# Experience in medical thoracoscopy: a 4-year retrospective study

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***Objective*** The aim was to document our experience in rigid medical thoracoscopy in the diagnosis of pleural effusion of undetermined origin in a 4-year retrospective study regarding its safety, complications, and diagnostic yield.

***Patients and methods*** Data of 134 patients who underwent medical thoracoscopy in Alexandria Main University Hospital, Chest Department, for diagnosing pleural effusion of undetermined origin were reviewed to assess the diagnostic yield, safety, and complications of rigid medical thoracoscopy.

***Results*** We reviewed records of 134 patients [62 (46%) males and 72 (54%) females]. Their mean age was 54±13.43 years. On combining histopathological and bacteriological examination results of thoracoscopic pleural biopsies, all patients were finally diagnosed, except for 13 (10%) patients who remained idiopathic; 97 (72%) patients were diagnosed as having malignant pleural effusion and 24 (18%) patients were diagnosed as having benign pleural effusion. The commonest complication encountered was postprocedural pain (35%), followed by subcutaneous emphysema (19%). Overall, the procedure was safe even in elderly patients. No procedure-related mortality was reported.

***Conclusion*** Medical thoracoscopy, in our experience, is a safe and well-tolerated procedure even in elderly patients with high diagnostic yield.

*Egypt J Bronchol* 2019 13:73–80



**Egyptian Journal of Bronchology** 2019 13:73–80

**Keywords:** exudative pleural effusion, malignant pleural effusion, rigid medical thoracoscopy

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**Received** 3 July 2018 **Accepted** 28 September 2018

## Introduction

The accurate diagnosis of pleural disease is considered a great challenge [1]. Nearly 25% of the cases seen in a pulmonologist practice involve the pleura. Of these cases, 25% remain undiagnosed, even after pleural fluid analysis and closed pleural biopsy [2].

As many as 50% of the patients in this undiagnosed group will be finally diagnosed with a malignancy [3]. If the facilities for medical thoracoscopy are available, medical thoracoscopy should be performed because of its high sensitivity in malignant and tuberculous pleural effusions [4]. We report here our experience with rigid medical thoracoscopy in the diagnosis of pleural effusion of undetermined origin in a 4-year retrospective study.

## Patients and methods

Data of 134 patients on whom medical thoracoscopy was performed in the duration between the year 2013 and 2017 at Chest Department, Alexandria Main University Hospital, Egypt, for diagnosis of pleural effusion of undetermined origin were retrospectively reviewed to assess the diagnostic yield and safety of rigid medical thoracoscopy. Patients were referred for thoracoscopy after failure to reach a definite diagnosis after thorough analysis of pleural fluid. Some patients underwent other less invasive procedures such as closed or image-guided pleural biopsies. Patients were all examined to make sure they were fit for the procedure and could lie in the recumbent position. Patients with extensive loculations and pleural adhesions were excluded. This study has been approved by the local institutional ethics committee.

All patients underwent initial clinical assessment, ECG, routine blood chemistry analysis, chest radiography, thoracentesis, contrast-enhanced computed tomography, and ultrasonography. Data collected include patient demographics, clinical status, and medical history including smoking habits, occupational exposure, and history of previous cancer. All patients underwent thoracentesis at least once. The pleural effusion was defined as exudative using Light's criteria [5]. Medical thoracoscopy was performed in after written informed consent was taken.

### Technique

The procedure was performed using a rigid thoracoscope in the endoscopy suite, with the patient under conscious sedation and local anesthesia or, rarely, general anesthesia. Patients were monitored regarding blood pressure and pulse rate; an



 DOI: 10.4103/ejb.ejb_50_18

electrocardiograph was attached, along with a pulse oximeter; and supplementary oxygen was provided to maintain oxygen saturation greater than 90%. Equipment used included a rigid thoracoscope (Karl Storz; GmbH and Co., Tuttlingen, Germany); a straightforward telescope with angled eye-piece, 10 mm in diameter, working length at 27 cm with 6-mm working channel; a metallic trocar 11 mm in diameter; cold (xenon) light source; an endoscopic camera attached to the eyepiece; a video monitor; and a recorder. A single port of entry was required in all patients.

