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A randomized trial comparing the diagnostic yield of rigid and semirigid thoracoscopy in undiagnosed pleural effusions

[**Running title**: RISE trial]

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ABSTRACT

Background and aim: Thoracoscopic pleural biopsy increases the diagnostic yield of pleural effusions undiagnosed after thoracentesis, and is superior to closed pleural biopsy**.** Medical thoracoscopy can be performed using the rigid thoracoscope or the semirigid thoracoscope (pleuroscope). In this randomized trial, we compare the efficacy and safety of the two thoracoscopes.

Methods: Patients with undiagnosed exudative pleural effusions were randomly assigned to undergo pleural biopsy either with rigid or the semirigid thoracoscope. The primary outcome was the diagnostic yield of the procedure while the secondary outcomes were requirement of sedative/analgesic agents, scar size, biopsy size and the operator's view of the procedure.

Results: Of the 145 screened patients with exudative pleural effusions, 90 were randomized to undergo thoracoscopy with the two thoracoscopes (n=45 each). The diagnostic yield of rigid thoracoscopy was superior to semirigid thoracoscopy (97.8% vs. 73.3%, p=0.002) on an intention-to-treat analysis but was similar (100% vs. 94.3%, p=0.18) in those with successful biopsy. The requirement of sedative/analgesic agents was higher in the rigid thoracoscopy arm. The scar size was slightly larger (mean±SD, 23.1±4 vs. 18.7±3.2 mm, p=0.0001), whereas the biopsy size was distinctly larger in the rigid arm (mean±SD, 13.9±4.4 vs. 4.4±1.4 mm, p=0.001). The operator rated visual analog scale (VAS) for the ease of taking a biopsy was significantly higher with the rigid instrument (mean±SD, VAS 86±12 vs. 79±12 mm, p=0.01) while the quality of image was superior in the semirigid arm (mean±SD, VAS 88±7 vs. 92±5 mm, p=0.002). The number of complications was similar in the two groups.

Conclusions: Rigid thoracoscopy was found to be superior to semirigid thoracoscopy overall but the diagnostic yield was similar if pleural biopsy could be successfully performed. Due to the

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small sample size, a larger study is required to define the usefulness and choice between the two procedures.

(Clinical trials.gov:NCT01726556)

Key-words: thoracoscopy, semirigid, pleural effusion, lung cancer, tuberculosis

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INTRODUCTION

About 20-40 percent of patients with pleural effusions remain undiagnosed despite pleural fluid analysis and closed pleural biopsy.[1-5] Medical thoracoscopy increases the diagnostic yield in these cases.[6] The sensitivity of thoracoscopy ranges from 80-100 percent in diagnosis of pleural effusions.[7] Rigid thoracoscopy, with or without video assistance has traditionally been the procedure of choice.[8, 9] A semirigid thoracoscope (pleuroscope) combining the features of rigid thoracoscope and flexible bronchoscope has been available since its first report in 1998.[10] Two recent systematic reviews have concluded that the semirigid pleuroscope is a safe, easy-to-handle and accurate tool in diagnosis of pleural effusions of undetermined origin.[11, 12] Another retrospective study found comparable histologic yields of the rigid and the semirigid thoracoscopes.[13] There is only one published randomized trial comparing the yield of the two instruments wherein the authors found comparable diagnostic accuracy of the two instruments, despite the smaller biopsy size obtained with the semirigid device.[14]

We hypothesized that the yield with rigid thoracoscopy would be better than semirigid thoracoscopy because of the larger biopsy size with the former and the fact that rigid thoracoscope allows better maneuverability in patients with adhesions. In this randomized trial, we compare the efficacy and safety of **ri**gid versus **s**emirigid thoracoscopy in undiagnosed **e**xudative pleural effusions (RISE trial).

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MATERIALS AND METHODS

This was a prospective study conducted between May 2011 and October 2012 in the Department of Pulmonary Medicine of this Institute, a tertiary care referral center. The protocol was approved by the Institute Ethics Committee and a written informed consent was obtained from all patients.

