Effectiveness of Video-Assisted Thoracoscopic Surgery in Undiagnosed Exudative Pleural Effusions

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Cite this article as: Dadaş E, Erdoğdu E, Toker A, et al. Effectiveness of Video-Assisted Thoracoscopic Surgery in Undiagnosed Exudative Pleural Effusions. Turk Thorac J 2019; DOI: 10.5152/TurkThoracJ.2018.18133.

OBJECTIVES: Undiagnosed pleural effusions mostly require histologic studies for a definite diagnosis. In addition, malignant pleural effusions responsible for a significant part of exudative pleurisy need palliative therapy. The purpose of our study is to research the effectiveness of video-assisted thoracoscopic surgery in definitive diagnosis and palliative treatment of unexplained non-parapneumonic exudative pleural effusions.

MATERIALS AND METHODS: The study included 263 patients with non-parapneumonic exudative pleurisy, which could not be diagnosed by an initial clinical, radiological, biochemical, microbiological, and cytological investigation in three centers. All patients underwent video-assisted thoracoscopic surgery for definitive diagnosis between January 2002 and January 2018. Patients’ data were retrospectively analyzed in terms of age, gender, symptoms, previously diagnosed cancers, computerized tomography of chest findings, histopathological diagnosis, cytological diagnosis, morbidity, mortality, and success rates of the procedure. Patient groups from the three centers were divided into three groups according to the center of the patient. The groups were compared statistically in terms of cytologic diagnosis rates.

RESULTS: The most common complaint was dysnea (66.5%). Of the 263 cases, 83 were previously diagnosed with cancer. The simple pleural effusion (66.5%) was the most frequent radiological finding. The success rate for definitive diagnosis was detected as 97%. Of all the cases, the rate of specific cytological diagnosis was detected to be 34%. The cytologic diagnosis rate was meaningfully lower in Group 1 than in Groups 2 and 3. The postoperative morbidity rate was detected as 9%.

CONCLUSION: Video-assisted thoracic surgery is not only a rapid and effective diagnostic method, but also a palliative therapeutic method. We think that it should be used immediately after initial diagnostic thoracentesis in undiagnosed exudative PE in the less experienced centers.

KEYWORDS: Exudative pleural effusion, definitive diagnosis, palliative therapy, video-assisted thoracoscopic surgery

INTRODUCTION

Pleural effusions (PE) represent extreme accumulation of pleural fluid in the pleural space, due to infectious and infiltrative pathologies affecting the pleura and lungs or resulting from impaired balance between the pleural fluid production and absorption as a consequence of various systemic diseases [1]. Congestive heart failure, pneumonia, and malignancy are the most common PE causes [2].

Pleural effusions obtained by diagnostic thoracentesis is divided into transudate and exudate fluid, according to light criteria [1]. There is usually no need for advanced laboratory and interventional diagnostic procedures in transudative PE. In the case of exudative pleurisy, precise etiologic diagnosis requires advanced biochemical and microbiological laboratory procedures, cytological studies, and tissue biopsies [3].

The purpose of our study was to investigate the effectiveness of video-assisted thoracic surgery (VATS) in diagnosis and palliative treatment of unexplained non-parapneumonic exudative PEs.

MATERIALS AND METHODS

This retrospective multicenter study conducted in three centers between January 2002 and January 2018 included 263 patients with non-parapneumonic exudative pleurisy that could not be diagnosed by initial clinical, radiological, biochemical, microbiological, and cytological investigations. The biochemical analyzes of pleural fluid included measur-
ing sugar, protein, triglycerides, and lactate dehydrogenase, while the microbiological analyses consisted of Gram stain, acid fast bacillus smear, and culture, and the pleural fluid adenosine deaminase (ADA) level measurements. All patients underwent detailed clinical evaluations with disease history and clinical examinations. Chest computerized tomography (CT) was performed to evaluate the pleural and parenchymal pathologies and assess the feasibility of thoracoscopy. All patients underwent VATS for definitive diagnosis and, if necessary, palliative therapy. The patients who could not undergo thoracoscopy due to advanced adhesions and did not tolerate general anesthesia or lung ventilation were not included in the study. All the patients underwent general anesthesia and double-lumen intubation at the lateral decubitus position. First, we placed a 10-mm port in the sixth intercostal space at the mid-axillary line and the second port in the fourth intercostal space at the anterior axillary line. After the lung was deflated and all pleural surfaces were observed, pleural fluid was fully aspirated and sent for cytology and culture. Biopsies were taken from the pathological lesions on the pleura. Talc pleurodesis was performed in each case diagnosed as malignant pleurisy by thoracoscopic observation. The trucut biopsies were performed incases where a lung mass was detected by chest CT. Also, patients with a peripheral pulmonary nodule underwent wedge resection by endostapler. Hemostasis was controlled by electrocautery. The procedure was completed by inserting a chest tube in the telescopic incision. The lung expansion was checked by chest X-ray. The chest drains were removed when the lung expanded and drainage was less than 50 mL per 24 hours.