The patient was positioned in the lateral decubitus position, with the normal lung in the dependent position and the arm raised above the head. The involved hemithorax was disinfected; 15–30 ml of lidocaine 2% was injected at the point of entry, through all layers of chest wall till the pleura. Thoracentesis was done under ultrasound guidance to confirm the presence of pleural fluid at the insertion site,. A single puncture, which involved a 1.5–2 cm incision in the mid-axillary line between the fourth and seventh intercostal spaces of the chest wall, was done, and a track was created by blunt dissection. A trocar was introduced, and the pleural cavity was punctured. All pleural fluid was aspirated using a small-diameter catheter, followed by full examination of the pleural cavity. Biopsy specimens (5–7 in number) of parietal pleura were taken as appropriate under direct vision. Finally, a chest tube was inserted and lung expansion was radiographically confirmed before removal of the tube. A chest radiography was taken within 24 h. The specimens obtained were preserved in 10% neutral buffered formalin or normal saline for microbiological examination as well. Subsequently, sections were examined by the pathologist knowing the clinical data. A final diagnosis was then made in light of the biopsy findings regarding both histopathological and microbiological examinations, and further investigations according to individual patient circumstances and the subsequent clinical course were done.

Statistical analyses of the data were done using IBM SPSS software package (IBM SPSS Statistics for Windows, Version 20.0.; IBM Corp. Armonk, New York, USA). Descriptive statistics including frequency, distribution, mean, median, SD, and interquartile range were used to describe different characteristics.

Kolmogorov–Smirnov test was used to examine the normality of data distribution. Comparisons between groups for categorical variables were assessed using $\chi^2$-test (Fisher or Monte Carlo). Student's *t*-test was used to compare two groups for normally distributed quantitative variables. The significance of the results was set at the 5% level of significance.

## Results

We enrolled 134 patients with undiagnosed exudative pleural effusion [62 (46%) males and 72 (54%) females] who were admitted to Alexandria Main University Hospital, Chest Department. Patients underwent medical thoracoscopy for diagnostic purposes using rigid instruments. The mean age of the enrolled patients was 54±13.43 years (range: 20–86 years). Demographic data regarding age, sex, smoking status, and asbestos exposure are illustrated in Table 1.

Among the studied patients, 26 (19%) patients gave history of previous malignancy.Breast cancer was the commonest, and none of our studied patients presented with history of lung cancer. Clinically, dyspnea (97%) was the commonest symptom at presentation followed by chest pain, weight loss, and cough (Table 1).

**Table 1 Demographics, history of neoplasm, and symptomatology of the studied patients**

| Demographic characteristics (*n*=134) | Result [*n* (%)] |
|---|---|
| Age (years) | 54±13.4 |
| Sex | |
| Male | 46 |
| Female | 54 |
| Smoking status | |
| Current or ex-smoker | 38 (28) |
| Passive or nonsmoker | 96 (72) |
| Asbestos exposure | 11 (8) |
| History of previous neoplasm | Total=26 (19) |
| Breast | 16 (61.5) |
| Colon | 1 (4) |
| Thyroid | 1 (4) |
| Breast and thyroid | 1 (4) |
| Bladder carcinoma | 2 (1.5) |
| Gastric cancer | 2 (1.5) |
| Ovarian cancer | 1 (4) |
| Endometrial cancer | 1 (4) |
| Lymphoma | 1 (4) |
| Clinical symptoms | |
| Dyspnea | 130 (97) |
| Chest pain | 74 (50) |
| Weight loss | 65 (48.5) |
| Cough | 60 (45) |
| Night sweating | 10 (25) |
| Fever | 26 (19) |
| Hemoptysis | 3 (2) |

**Table 2 Pleural fluid cytology in different primary tumors**

| | *P* | Unadjusted OR | 95% CI | | Adjusted OR | 95% CI | |
|---|---|---|---|---|---|---|---|
| | | | LL | UL | | LL | UL |
| Primary | | | | | | | |
| Lung | 0.048* | 0.329* | 0.110 | 0.990 | 0.784 | 0.207 | 2.968 |
| Breast | 0.008* | 4.581* | 1.491 | 14.075 | 5.156* | 1.344 | 19.779 |
| Colon | 0.033* | 12.5* | 1.227 | 127.311 | 17.40* | 1.495 | 202.470 |

CI, confidence interval; LL, lower limit; OR, odds ratio; UL, upper limit. *$P \leq 0.05$, statistically significant.

Pleural effusion showed lymphocytic predominance in 87 (65%) patients, and most of them were finally diagnosed as malignant effusion (72%). Patients with very high levels of pleural lactate dehydrogenase (LDH) (>2000) were all finally diagnosed as malignant as well.

