

Comparing the diagnostic accuracy of semi-rigid and rigid pleuroscopy in diagnosis of exudative lymphocyte dominant pleural effusion with

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ABSTRACT

Background and Objectives: Pleuroscopy is an appropriate technique for visualization and biopsy of the pleural lesions, performed by two different techniques. In this study, we aimed to investigate the diagnostic accuracy of semi-rigid and rigid pleuroscopy in patients with lymphocyte dominant exudative pleural effusion. **Materials and Methods:** In this study, patients with lymphocyte dominant pleural effusion with negative results for tuberculosis who referred to Imam Khomeini Hospital, Ahvaz, Iran; from 2018 to 2019 were selected by census method and randomized to undergo semi-rigid or rigid pleuroscopy (30 in each group). Patients' demographic, such as age and gender, were recorded and the pathologic results reported by the two pleuroscopy methods were compared and sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were reported for each method. All statistical analyses were performed using SPSS v. 21. **Results:** Thirty patients were included in each group. The frequency of tuberculosis, malignancy, and other causes of pleural effusion had no difference between the two methods ($P > 0.05$). Semirigid pleuroscopy had a sensitivity of 81.5%, specificity of 66.6%, PPV of 75.6%, and NPV of 74%, while the relevant values in rigid pleuroscopy were 87.2%, 68.4%, 87.2%, and 68.4%, respectively. **Conclusion:** These results, consistent with previous studies, indicated that both semi-rigid and semi-flexible pleuroscopy methods are accurate for diagnosis of lymphocyte dominant pleural effusion when performed by skilled specialists and other considerations, such as availability and costs, can be used for selection of each method.

Keywords: Pleural effusion, sensitivity and specificity, thoracoscopy

Introduction

Pleural effusion refers to the abnormal fluid accumulation in pleural space, as a result of imbalance between formation and removal of the pleural fluid.^[1] Pleural effusion is not a disease

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itself, but a presentation of a disease;^[2] therefore, its prevalence and management depends on the underlying diseases,^[3] which not only include diseases inside the thorax (like pulmonary and cardiac diseases), but also outside the thorax (such as hepatorenal diseases).^[1] Radiologic examination and other imaging techniques can confirm the diagnosis of pleural effusion, but cannot diagnose its cause,^[4] therefore, analysis of the fluid by thoracentesis can categorize help diagnosis of the underlying disease and narrow the differential diagnosis.^[5,6] by categorizing the pleural fluid into transudative and exudative based on Light's criteria (levels of lactate dehydrogenase (LDH) and protein) or

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measurement of other parameters in the pleural fluid (such as pH, amylase, triglyceride, procalcitonin, and tumor markers).^[7-9]

Other tools are also used for diagnosis of the cause of pleural effusion, such as ultrasonography, radiography, and other imaging techniques, while direct observation is considered the most accurate diagnostic tool.^[10] One of the methods with direct observation is video assisted thoracic surgery (VATS), which can help diagnosis and management at the same time, but it requires general anesthesia and is therefore associated with the risk of complications.^[11] Pleuroscopy or medical thoracoscopy is a minimally invasive technique,^[12] which inserts trocars (by single or double puncture) into the thorax under local anesthesia.^[13] It is a safe and well-tolerated procedure, most commonly used in cases with exudative pleural effusion, and is considered as an appropriate alternative to VATS.^[14] It can not only provide direct observation, take biopsies, and drain the pleural fluid, but also enables management, such as pleurodesis.^[15] It can be performed using rigid or flexible (semi-rigid or flex-rigid) scopes, each with their own advantages and disadvantages.^[16]

Examination of different angles of the pleural space with a rigid metal tube can impose pressure on the ribs and increase patients' discomfort, while the smaller diameter and flexible tip of the flex-rigid thoroscopes allow for maneuvering between the ribs and thorough examination of pleural surfaces.^[17] On the other hand, the larger working channel provided by the rigid technique allows for larger biopsy specimens, which specimens of flexible thoroscopes are also adequate.^[18] Although the technical differences between have been outlined, few studies have compared the diagnostic accuracy of the two techniques of pleuroscopy,^[19,20] while none have addressed its diagnostic accuracy in cases with lymphocyte dominant exudative pleural effusion. Therefore, in this study, we aimed to investigate the diagnostic accuracy of flexible and rigid pleuroscopy in patients with lymphocyte dominant exudative pleural effusion.