Patients’ data were retrospectively analyzed in terms of age, gender, symptoms, previously diagnosed cancers, chest CT findings, histopathological diagnosis, cytological diagnosis, morbidity, mortality, and procedure success rates. Patient groups from the three centers were divided into three groups according to the center of the patient. The groups were compared statistically in terms of cytologic diagnosis rates. The Ethics Committee of Adıyaman University Medical School approved the study protocol (5/22/2018, 2018/4-6).

**Statistical Analysis**

We conducted the study according to the principles of the Declaration of Helsinki. We used the Statistical Package for the Social Sciences (SPSS Inc.; Chicago, IL, USA) software for statistical analysis. A chi-squared test was utilized to compare the differences between the groups. A p-value < 0.05 was considered to be statistically significant.

**RESULTS**

The majority of cases were male patients (161 males and 102 females). The most common complaint was dyspnea 66.5%. One hundred and eighty cases had no malignant disease, whereas 83 cases had previously diagnosed cancer. Single PE (66.5%) was the most frequently observed radiological finding. Clinical and radiological characteristics of 263 patients are presented in Table 1. The histopathological data could be obtained from 249 of 263 patients. The definitive diagnosis was achieved in 242 (97.2%) of 249 patients, while the specific diagnosis was not obtained in only 7 (2.8%) patients. The success rate for definitive diagnosis was detected at 97%. The success rate of palliative therapy was found to be 95%. The histopathological characteristics are presented in Table 2. Cytopathological data were obtained from 195 patients. The specific cytological diagnosis was set in only 67 of 195 patients. The cytologic diagnosis rate was significantly lower in Group 1 than in Groups 2 and 3 (p=0.000).

| Table 1. Clinical and radiological characteristics |
|---------------------------|------------------|
| Variables                | Number (%)       |
| Mean age (year)          | 59.54±14.92      |
| Gender                   |                  |
| Male                     | 161 (61.2)       |
| Female                   | 102 (38.8)       |
| Symptoms                 |                  |
| Dyspnea                  | 175 (66.5)       |
| Chest pain               | 41 (15.6)        |
| Cough                    | 34 (12.9)        |
| Weight loss              | 4 (1.4)          |
| Hemothysis               | 7 (2.7)          |
| Fever                    | 2 (0.8)          |
| Previously diagnosed cancers |           |
| Lung cancer              | 36 (13.7)        |
| Extrathoracic cancers    | 47 (17.9)        |
| Total                    | 83 (31.6)        |
| Chest CT findings        |                  |
| Single pleural effusion  | 175 (66.5)       |
| Pleurisy + pleural nodule/Diffuse thickening | 50 (19.0)       |
| Pleurisy + Lung mass     | 38 (14.5)        |
| CT: computed tomography  |                  |

| Table 2. Histopathological characteristics |
|--------------------------------------------|
| Histopathologic diagnoses                | Number (%) |
| Malign disease                            |            |
| Lung cancer                               | 52 (20.9)  |
| Malignant pleural mesothelioma            | 39 (15.7)  |
| Breast cancer                             | 17 (6.8)   |
| Gastric cancer                            | 5 (2)      |
| Non-Hodgkin lymphoma                      | 4 (1.6)    |
| Soft tissue sarcoma                       | 3 (1.2)    |
| Undifferentiated round cell tumor          | 3 (1.2)    |
| Others                                    | 11 (4.2)   |
| Total                                     | 134 (55)   |
| Benign diseases                           |            |
| Chronic nonspecific inflammation          | 67 (26.9)  |
| Tuberculosis                              | 19 (7.6)   |
| Reactive mesothelial hyperplasia           | 16 (6.4)   |
| Others                                    | 6 (2.4)    |
| Total                                     | 108 (45)   |
behind the VATS [15,16].

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pproximately 60% in patients with MP [11]. Factors such as the type 
of tumor, pleural tumor burden, and expertise of the cytolo 
gist determine the success rate of cytologic diagnostic studies 
[12]. Traditionally, when the pleural fluid cytologic diagnos 
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As a more current practice, the pleural biopsy can be per 
formed under the guidance of a chest CT or ultrasound 
(USG). According to a prospective study performed by Metintas et al. [17], diagnostic sensitivity of the chest CT 
guided-needle pleural biopsy in patients with PE is approxi 
mately 82%. It was detected that the chest USG-guided 
needle pleural biopsy had a 66% diagnostic sensitivity in 
the same study. But the imaging-guided pleural biopsies re 
quire experienced interventional radiologists, and it is not 
possible in all hospitals. In general, approximately 50% of 
all patients with PE cannot be diagnosed after the initial 
diagnostic thoracentesis [8].