Among 97 patients finally diagnosed as malignant, pleural fluid sample showed cancer cells in only 21 patients, meaning that diagnostic yield of cytopathological examination was only 22%. Furthermore, the cytopathology report never mentioned the type of malignancy nor the primary tumor organ. All patients with positive fluid cytology result were confirmed to be malignant after tissue diagnosis obtained from medical thoracoscopy. Therefore, the false-positive rate of cytopathologic diagnoses was 0%.

Comparing both cytology-positive and cytology-negative groups among patients with malignant pleural effusion (MPE), there were no statistically significant differences found regarding age and sex, nor any of the histological subtypes. The only statistically significant differences between both groups were found regarding certain primary tumor organs as follows (Table 2): the lung was associated with negative cytology results ($P$=0.048), and both the breast ($P$=0.008) and the colon ($P$=0.033) were associated with positive cytology results.

Regarding macroscopic appearance of pleural lesions during medical thoracoscopy, the most common finding was pleural nodules, followed by fibrinous pleural peel, pleural adhesions, pleural plaques, and finally pleural masses (Table 3). The costal pleura was the most commonly affected site by metastatic pleural lesions (in 98% of patients with metastatic malignant effusions) followed by diaphragmatic (84%) and then visceral pleura (52%).

**Table 3 Distribution of studied cases according to thoracoscopic macroscopic appearance ($n$=134)**

| Findings | *n* (%) | Diagnosis |
|---|---|---|
| Adhesions | 49 (37) | 25 malignant, 1 coexisting malignancy and TB,13 TB, 1 TB empyema, 1 empyema, 1 brucellosis, and 7 idiopathic |
| Fibrinous peel | 57 (43) | 36 malignant, 1 coexisting malignancy and TB, 12 TB, 1 TB empyema, 1 empyema, 1 brucellosis, and 5 idiopathic |
| Plaques | 37 (28) | 30 malignant, 1 coexisting malignancy and TB, 2 TB, and 4 idiopathic |
| Nodules | 106 (77) | 84 malignant, 16 TB, 1 brucellosis, 1 empyema, and 4 idiopathic |
| Masses | 26 (19) | All malignant |

### Diagnostic yield of medical thoracoscopy

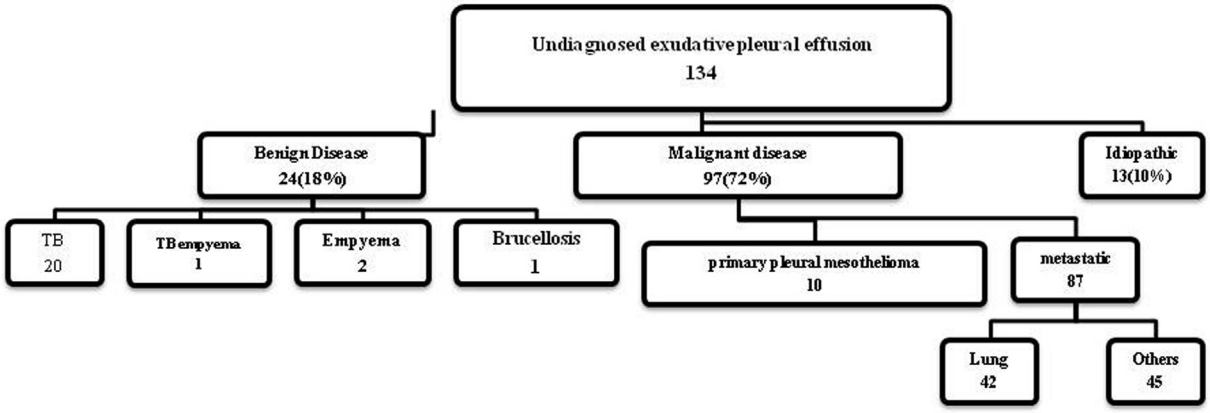
Combining the results of rigid thoracoscopy (including histological and bacteriological examination of pleural biopsies) with other investigations guided by the patient clinical course, all our patients were finally diagnosed except 13 (10%) patients who remained idiopathic (nonspecific pleuritis) (Fig. 1).

Regarding patients with malignant pleural disease, 10 patients were diagnosed as having primary pleural mesothelioma. The frequency of primary tumor organ among the 87 patients with metastatic pleural disease, with no respect to the sex of the patients, was as follows; the lung was the most common primary organ (48%), and the next three primary organ sites encountered in order of descending frequency were breast (20%), ovary (5%), and colon (5%). In 9 (10%) patients, the primary site of the neoplasm was never determined (Fig. 2).