Materials and Methods

Study design

This study included all patients who referred to Imam Khomeini Hospital, Ahvaz, Iran, from 2018 to 2019 for thoracoscopic examination. The protocol of the study was approved by the Ethics Committee of Jundishapur University of Medical Sciences (code: IR.AJUMS.REC.1398.201) the date of the approval was in September 2019. The study sample size was calculated at 30 in each group and patients who had the inclusion criteria were considered for recruitment into the study. First, the researcher explained the study objectives to the eligible patients and asked them to read and sign the written informed consent.

The inclusion criteria for this study consisted of patients with lymphocyte dominant pleural effusion with negative results for tuberculosis (TB) who referred to the study place during the study period and gave consent to participate in the study. The characteristics of pleural fluid were determined based on the

results of pleurocentesis; lymphocyte dominant was defined as >50% lymphocytes in the pleural fluid.

Patients' demographics, including age and gender were extracted from the patients' records. The eligible patients were randomized by table of random numbers, to undergo semi-rigid or rigid pleuroscopy (30 in each group). The procedures were performed by collaboration of Thoracic surgeon and pulmonologist using Olympus (EVIS EXERA LFT-160) Rigid and semi-rigid pleuroscopes. The results of thoracoscopic examination were recorded by the researcher. One biopsy was taken from all patients and sent to the laboratory for examination by an experience pathologist. Patients with unsuccessful biopsy were excluded from the study. The results of each of the methods were compared with the pathologic results and the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were reported for each method.

Statistical analysis

The collected data were input into the statistical software IBM SPSS Statistics for Windows version 21.0 (IBM Corp. 2012. Armonk, NY: IBM Corp.), used for all of the statistical analyses. First, the descriptive results were reported by mean \pm standard deviation (SD) for quantitative variables and by frequency (percentage) for categorical variables. One-sample KolmogorovSmirnov test showed that data were normally distributed ($P > 0.05$) and the equality of variances was confirmed by the Levene's test ($P = 0.180$). Continuous variables were compared between the groups using *t* test and categorical variables were compared using Chi-square test. The sensitivity, specificity, PPV, and NPV of each thoracoscopic method were reported by comparing the results with the gold standard, pathologic results. *P* values of 0.05 or less were considered statistically significant.

Results

Of 60 patients included into the study, 49 (80.3%) were male and 12 (19.7%) were female. Thirty patients were studied in rigid group (consisting of 24 male and 6 female) and thirty in semirigid group (consisting of 25 male and 6 female) without significant difference in their sex distribution ($P = 0.100$). The mean \pm SD of participants' age was 49.10 ± 17.29 years, which was not different between the rigid and semi-rigid groups (47.10 ± 3.66 vs. 51.03 ± 15.85 years, respectively; $P = 0.379$).

The results of pathologic examination revealed malignancy in 8 cases of the rigid group and 6 cases of semi-rigid group without significant difference between the groups ($P = 0.384$) and TB was reported in 8 cases of the rigid group and 5 cases of semi-rigid group without significant difference between the groups ($P = 0.235$). The frequency of other causes of pleural effusion, including nonspecific inflammation, sarcoidosis or rheumatoid nodule, and undiagnosed cases, was also not different between the groups ($P > 0.05$), as shown in Table 1. Subtype of different malignancies that obtained by Rigid and Semi-rigid pleuroscope were shown in Table 2.