Patients: Patients were included in the study if they met the following criteria: (a) age ≥12 years; (b) exudative pleural effusion by Light's criteria[15] where a specific diagnosis was not obtained after two cytological and/or microbiological examinations. Closed pleural biopsy is not routinely performed at our center. Patients with any of the following were excluded: PaO_2/FiO_2 ratio <300, hemodynamic instability, myocardial infarction or unstable angina in the last six weeks, lack of pleural space due to adhesions, uncorrected coagulopathy, and failure to provide informed consent. We also excluded patients with pleural fluid adenosine deaminase levels >70 U/L and clinical picture consistent with diagnosis of tuberculous pleural effusion. All patients underwent complete blood count, liver and renal function tests, coagulation profile and an electrocardiogram. Computed tomography (CT) of the chest was obtained in patients where chest radiograph showed significant parenchymal abnormality or loculated effusion. The effusion was categorized as small (<1/3rd of hemithorax), moderate (1/3rd-2/3rd of hemithorax), large (>2/3rd of hemithorax), and massive (unilateral opaque hemithorax with contralateral mediastinal shift). Chest ultrasound was done in selected patients to exclude significant pleural loculations as most of the patients presented late at our center with many of them already on treatment including antibiotic and/or antituberculosis therapy.

Randomization: The subjects were randomly assigned to either rigid thoracoscopy (10 mm outer diameter, working channel 5 mm, 8912.402, Richard Wolf, Germany) arm or semirigid

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thoracoscopy (7 mm outer diameter, working channel 2.8 mm, LTF-160, Olympus Medical, Japan) arm. The randomization sequence was computer generated and the assignments were placed in opaque sealed envelopes. Each patient's assignment to a particular group was made sequentially. Blinding of treatment allocation was not possible. If successful pleural examination could not be performed with the semirigid instrument, the rigid device was subsequently used.

Procedure: Thoracoscopy was performed in the bronchoscopy suite on a spontaneously breathing patient (fasting for eight hours) under conscious sedation (titrated using midazolam, pentazocine and tramadol) using full aseptic precautions. Blood pressure was monitored every 10 minutes while oxygen saturation, heart rate and rhythm were monitored continuously. Supplemental oxygen was administered via air-entrainment mask. The operators were consultant pulmonologists or pulmonary fellows with two-and-a half years of training and having assisted in at least 25 procedures under the direct supervision of one of the consultants. The consultants were equally trained in both rigid and semirigid thoracoscopy.

A single entry site was selected in the fourth or fifth intercostal space along the midaxillary line with the patient in lateral decubitus position and involved side upward. The site was infiltrated with 2% lidocaine and 1-3 cm skin incision was made. A blunt dissection was used to enter the pleural space; the incision was extended if required. The trocar supplied with the respective thoracoscopes (rigid: trocar sleeve with magnetic ball valve [8923.123, Richard Wolf] and trocar with blunt conical tip [8923.103, Richard Wolf]; semirigid: flexible trocar [MAJ-1058, Olympus]) was inserted followed by introduction of the thoracoscope. Pleural fluid was aspirated while air was allowed to enter the pleural space. The parietal, visceral, and diaphragmatic pleura were inspected and biopsies (6-8 with semirigid and 2-4 with rigid) were performed under direct vision in all suspect areas of the parietal pleura. Biopsies were performed

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using the respective biopsy forceps (rigid [8393.09135, Richard Wolf, 5 mm diameter]; semirigid [FB-55CR, Olympus, 2 mm diameter]).

If there were fibrous adhesions that precluded biopsy with the semirigid device, patients were crossed over to the rigid thoracoscopy arm, and adhesiolysis was performed followed by pleural biopsy. If an adequate pleural space could not be created even with the rigid scope, the procedure was stopped. A 24-28F intercostal drainage tube was inserted before wound closure to evacuate air and fluid. If the thoracoscopic findings suggested malignancy (variable sized nodules), talc poudrage was done during the procedure, or was performed later by instilling talc slurry (or iodopovidone) through the chest tube. Chest radiographs were obtained three hours after the procedure. Chest tube was removed only once the drainage decreased to <50 mL/day for two consecutive days and the effusion was non-purulent.