Regarding the histological subtype of malignancy, adenocarcinoma was the most common, seen in 61 (63%) patients. The next three subtypes in descending order were mesothelioma (10%), large cell carcinoma (9%), and infiltrating ductal carcinoma (5%). Among patients with primary lung cancer (42 patients), adenocarcinoma was the most common (29 out of 42, 69%), followed by large cell carcinoma (six out of 42 patients, 14%).

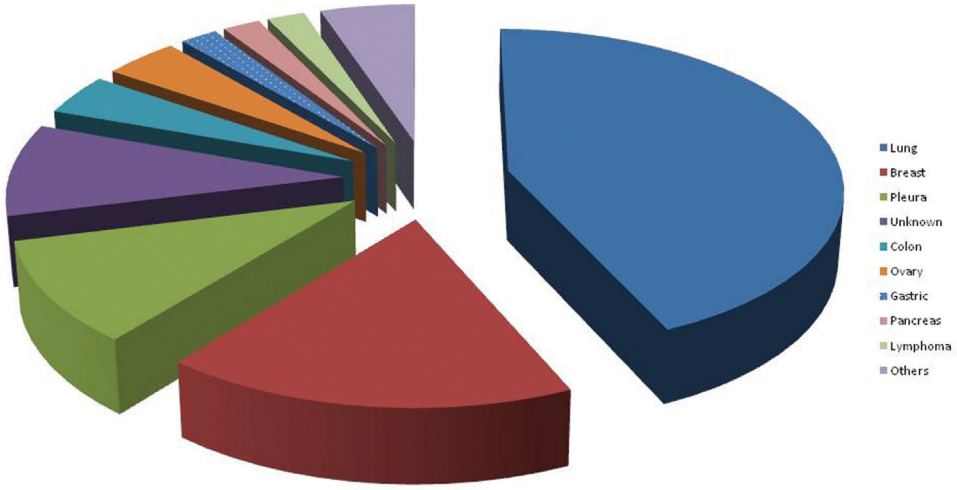
The procedure was performed safely without major complications. It was well tolerated even with elderly patients (Fig. 3). In general, patients found that the procedure caused only minor discomfort; those with previous history of image-guided biopsies considering the previously performed pleural biopsy to be more painful.

**Figure 1**




Distribution of studied patients according to the final diagnosis.

**Figure 2**




Distribution of patients finally diagnosed as having malignant pleural effusion according to the primary tumor organ.

The following complications were not reported in any of our patients: malignant seedling of the wound, pulmonary embolism, and persistent air leak, even those two patients from whom visceral pleural biopsy was obtained. None of our patients took prophylactic antibiotics, anticoagulants, or radiotherapy. Reversal of sedation was not required in any patient, and there was no reported procedure-related mortality.

Average duration of chest tube drainage was 2 days (interquartile range=2–3 days), and the median hospital stay was 3 days (interquartile range=2–5 days).