Because of the limiting reasons mentioned above, in many 
centers including ours, a non-diagnostic thoracentesis is 
followed by thoracoscopy [18]. Our study showed that 
the most common symptom and chest CT finding were dyspnea and single PE. The clinical and radiological fea 
tures were similar to the world literature [5,18,19]. We 
detected that in our large study group, VATS had high 
diagnostic success with favorable morbidity and mortality 
rates. In our study, which included patients from three dif 
fent centers, the rate of cytologic specific diagnosis was 
similar to the one in the world literature in Groups 2 and 3 
[11,20]. However, the rate of cytologic specific diagnosis 
in Group 1 was very low, which should be taken under 
consideration. There is no doubt that the reason for this 
is the absence of an experienced cytopathologist in this 
center. Furthermore, it should also be kept in mind that the 
presence of experienced interventional radiologist outside 
advanced centers is almost impossible. Therefore, since 
there are no experienced radiologists and cytologist in our 
center, it is almost impossible to diagnose pleural patholo 
gies with pleural biopsy by imaging or cytology of pleural 
fluid. Moreover, single PE is the most frequently observed 
radiological feature for PE, and therefore, the probability of 
a diagnostic closed pleural biopsy is very low. On the 
other hand, we believe that rapid and highly successful 
diagnostic methods should be used early on in cases of 
unexplained exudative PE due to the need for definitive 
diagnosis, initiation of specific or palliative treatment, and 
prognosis determination.

DISCUSSION

Many recent studies have investigated some novel cancer bio 
markers including ADA, tumor necrosis factor, interleukin-6, 
ceroreactiveprotein, carcinoembryonic antigen [4], vascular 
endothelial growth factor [5], reactive oxygenemetabolites 
[6], and ceruloplasmine [7] in pleural fluid for discriminating 
between malignant pleurisy (MP) and benign pleurisy (BP), but 
there is still a lack of diagnostic MP markers with sufficient 
sensitivity and specificity, which drove us to find and test novel 
biomarkers [8,9]. Of these biomarkers, only ADA shows high 
sensitivity and specificity for tuberculosis (TBC) pleurisy. If a 
patient has a lymphocytic pleurisy and an ADA level greater 
than 45 U/mL., it is highly probable that PE is dependent on the 
TBC pleuritis. In such patients, it is not necessary to confirm the 
diagnosis of TBC pleuritis by pleural biopsy [10].

Cytologic studies of the pleural fluid may reveal if pleurisy 
is malignant or benign. A positive cytology rate is approxi 
mately 60% in patients with MP [11]. Factors such as the type 
of tumor, pleural tumor burden, and expertise of the cytolo 
gist determine the success rate of cytologic diagnostic studies 
[12]. Traditionally, when the pleural fluid cytologic diagnos 
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behind the VATS [15,16].

The cytological characteristics are presented in Table 3. The 
postoperative morbidity rate was detected as 9% (n=24; Ta 
ble 4). Also, the mortality rate was 2.7% (n=7).

Table 3. Cytopathological characteristics and comparison of three study groups

| Morbidities | Group 1 (%) | Group 2 (%) | Group 3 (%) | p* |
|-------------|-------------|-------------|-------------|----|
| Specific diagnosis established | 1 (2.2) | 41 (41.8) | 25 (48.1) | 0.000 |
| No specific diagnosis established | 44 (97.8) | 57 (58.2) | 27 (51.9) | 0.000 |
| Total number | 45 | 98 | 52 | 0.000 |

*Pearson chi-squared test; Group 1: Adıyaman University School of Medicine, Thoracic Surgery Department; Group 2: Istanbul University 
Istanbul School of Medicine, Thoracic Surgery Department; Group 3: University of Health Sciences Istanbul Dr.Siyami Ersek Thoracic and 
Cardiovascular Surgery Training and Research Hospital, Thoracic Surgery Department

Table 4. Postoperative morbidities

| Morbidities | Number (%) |
|-------------|------------|
| Prolonged airleak | 7 (2.7) |
| Prolonged drainage | 6 (2.3) |
| Pneumonia | 3 (1.1) |
| Atrial fibrillation | 3 (1.1) |
| Expansion defect | 2 (0.8) |
| Hemorrhage | 2 (0.8) |
| Wound infection | 1 (0.4) |
| Total | 24 (9.1) |
Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Adıyaman University Medical School (5/22/2018, 2018/4-6).

Informed Consent: Due to the retrospective design of the study, informed consent was not taken.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - E.D.; Design - E.D.; Supervision - A.T., T.O.; Resources - E.D.; Materials - E.D., E.E.; Data Collection and/or Processing – E.D., E.E., N.E.; Analysis and/or Interpretation - E.D., E.E.; Literature Search - E.D., E.E., N.E.; Writing Manuscript - E.D.; Critical Review - A.T.; Other - T.O.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

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