Outcome: We recorded the clinical history, pleural fluid examination findings and thoracoscopic findings on a standard data entry sheet. The primary outcome was the diagnostic yield of the procedure defined as (a) pleural biopsy yielding a definite histopathology or microbiologic etiology; or, (b) histopathologic findings (nonspecific pleuritis) consistent with subsequent clinical course and response to treatment. The primary outcome is reported on an intention-to-treat basis i.e. the results are reported based on the initial treatment assigned (semirigid or rigid) and not on the treatment eventually received. Patients crossed from semirigid to rigid were considered as failures of the semirigid arm irrespective of results with rigid thoracoscopy. We also calculated the diagnostic yield in the two arms in patients who underwent a successful biopsy. The secondary outcomes were requirement of sedative/analgesic agents, scar size (maximal length), biopsy size (longest axis length) and the operator's view of the procedure. The operators recorded the quality of image, ease of maneuvering, ease of taking a biopsy and the

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expectation that biopsy will reveal a definitive histological diagnosis on visual analog scale (VAS) from 0 to 100. The duration of intercostal tube drainage and complications were also recorded. The complications were classified as major (empyema, major hemorrhage [drop in hemoglobin by 1 gm/dL or requiring blood transfusion], persistent air-leak >3 days, re-expansion pulmonary edema) and minor (subcutaneous emphysema, operative site infection, non-infective fever and minor hemorrhage) as previously described.[16] All patients were followed up for at least three months following the procedure.

Statistical analysis: Data are expressed as mean ± standard deviation (SD), or percentage. Differences in continuous variables between the two groups were compared using student's t test (or Mann-Whitney U test); while differences in categorical data were compared using the chi-square test (or Fisher's exact test). A p value of less than 0.05 was considered statistically significant.

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RESULTS

During the study period, 145 patients with exudative pleural effusions were managed; 90 (mean [SD] age, 51.5 [14.3] years; 62 (68.9%) men) were randomized to undergo thoracoscopy with patients equally distributed between the two arms (Figure 1). The baseline characteristics of the patients are shown in Table 1. There was no significant difference in any of these characteristics. Dyspnea, chest pain, cough and fever were the most common symptoms in order of frequency. The effusion was large to massive in 35.5% and bilateral in eight (8.9%) patients. In the semirigid arm, the thoracoscope could not be maneuvered in 10 patients because of adhesions. Seven patients were crossed over to the rigid thoracoscopy arm while in three patients, the procedure was abandoned due to absolute lack of pleural space. Of the seven crossed over patients, rigid thoracoscopy and biopsy could be performed in three patients after adhesiolysis while in the remaining four patients, rigid thoracoscopy also could not be performed due to extensive adhesions. In the rigid thoracoscopy arm, the thoracoscope could not be manipulated in the pleural cavity in one patient, and the procedure was abandoned (Figure 1). Thus the procedure could be completed in 82 of the 90 randomized patients. Although higher in the semirigid group, the number of procedures interrupted (10/45 in the semirigid group, 5/52 in the rigid group; p=0.09) were not statistically different between the two groups. Of the eight failed cases, loculations were observed by any method (ultrasound, chest radiograph or CT chest) in four cases while loculations were observed in 20 of the 82 patients with successful biopsy (p=0.8). The procedures were performed primarily by fellows under direct supervision of the consultants.

The diagnostic yield of rigid thoracoscopy (44/45, 97.8%) was superior to semirigid thoracoscopy (33/45, 73.3%) on an intention-to-treat (ITT) analysis (p=0.002). However, the

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yield was similar when only those in whom biopsy was done were considered (p=0.18) (Table 2). The requirement of sedative/analgesic agents was higher in the rigid thoracoscopy arm (Table 2). The scar size was slightly larger (mean, 23.1 vs. 18.7 mm) in the rigid versus the semirigid arm (Table 2); however, the biopsy size was significantly larger in the rigid thoracoscopy group (median, 14 mm vs. 4 mm). The VAS for ease of taking biopsy was significantly higher in the rigid arm (p=0.01) while that for the quality of image was significantly higher in the semirigid arm (p=0.002) (Table 2). The duration of procedure was similar in the two groups.

