used only in a few countries, and because it is a new procedure, the outcomes, the frequency of misdiagnoses, and the resulting complications are different from those experienced by the European and American patients.

**Background:** One of the most common indications for pleuroscopy is undiagnosed pleural effusion, which comprises about 25% of all cases of pleural effusions, which remain undiagnosed despite primary tests. Pleuroscopy was performed for the first time in Iran in Masih Daneshvari hospital located in Tehran. The aim of this study was to assess the diagnostic yield of pleuroscopy performed in this center in Iran.

**Materials and Methods:** Three-hundred patients with undiagnosed pleural effusions were enrolled in this study. For all patients, primary tests including pleural effusion analysis, cytology and closed pleural biopsy (if needed) were conducted and all of them were inconclusive. The semirigid thoracoscopy (pleuroscopy) was performed for all patients for diagnostic purposes.

**Results:** Eighty-seven percent of the pleuroscopies were diagnostic and 67% of them were diagnosed as malignancy while the rest were diagnosed as tuberculosis. Only 11 patients developed minor complications.

**Conclusion:** In conclusion, pleuroscopy is a safe procedure when performed by a skilled and experienced practitioner; it has a high diagnostic yield and results in only minor complications.

**Key words:** Pleuroscopy; Pleural effusion; Diagnosis; Thoracoscopy

Observation of the pleural cavity by pleuroscopy dates back to 1991(2). Over the ensuing decades, and particularly in this new era of high-tech video endoscopy and advanced anesthesiology, pleuroscopic diagnosis has become increasingly effective. Pleuroscopy is associated with a small probability of major complications (1.95%)(3), and mortality is very rare, similar to the risks of transbronchial biopsy (0.22-0.66%) and mediastinoscopy (0.17%)(4). Furthermore, pleuroscopy can be used multiple times without any risk of death or disability (5).

Clinicians in three Asian countries currently use this technique, and researchers in these countries have reported their results in patients with undiagnosed pleural effusions. With “success” defined as conclusive diagnosis, researchers in Thailand (6) reported the use of pleuroscopy in 86 patients with a success rate of 95.2%; researchers in Hong Kong (7) reported a success rate in 20 patients with 70% success rate; and researchers in India reported a success rate of 74.5% (8).

The aim of this study was to demonstrate the utility of pleuroscopy in patients with diagnostically unclear pleural effusions.

## **MATERIALS AND METHODS**

This study included all patients referred to Masih Daneshvari Hospital in Tehran, Iran, from June 2013 to April 2015 with undiagnosed pleural effusion despite primary tests, such as thoracentesis, biochemical and serological tests, and closed pleural biopsy. Pleuroscopies were done in the bronchoscopy ward where bronchoscopic procedures were performed. Written informed consent for medical thoracoscopy was obtained from the patients. All patients underwent primary tests, including pleural fluid analysis, which examined pleural fluid protein level, glucose level, cell count and differentiation, and lactate dehydrogenase level; pleural fluid serologic test, which was conducted three times, and closed pleural biopsy if needed according to the patient’s computed tomography (CT) scan results. All primary tests of all patients were inconclusive. If patients underwent a procedure for therapeutic purposes, they were excluded from the study. If they were hemodynamically unstable, they were excluded from the study as well because of the increased risk of hemorrhage. Patients with platelet levels less than 75,000/microL and prothrombin time (PT) of more than 10 seconds were also excluded.

We recorded basic patient information, including age, sex, results of lab tests including complete blood count, coagulation (PT, partial thromboplastin time and international normalized ratio), medication history,

medical history (including chronic diseases such as hypertension and diabetes mellitus), and any history of coagulopathy and cardiac diseases.

The pleuroscopy team comprised one or two pulmonary fellows, one faculty member, and one or two nurses to assist during the procedure.

Patients were positioned in the lateral decubitus position with the pleural effusion side facing up and their hands were positioned over their heads to widen the intercostal space. Cardiac monitoring and oxygen saturation were observed during the procedure. Patients received oxygen via nasal cannula during the pleuroscopy.