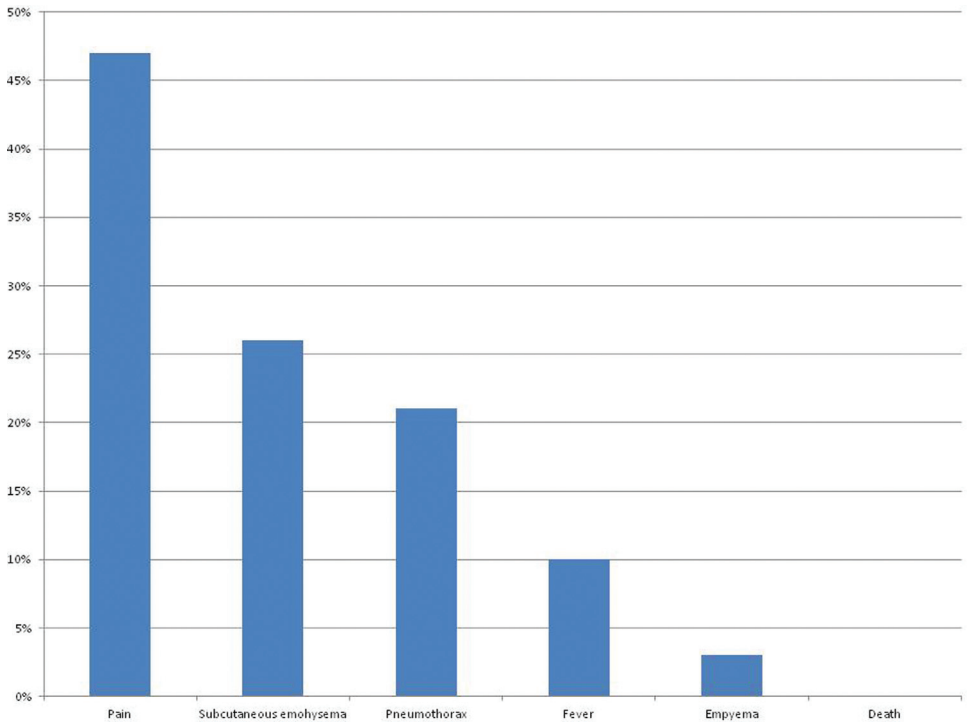
## Discussion

In our study, we have presented the data on 134 patients who underwent medical thoracoscopy using rigid thoracoscope for diagnosis of exudative pleural effusions in whom initial diagnostic workup was inconclusive.

Pleural fluid analysis showed that patients with very high levels of pleural LDH (>2000 or 5000 IU/l) were all finally diagnosed as having malignant effusion, whereas LDH levels from 1000–2000 were finally diagnosed as having malignant, tuberculous, empyema, or idiopathic effusion. Thus, LDH level more than 2000 IU/l can be a useful indicator of pleural malignancy and can narrow differential diagnosis. Other study reported that LDH level more than 1000 IU/l narrowed the differential diagnosis to empyema, a complicated parapneumonic effusion, cholesterol pleural effusion, rheumatoid pleurisy, or lymphoma [6].

Pleural fluid cytological examination was done preoperatively in all patients; it showed positive

**Figure 3**




Frequency of medical thoracoscopy-related complications.

results for malignancy in 21 of 97 malignant patients (diagnostic yield 22%). Although being positive in those 21 patients, we still performed thoracoscopy, as the pathology only described them as positive for malignant cells without mentioning the type of malignancy or its primary. Similarly, Boutin *et al.* [7] reported that it was difficult to determine the type and origin of cancer by thoracentesis. So thoracoscopic biopsy is highly needed even in positive pleural fluid for malignant cells.

The histopathological type of malignancy among patients with positive fluid cytology results was adenocarcinoma in more than 70%. This agrees with the finding of Hooper *et al.* [8] who reported that detection rate by cytology for adenocarcinoma is higher than that of squamous cell carcinoma, mesothelioma, or lymphoma. Tumor markers in the pleural fluid were not measured as they proved of no value in previous study [9]. If the cutoff level is set high enough so that there are no false positives, the sensitivity of the test falls to less than 50% [10].

Among the patients with metastatic pleural disease, the costal part of parietal pleura was the most commonly affected site by metastatic pleural lesions (98%) followed by diaphragmatic (84%) and then visceral pleura (52%). This finding supports the concept that the low reliability of pleural needle biopsy results in MPE does not relate to the type of needle used, rather it relies upon the fact that there are metastatic locations that may not be reached with this method, because on employing 'blind' biopsy, we explore only the costal pleura. In contrast to malignant effusion, the diagnostic yield in tuberculous pleuritis is high (around 75%) [11,12]. So we recommend performance of medical thoracoscopy directly in any patient suspected to have malignancy bypassing the step of closed pleural biopsy unless the general condition of the patient does not allow safe procedure or in the presence of evident localized accessible pleural lesion in the absence of or the presence of minimal pleural effusion.

Combining the results of rigid thoracoscope (including histological and bacteriological examination of pleural biopsies) with other investigations guided by the patient clinical course, all our patients were finally diagnosed, except for 13 (10%) patients who remained idiopathic; 97 (72%) patients were diagnosed as having MPE and 24 were diagnosed as having benign pleural effusion (Fig. 1). This means that most of our patients were finally diagnosed as having MPE. This agrees with the statement of American Thoracic Society (ATS) that more than half of exudative effusions are attributable to malignancy [13]. Ng *et al.* [14] found pleural malignancy in 45.5% of patients with undiagnosed pleural effusions subjected to thoracoscopy.

All our patients were finally diagnosed, except for 13 (10%) patients who remained idiopathic (nonspecific pleuritis). The sensitivity and specificity of diagnostic thoracoscopy in our study were 90 and 100%, respectively, signifying a high diagnostic yield and matching that of previous studies which reported diagnostic yield up to 95% for malignancies and 100% for benign diseases. Kendall *et al.* [15] reported thoracoscopic pleural biopsy yield to be 83%. Tscheikuna colleagues also reported their experience, and thoracoscopy was diagnostic in 95% of 34 patients. On the contrary, Ng *et al.* [14] reached diagnosis with thoracoscopic pleural biopsy in only 45.5% (10/22) patients with undiagnosed pleural effusions.