The thoracoscopic and histopathological findings are shown in Table 3. Adhesions and nodules were found in 53 and 54 patients respectively on thoracoscopic examination (Table 3). The presence of nodules predicts high odds for obtaining a definitive histological diagnosis on pleural biopsy (Table 4). The presence of variable sized nodules suggests higher odds for malignancy while the odds for tuberculosis are higher with uniform sized nodules. Diffuse distribution of nodules predicted the diagnosis of tuberculosis (Table 4).

The most common definitive histological diagnosis made on pleural biopsy was malignancy followed by tuberculosis (Table 3). One patient with an established diagnosis of sarcoidosis was diagnosed as sarcoidosis-related pleural effusion based on the histopathology finding of compact granulomas, and resolution of the effusion with glucocorticoids. Another patient, a known case of allergic bronchopulmonary aspergillosis (ABPA) was found to have pleural effusion secondary to ABPA; she was treated with steroids and voriconazole and did not have recurrence of pleural effusion. One patient, a known case of rheumatoid arthritis was found to have rheumatoid pleurisy and improved on treatment with steroids. Pleural biopsies from 32 patients were reported as non-specific inflammation or fibrinous pleuritis, and the followup data of these patients is shown in Table 5. In two of the 32 patients, a final diagnosis of tuberculous

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pleural effusion was made (both in the semirigid arm), and was considered as failure of the procedure (Table 5). In one of these patients, the diagnosis was made on the basis of demonstration of necrotizing granulomatous inflammation on transbronchial lung biopsy. The other patient was given empiric anti-tuberculosis treatment (in view of a positive tuberculin skin test and non-response to antibiotics) and showed response to the same. Pleural biopsy could not be obtained in a total of eight patients. Six of these patients were diagnosed as inadequately treated parapneumonic effusion and were given prolonged antibiotic therapy. One patient with chronic kidney disease (CKD) was given empiric anti-tuberculosis therapy. Another patient was diagnosed as tuberculous pleural effusion based on positive sputum mycobacterial cultures.

There were no deaths attributed to the procedure. Twenty-five complications were encountered in 82 patients. The major complications included empyema, peristent air leak and re-expansion pulmonary edema but there was no instance of major bleeding. The minor complications included subcutaneous emphysema, fever, small amount of bleeding after biopsy and operative site infection. The complication rate was not significantly different between the two arms (Table 6). Empyema occurred in four patients, which necessitated treatment with intravenous antibiotics. Four patients had air leak lasting more than three days which recovered spontaneously. Three patients developed hypoxia after the procedure along with the appearance of new onset bilateral lung opacities. They were diagnosed as re-expansion pulmonary edema and were treated with oxygen and supportive treatment. The intercostal tube remained for a mean (SD) duration of 5.6 (6.6) days and was not different between the two groups. The patients were followed up for a median (range) duration of 10 (3-17) months.

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DISCUSSION

In this study, rigid thoracoscopy was found to be superior to semirigid thoracoscopy on an intention-to-treat analysis but the yield was similar if pleural biopsy could be successfully performed. Rigid thoracoscopy could be performed successfully in three patients in whom semirigid thoracoscopy was unsuccessful. Further, none in the rigid arm had any failure of diagnosis whereas a diagnosis of tuberculous pleuritis was missed in two patients in the semirigid arm.

In pleural effusions undiagnosed by thoracocentesis, closed pleural biopsy increases the yield by about 10% and 40% in malignant and tuberculous pleural effusions, respectively; while the diagnostic yield of thoracoscopy is about 93% in both malignant and tuberculous pleural effusions.[7] Hence, in many centers including ours, a non-diagnostic pleurocentesis is followed by thoracoscopy. Thoracoscopy can be performed either using the conventional video-assisted thoracic surgery (VATS) or "medical thoracoscopy". Medical thoracoscopy is performed under local anesthesia and conscious sedation while VATS requires general anesthesia and single lung ventilation. For diagnostic pleural biopsy, VATS is rarely required as medical thoracoscopy is highly efficacious and cost-effective. The unfamiliarity of the pulmonary physician with the rigid instrument, and familiarity with the flexible bronchoscope has led various investigators to attempt thoracoscopy, even with a fiberoptic bronchoscope.[17-20]