Table 1: The diagnostic results reported by each type of pleuroscopy

	Rigid pleuroscopy	Semi-rigid pleuroscopy	P
Malignancy	8	6	0.384
Tuberculosis	8	5	0.235
Nonspecific inflammation	7	8	0.082
Sarcoidosis	1	2	0.764
Aspergillosis	1	0	0.936
Rheumatoid nodule	2	4	0.074
Undiagnosed	3	4	0.056
Total	30	30	-

All values are reported as number of patients; P values are the results of Chi square test, and values <0.05 are considered significant

Table 2: Different subtypes of malignancies obtained in biopsy results with Rigid & Semirigid pleuroscopy

Subtype of Malignancies	Rigid pleuroscopy	Semi-rigid pleuroscopy	P
Adenocarcinoma	4	3	>0.05
Small cell carcinoma	1	0	>0.05
Squamous cell carcinoma	1	1	>0.05
Mesothelioma	2	1	>0.05
Lymphoma	0	1	>0.05

P-values are the results of Chi square test, and values <0.05 are considered significant

In Rigid pleuroscopy group, there was three person with non-diagnostic biopsy results, that in two of them pleural effusion decreased in follow up that rise probability of inflammation and infectious process. One of them in follow up had arthritis and positive antinuclear antibody that finally had a diagnosis of Lupus pleuritis because of positive ANA titer in pleural analysis. In semirigid group, there were four patients with non-diagnostic biopsy that three of them underwent sonography-guided biopsy because of pleural thickening and results was two cases of adenocarcinoma and one case had granuloma with necrosis suggestive of TB. One of them had no consensus for more diagnostic procedures.

Comparing the diagnostic accuracy, the results revealed a sensitivity of 81.5%, specificity of 66.6%, PPV of 75.6%, and NPV of 74% for semi-rigid technique, while the relevant values in rigid pleuroscopy were 87.2%, 68.4%, 87.2%, and 68.4%, respectively.

Discussion

In this study, we examined the diagnostic accuracy of semi-rigid and rigid pleuroscopy in patients with lymphocyte dominant exudative pleural effusion without TB. The results showed that the frequency of causes of pleural effusion reported by the two methods were similar. Studying the diagnostic accuracy of the two methods also revealed acceptable sensitivity and specificity for both methods without significant difference between the methods.

Considering the demographic characteristics of our participants, the results showed that 80% of our study population was male,

which indicates the male dominance of pleural effusion. This finding has been reported previously. In the study by Kiani and colleagues, 300 patients with undiagnosed pleural effusion undergoing pleuroscopy were examined, of whom 64% were men.^[21] These results confirm that of ours and suggest the male dominance in patients with pleural effusion. Not only patients with undiagnosed pleural effusion are dominantly male, the results of previous studies have also determined that the same sex distribution is observed in patients with pleural effusion generally.^[22,23] The mean age of our participants was 49.10 ± 17.29 years, which is similar to the results of previous studies.^[21-23] The important results of our study was no significant difference in mean age or sex distribution of the groups, which eliminated the confounding effect of demographic characteristics of patients on the main outcome of the study.