From the present study, we conclude that medical thoracoscopy, in addition to its very high diagnostic yield, has several other advantages as previously mentioned in other studies [13,16]. It can assess metastatic spread of lung cancer to the pleura for proper staging, and the presence of pleural metastasis is defined as M1a (from T4), representing a corresponding change from stage IIIB to stage IV [16]. Thus, pleuroscopy can determine operative eligibility by determining if the pleural effusion is paramalignant or due to metastases [13].

Similar to our results, Khaleeq and Musani [17] reported that lung cancer was the most common cause of MPE in men, and breast cancer in women, and the two combined account for two-thirds of all MPE. In comparison with metastatic pleural malignancy, malignant mesothelioma was rare (10/97 patients, 10%). Diagnosis of mesothelioma was confirmed by immunocytochemical studies using mainly calretinin, TTF1, and pancytokeratin. Asbestos exposure was reported only in three (30%) of those 10 patients. This rare incidence of mesothelioma as a cause of malignant pleural disease was also reported in a recent study in India that could diagnose only one case of mesothelioma, whereas 16 out of the 17 cases were owing to pleural metastasis [18].

In agreement with our study, another study postulated that the most common subtype of metastatic pleural carcinoma was adenocarcinoma (38%) [12]. Among patients with metastatic effusion from lung cancer, adenocarcinoma was the most common type as well representing 70% (28/40). These findings agree with those of others [18].

Regarding macroscopic appearance of pleural lesions during thoracoscopy, the most common finding was pleural nodules, followed by fibrinous pleural peel, pleural adhesions, pleural plaques, and finally pleural masses. All patients who had apparent pleural masses were proved malignant after histopathology, whereas only 81% and 80% of patients with pleural plaques and nodules, respectively, proved malignant. On the contrary, patients with thoracoscopic findings like pleural adhesions and fibrinous pleural peel showed final diagnosis of lower malignancy rates of 51 and 63%, respectively. In our opinion, macroscopic appearance can predict or suggest the nature of disease whether benign or malignant in most cases, but still it should be complemented by not only histopathological examination but also microbiological examination. Enk and Viskum [19] in their study reported that the thoracoscopic appearances were reliable. Furthermore, there was no relation between the morphology of the metastasis and the histologic subtype, as most metastatic pleural carcinoma appeared macroscopically as nodules of different sizes mostly in lower part of costoparietal pleura, masses, diffuse thickening, or increased vascularity. Mesothelioma had similar appearance.

When medical thoracoscopy is used in the diagnostic workup of pleural effusions, the percent of idiopathic pleural effusions usually falls markedly below 10% [20]. In this study, a specific diagnosis was not reached in thirteen patients (13/134) (10%) after exhausting all needed investigations according to each individual patient. Problems may occur because concerns exist whether this histopathological diagnosis truly points to a benign disease, or if MT observation and sampling failed to accurately detect malignancy.

Another factor to be put into consideration before deciding the plan for these patients is the thoracoscopist impression. Boutin *et al.* [21] concluded in their study that some endoscopic characteristics, such as nodules, polypoid masses, and 'candle wax drops,' were highly suggestive of malignancy; nevertheless, early-stage mesothelioma can resemble pleural inflammation.

According to the literature, two methods can be applied. First, a 'wait and see' approach which can be suitable for most of these patients because the rate of false negatives is not so high and we support this method unless there were extensive adhesions in the pleural space or any obstacle that prohibited the thoracoscopy procedure, then Video-assisted Thoracoscopic surgery (VATS) or open biopsy should follow [22].

Nevertheless, the patients should be monitored through chest radiographies, and others suggest that

if subsequent pleural fluid analysis reveals lymphocytosis, then thoracoscopy should be repeated [23]. In our study, none of our patients underwent redo thoracoscopy or open surgery; only follow-up, repeated tapping, and cytology in case of effusion recurrence and other investigations were continued as needed according to individual cases. The diagnoses after open thoracotomy are apparently not much superior, as shown in a study from the Mayo Clinic [24]. Auto fluorescence video thoracoscopy or narrow-band imaging may aid in future to avoid false-negative results [25].