After administration of local anesthesia (lidocaine 10%), a 1-cm incision was made on the mid-axillary line above the costal ridge over the intercostal space. The location of thoracoscope entry was mainly between the 4th and 7th intercostal space, but if sonography and CT scan results indicated lower pleural cavity abnormalities, the pulmonologist inserted the thoracoscope through lower incisions. After thorough visualization of the pleural cavity, biopsies were taken from abnormal findings and preserved in formalin for histopathological analysis and in normal saline for mycobacterial cultures.

After the procedure, a chest tube was inserted in the place of the thoracoscope insertion. Also after the procedure, a control chest X ray was taken from all patients for probable pneumothorax, which sometime happens after the procedure. All patients were under observation for 2 hours and were then discharged with the recommendation to visit their pulmonary physician in the coming weeks for clinical follow-up.

SPSS 18 software was used for statistical analysis. Descriptive analysis was performed. Categorical variables were reported as frequency (%), and quantitative variables were reported as mean  $\pm$ SD.

## **RESULTS**

Three-hundred patients with undiagnosed pleural effusion were included in this study. The patients’ mean

age was  $51 \pm 14.7$  years (range: 34-73 years). There were 192 (64%) men and 108 (36%) women. Sixty-one percent had right-sided pleural effusion and 39% had left-sided pleural effusion. Large, medium, and small pleural effusion was detected in 29%, 48%, and 23% of patients, respectively.

In this study, adhesion, nodule, inflammation, and mass were abnormal pleuroscopy findings. Two-hundred and sixty-one patients (87%) had definitive thoracoscopic pleural biopsy, and 39 (13%) expressed nonspecific inflammation, or there was inadequate sample present. Twelve patients with empyema underwent adhesiolysis during pleuroscopy. In the group of patients with definitive diagnosis, 165 (63%) had malignancy; other patients were diagnosed with tuberculosis. Of those 39 patients with undiagnosed pleuroscopy, four underwent open-lung biopsy, which resulted in a diagnosis of adenocarcinoma. The remaining patients with undiagnosed pleuroscopy did not consent to undergo video-assisted thoracoscopy (VAT) or open-lung biopsy.

According to clinical findings, 20 patients were recommended to be under close observation, and 15 patients were diagnosed with uremia, pleural effusion, tuberculosis, abdominal abscess, heart failure, pulmonary thromboembolism and rheumatoid arthritis.

Among malignant histopathological diagnoses, adenocarcinoma was the most prevalent (67%), followed by small-cell carcinoma (25%) and mesothelioma (8%).

Minor complications related to the procedure occurred in only 11 patients: 5 cases of subcutaneous emphysema, 4 cases of minor bleeding, and 2 cases of mild fever; all of which were cured with conservative measures.

Two patients died because of ventricular fibrillation on the day of pleuroscopy. The patients were unresponsive to resuscitation. Both patients were discovered to have highly advanced adenocarcinoma.

## DISCUSSION

This study enrolled 300 patients who underwent pleuroscopy for pleural effusion. All of their primary tests were inconclusive. Two-hundred sixty-one (87%) of the

pleuroscopic procedures were diagnostic; of these, 63% resulted in a diagnosis of malignancy, and the rest resulted in a diagnosis of tuberculosis.

Pleural cavity inspection was first performed in 1910, mainly for tuberculosis-led pneumothorax diagnosis, and the utility of the procedure decreased with new and effective tuberculosis medications (2). One of the most prevalent indications for pleuroscopy is undiagnosed pleural effusion; of these cases, 50% will eventually turn out to be malignant pleural effusions (9).

VAT is another technique with more diagnostic yield for pleural abnormality detection as compared to pleuroscopy, which is more aggressive, not available in all centers, and is one of the two diagnostic modalities (the other is open-lung surgery, performed for two of our patients with undiagnosed pleuroscopy) performed when pleuroscopy results are inconclusive (10).