The main outcome in our study was the diagnostic accuracy of the two methods of pleuroscopy. Comparison of the results between the two groups of patients undergoing rigid and semi-rigid pleuroscopy showed that both methods of pleuroscopy had a high diagnostic accuracy. Pleuroscopy is suggested as a safe and efficient method for diagnosis of undiagnosed cases of pleural effusion that can be performed by two techniques: rigid and semi-rigid pleuroscopy. The technical differences between the methods have resulted in advantages and disadvantages for each, consisting of easier maneuvering between the ribs by flexible instruments in semi-rigid method, resulting in less pain and discomfort for the patients, beside the larger working channel in rigid method.^[17,18] Dhooria *et al.* have reported that the rigid method causes more pain and a larger scar, while the semi-rigid method resulted in higher quality images; therefore, they concluded that the semi-rigid pleuroscopy provides a better image with lower rates of complications by combining the rigid and flexible features.^[20] In the meantime, their investigation about the diagnostic accuracy did not result in suggestion of one method as a more accurate one. Randomization of 90 subjects with undiagnosed exudative pleural effusion to rigid or semi-rigid pleuroscopy showed that the diagnostic yield of rigid pleuroscopy was significantly higher than that of semi-rigid (97.8% vs. 73.3%, respectively) using intension-to-treat analysis; however, considering patients with successful biopsy, they reported a diagnostic yield of 100% for rigid and 94.3% for semirigid pleuroscopy, which was not statistically different between the groups.^[20] Since we have considered the results of pleuroscopy with the pathologic results, obtained by biopsy, their final results are consistent with ours, suggesting similar diagnostic accuracy of these two methods. However, the method of analysis in their study was different from that of ours, as they reported diagnostic yield and performed intension-to-treat analysis, while we have calculated the diagnostic accuracy of the methods by sensitivity, specificity, NPV, and PPV. If we consider the diagnostic yield similar to sensitivity, the diagnostic accuracy reported by Dhooria *et al.* is greater than that of ours for both methods, as the results of our study revealed sensitivity of 81.5% for semi-rigid method and sensitivity of 87.2% for rigid method. Rozman *et al.* have also reported the diagnostic accuracy of rigid method at 100%

and that of semi-rigid at 97.6%,^[18] and in the study by Shaheen and colleagues, investigation of 40 patients with undiagnosed exudative pleural effusion indicated the diagnostic yield at 80% for flexible and 95% for rigid pleuroscopy.^[24] The diagnostic yield of all of the above-mentioned studies.^[18,20,24] are greater than the results of our study. These differences between the results of studies could be due to different frequency of diseases present in the study populations of the studies, as well as the difference in the experience/skills of the operator.

Considering the results of pathologic examination of rigid pleuroscopy, the frequency of malignancy and TB were the same (diagnosed in 8 cases), while considering the results of semirigid pleuroscopy, 6 cases were diagnosed with malignancy and 5 with TB. The results of our study indicates malignancy and TB as the two most common findings, while some studies investigating patients by pleuroscopy have revealed malignancy as the most common finding.^[25] In an Indian study, the results of semi-rigid pleuroscopy revealed malignancy as the first most common diagnosis, while TB was reported as the second most common diagnosis.^[26] This difference among the studies could be due to the fact that we have only included patients with exudative pleural effusion, especially lymphocyte dominant cases, which are both frequently observed in extrapulmonary TB.^[27] Another reason for this difference could be due to the different frequency of TB in the study populations of the studies.^[28] Furthermore, the high value of TB reported by our results refers to the importance of TB in our study, as we had excluded patients with diagnosis of TB as the cause of pleural effusion, according to the results of pleurocentesis. The results of our study confirms that TB is still a major health concern globally and is of significant importance in developing countries, despite the efforts of the World Health Organization to end TB.^[29,30] As Iran is a country with a significant prevalence of TB, especially drug-resistant cases, more attention should be paid to this issue in Iranian population.^[31]

This study compared the pleuroscopic results of two groups with similar demographics and determined the diagnostic accuracy of the two methods of pleuroscopy, namely rigid and semirigid, for the first time in Iranian population. However, this study also had some limitations. First, the patients' enrollment into the study were convenient and nonrandom, which increases the chance of bias in our results. In addition, the sample size of our study was limited, and we did not follow patients to determine the long-term outcomes.

Conclusion

In conclusion, the results of our study revealed that rigid and semi-rigid pleuroscopy can be used for diagnosis of cases with lymphocyte dominant exudative pleural effusion, who remained undiagnosed by previous investigations, including chest X-ray and pleurocentesis. The results showed that the two methods had no difference in reporting the pathologic results, including malignancy, TB, and other causes of pleural effusion. Considering the fact that the results of our study revealed similar diagnostic

accuracy between these two methods, future studies can perform a comprehensive review on different aspects of these methods, including patients' and operators' satisfaction or the costs and availability of these methods to suggest one as a superior method.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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