In our hands, thoracoscopy was well tolerated by all patients, causing little more discomfort than insertion of a chest drain. Our study represents high incidence of minor but not major complications. A Previous study reported major complication (death, hypercapnic respiratory failure, empyema, sepsis, and pulmonary embolism) and less serious complication (insignificant pneumothorax, subcutaneous emphysema, fever, severe pain) rates of 1.9 and 5.5%, respectively [26]. Another study reported 0.3–0.4% incidence of major bleeding [27].

The risk of bleeding was very low in our study owing to certain precautions, as the least prothrombin activity and INR were 59 and 1.4%, respectively; biopsy was taken from the pleura overlying the ribs (to avoid damaging intercostal vessels). None of our patients were on anticoagulant therapies. Patients at high risk for clotting with anticoagulation interruptions were considered for 'bridging therapy' with heparin or low-molecular-weight heparin given by subcutaneous injection [28].

No lung injury or any organ injury was reported in any of our patients. Some authors recommend induction of pneumothorax before thoracoscopy. However, direct introduction of a blunt trocar into the thoracic wall, without prior induction of pneumothorax, is in our experience safe if enough pleural fluid was present. Lung deflation was surprisingly well tolerated in most patients presumably because the effusion had already caused partial lung collapse, so that further deflation was barely felt, and possibly because of improved matching of ventilation and perfusion with the dependent ventilated lung better perfused. Reexpansion pulmonary edema was not a common finding because fluid drainage was replaced in the same time with pneumothorax through suctioning with a small-diameter suction inserted relative to diameter of the trocar. Respiratory insufficiency during thoracoscopy was not a complication in our study and has not been mentioned as a complication in previous series as well [29].

Overall, unexpandible lung was present in 21 (16%) patients. Before thoracoscopy, only two patients showed radiographically ipsilateral mediastinal shift and seven patients showed central mediastinum. Our results were similar to those reported in the literature [30], so radiology alone proved inaccurate in predicting postoperative complication with unexpandible lung.

Invasion of the thoracoscopy site by mesothelioma is reported. In our study, none of the patients developed this complication despite not giving prophylactic radiotherapy which is often recommended [7]. Empyema occurred in three (2%) patients. No prophylactic antibiotics were given to our patients. Other studies reported its incidence as 0.5–2.7% [27].

The procedure did not need to be terminated because of pain, dyspnea, or hemodynamic instability, and there were no perioperative complications that necessitated open surgery and blood transfusion. Moreover, pulmonary embolism was not reported in any of our patients despite not giving prophylactic anticoagulation. There was no procedure-related mortality among our patients, and this agrees with the results of other studies, which report that death is extremely rare. Only one fatality of 8000 patients was reported in one study [7].

Our median length of hospital stay is good at 3 days, which compares favorably with most studies in the literature [4,21,30].

In conclusion, medical thoracoscopy, in our local experience, is a safe and tolerated procedure even in elderly patients, with high diagnostic yield.

#### Financial support and sponsorship
Nil.

#### Conflicts of interest
There are no conflicts of interest.

## References

1 Poe RH, Israel RH, Utell MJ, Hall WJ, Greenblatt DW, Kallay MC. Sensitivity, specificity, and predictive values of closed pleural biopsy. *Arch Intern Med* 1984; **144**:325–328.

2 Prakash UB, Reiman HM. Comparison of needle biopsy with cytologic analysis for the evaluation of pleural effusion: analysis of 414 cases. *Mayo Clin Proc* 1985; **60**:158–164.

3 Hassanein E, Hatata E, Helal S, Ibrahim E, Baess A. Rigid medical thoracoscopy in management of exudative pleural effusion. *Chest* 2014 ? **145**:289A.

4 Shoukri A. Medical thoracoscopy: past, present, and future. *Egypt J Bronchol* 2013; **7**:50–52.

5 Light RW, McGregor MI, Luchsinger PC, Ball WC. Pleural effusions: the diagnostic separation of transudates from exudates. *Ann Inter Med* 1972; **77**:507–513.

**6** Sahn SA, Heffner JE. Pleural fluid analysis. In: Light RW, Lee YCG, editors. *Textbook of pleural diseases*. UK: Hodder A; 2008. 209–226.

**7** Boutin C, Viallat JR, Cargnino P, Farisse P. Thoracoscopy in malignant pleural effusions. *Am Rev Respir Dis* 1981; **124**:588–592.

**8** Hooper C, Gary Lee YC, Maskell N. Investigation of a unilateral pleural effusion in adults: British Thoracic Society Pleural Disease Guideline 2010. *Thorax* 2010; **65**(Suppl 2):ii4–ii17.