There are two types of thoracoscopy: rigid thoracoscopy and semi-rigid thoracoscopy (pleuroscopy). Semi-rigid thoracoscopy (pleuroscopy) was first used in 1970 (11) and was designed for pulmonologists who were familiar with bronchoscopy instruments. In the past, pulmonologists performed rigid thoracoscopy under local anesthesia. Because the procedure is relatively invasive under local anesthesia and also because of pulmonologist's unfamiliarity with rigid instruments, it was not popular (12).

Although rigid thoracoscopy can obtain samples with higher diagnostic value than semi-rigid thoracoscopy (specifically regarding mesothelioma diagnosis)(13,14), when rigid thoracoscopy is not available, semi-rigid thoracoscopy can yield diagnoses that are comparable in prevalence.

Definitive contraindications of pleuroscopy are pleural adhesions, patients unable to lie in the lateral decubitus position, and patients with severe coagulopathy; severe cough and hypoxia are relative contraindications (15). In our study, all the necessary tests were conducted prior to the pleuroscopy procedure, and the patients' physical status was thoroughly assessed.

Major complications of the procedure include ventricular tachycardia that is unresponsive to resuscitation, continuous air leak, and extensive subcutaneous emphysema. Minor complications include minor bleeding, mild fever, and temporary air leaks (3,4). In our study, minor complications occurred in only 3% of patients, which is less than a study in Canada (3) that reported a minor complication rate of 5.5%.

In a study in Thailand (6) among 142 patients arranged to undergo pleuroscopy, 86 pleuroscopies were performed for patients with undiagnosed pleural effusions; diagnostic yield was 95%. Malignancy, found in 45% of cases, was the most common diagnosis.

In a study in Hong Kong (7), of 20 patients with exudative pleural effusion who underwent pleuroscopy, this procedure was diagnostic for 14 (70%) patients. Minor complications, such as self-limited fever, local emphysema, and temporary air leak occurred in 20% of patients, and no deaths were reported.

In studies done in India (16-19), diagnostic yield of pleuroscopy was found to be 67%, 73%, 80%, and 97% in studies with sample sizes of 21, 45, 25, and 68 patients, respectively. Among all the diagnoses, malignancy was the most common, and in those cases the most common finding was adenocarcinoma; the second prevalent finding was tuberculosis except in one study (18) which pleuritis was more prevalent than tuberculosis. In two studies (16,18), no significant complication was reported. One other study (19) reported minor complications in 5% of patients, which is a rate similar to the one found in our study (5.3%). Yet another study reported a minor complication rate of 13% and major complication rate of 6% among 45 patients (17).

In a study conducted in Egypt, pleuroscopy was performed in 40 patients with exudative pleural effusion; 95% of the procedures were conclusive among diagnosed pleural effusions; 28 patients presented with pleural nodule and 10 patients of these 28 patients were diagnosed with mesothelioma, which had a higher prevalence in comparison with other studies (20).

Loddenkemper (21) demonstrated the diagnostic yield

of pleural effusion analysis, closed pleural biopsy and medical thoracoscopy for malignancy and tuberculosis, which was 62% and 28%, respectively after pleural fluid was analyzed, 44% and 51%, respectively after closed pleural biopsy was performed, 74% and 61%, respectively by the two mentioned tests combined and 95% and 99%, respectively after pleuroscopy was done.

A limitation of our study was the bias caused by assessing patients referred to a tertiary center (Masih Daneshvari Hospital) where all tuberculosis and complicated lung disease patients are referred. Also, the refusal of some patients with undiagnosed pleural effusion after pleuroscopy to undergo VAT or open-lung biopsy led to some pleural effusions remaining undiagnosed.

In conclusion, pleuroscopy is a safe procedure when performed by a skilled and experienced practitioner; it has a high diagnostic yield and results in only minor complications. It is recommended for patients with undiagnosed pleural effusions.

#### Conflict of interest

The authors declare no conflict of interest.

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