**9** Lee YC, Knox BS, Garrett JE. Use of cytokeratin fragments 19.1 and 19.21 (Cyfra 21-1) in the differentiation of malignant and benign pleural effusions. *Aust N Z J Med* 1999; **29**:765–769.

**10** Janssen JP, Thunnissen FBJM, Visser FJ. Comparison of the 2.0 mm and 3.5 mm minithoracoscopy set to standard equipment for medical thoracoscopy. *Eur Respir J* 2003; **22**:S541.

**11** Tomlinson JR. Invasive procedures in the diagnosis of pleural disease. *Semin Respir Med* 1987; **9**:31–36.

**12** Cantó A, Ferrer G, Romagosa V, Moya J, Bernat R. Lung cancer and pleural effusion. Clinical significance and study of pleural metastatic locations. *Chest* 1985; **87**:649–652.

**13** American Thoracic Society. Management of malignant pleural effusions. *Am J Respir Crit Care Med* 2000; **162**:1987–2001.

**14** Ng TH, How SH, Kuan YC, Hasmah H, Norra H, Fauzi AR. Medical thoracoscopy: Pahang experience. *Med J Malaysia* 2008; **63**:298–301.

**15** Kendall SW, Bryan AJ, Large SR, Wells FC. Pleural effusions: is thoracoscopy a reliable investigation? A retrospective review. *Respir Med* 1992; **86**:437–440.

**16** Rami-Porta R, Crowley JJ, Goldstraw P. The revised TNM staging system for lung cancer. *Ann Thorac Cardiovasc Surg* 2009; **15**:4–9.

**17** Khaleeq G, Musani AI. Emerging paradigms in the management of malignant pleural effusions. *Respir Med* 2008; **102**:939–948.

**18** Mootha VK, Agarwal R, Singh N, Aggarwal AN, Gupta D, Jindal SK. Medical thoracoscopy for undiagnosed pleural effusions: experience from a tertiary care hospital in north India. *Indian J Chest Dis Allied Sci* 2011; **53**:21–24.

**19** Enk B, Viskum K. Diagnostic thoracoscopy. *Eur J Respir Dis* 1981; **62**:344–351.

**20** Loddenkemper R. Thoracoscopy: results in non cancerous and idiopathic pleural effusions. *Poumon Coeur* 1981; **37**: 261–264.

**21** Boutin C, Cargnino P, Viallat JR. Thoracoscopy in the early diagnosis of malignant pleural effusions. *Endoscopy* 1980; **12**:155–160.

**22** Venekamp LN, Velkeniers B, Noppen M. Does 'idiopathic pleuritis' exist? Natural history of non-specific pleuritis diagnosed after thoracoscopy. *Respiration* 2005; **72**:74–78.

**23** Janssen J, Ramlal S, Mravunac M. The long-term follow up of exudative pleural effusion after nondiagnostic thoracoscopy. *J Bronchol* 2004; **11**:169–174.

**24** Ryan CJ, Rodgers RF, Unni KK. The outcome of patients with pleural effusion of indeterminate cause at thoracotomy. *Mayo Clin Proc* 1981; **56**:145–149.

**25** Schonfeld N, Schwarz C, Kollmeier J, Blum T, Bauer TT, Ott S. Narrow band imaging (NBI) during medical thoracoscopy: first impressions. *J Occup Med Toxicol* 2009; **4**:24–29.

**26** Menzies R, Charbonneau M. Thoracoscopy for the diagnosis of pleural disease. *Ann Intern Med* 1991; **114**:271–276.

**27** De Campos JR, Vargas FS, de Campos Werebe E, Cardoso P, Teixeira LR, Jatene FB, Light RW. Thoracoscopy talc poudrage: a 15-year experience. *Chest* 2001; **119**:801–806.

**28** Douketis DJD. *BRIDGE Study, Duke Clinical Re search Institute, Durham, NCSt*. Ontario, Canada: Joseph's Healthcare Hamilton, Ontario, Canada Circulation, 2012.

**29** Migliore M, Giuliano R, Aziz T, Saad RA, Sgalambro F. Four-step local anesthesia and sedation for thoracoscopic diagnosis and management of pleural diseases. *Chest* 2002; **121**: 2032–2035.

**30** Sakuraba M, Masuda K, Hebisawa A, Sagara Y, Komatsu H. Diagnostic value of thoracoscopic pleural biopsy for pleurisy under local anaesthesia. *ANZ J Surg* 2006; **76**: 722–724.