The semirigid thoracoscope (pleuroscope) has been designed to combine the best feature of rigid as well as flexible instruments with a proximal rigid shaft and a distal flexible tip, and can be maneuvered akin to the flexible bronchoscope. However, unlike the rigid thoracoscope, the semirigid instrument can be used only for pleural biopsy and usually cannot be used for adhesiolysis. In the only randomized controlled trial reported till date, the diagnostic accuracy

was 100% and 97.6% for rigid and semirigid thoracoscopy, respectively.[14] However, in this study, patients with lack of pleural space were excluded from the analysis,[14] while in our study an ITT analysis was performed by including those patients also in whom the procedure was abandoned. In another retrospective study, the diagnostic yield of the two procedures was comparable (rigid: 96.3% vs. semirigid: 92.3%) but the procedures were performed by different operators at different hospitals.[13] In both of the previous studies, majority of the patients were those with malignant pleural effusion while in our study only 30% of patients constituted those with malignant effusion.

In this study, the pleural space could not be negotiated in eight cases and the procedure had to be stopped. Our hospital is the tertiary referral center for a large population (about 6 million), and most of the patients presented late at our center (mean duration of 27 days after onset of symptoms). Many of them were already on treatment including antibiotics and/or antituberculosis therapy. In developing countries, differentiating inadequately treated parapneumonic effusions from tuberculous effusions remains a challenge,[21] and 38% of patients in this study belonged to this category. Moreover, 36% (32/90) of our patients had pleural biopsy diagnosis of nonspecific inflammation or fibrinous pleuritis due to inclusion of patients with subacute empyemas. Thoracoscopy helped in ruling out tuberculosis, and we could stop anti-tuberculosis therapy in 11 patients. These reasons might also explain a higher proportion of adhesions encountered during thoracoscopy in our series (59%) as compared to previous reports (between 30 and 40%), and failure to obtain a pleural biopsy.[22, 23] Also, the duration of the post-procedure tube drainage was longer because many of our patients were those of tuberculous and parapneumonic effusions in contrast to other reports where the majority of the patients are those with malignant effusions.[14]

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The decision to choose semirigid or rigid thoracoscopy depends on the extent of adhesions on imaging. Our study suggests that semirigid thoracoscopy is unlikely to help in those with extensive adhesions, and one should directly resort to rigid thoracoscopy or VATS.[6] Although all the investigations (namely chest radiograph, ultrasound and CT chest) were not performed in every patient in this study, we believe that ultrasound is the best diagnostic modality of the three as it offers realtime images. Occasionally, in some patients with no significant adhesions on ultrasound, we encountered extensive adhesions during thoracoscopy, especially in those with minimal effusions.

The complication rate was similar in the two arms. More patients in the rigid arm had persistent air leak and/or empyema which was attributed to extensive adhesiolysis. Many of these patients with adhesions were finally diagnosed as complicated parapneumonic effusions (ten of the 11 patients with complicated parapneumonic effusions had adhesions) with higher chances of secondary infection. The requirement of sedative and analgesics was slightly higher with rigid thoracoscopy as the scope is bigger and maneuvering the scope causes greater pain. Also, adhesiolysis was performed only with the rigid scope thus increasing the requirement of these drugs. Rigid thoracoscopy requires a larger port, which results in a bigger scar while the semirigid scope leaves a smaller scar. The operators found it easier to take a biopsy with the rigid forceps that accompanies the rigid scope. This is in agreement with the experience of other interventional pulmonologists.[10, 14] Despite a larger biopsy size with rigid thoracoscopy, the diagnostic yield was similar in the two groups, which is in congruity with the findings of Rozman et al.[14] However, a recent study does suggest a higher yield of larger biopsy size with semirigid thoracoscopy using a diathermic knife.[24]

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The presence of nodules on thoracoscopic examination increased the probability of achieving a definite histological diagnosis on biopsy with variable sized nodules increasing the odds of malignancy and uniform sized nodules increasing the odds for tuberculosis. Also, the finding of diffuse nodules suggests a diagnosis of tuberculosis. It has been previously suggested that availability of frozen section examinations of pleural biopsies during pleuroscopy might enable the endoscopist to decide on whether to proceed to pleurodesis in the same thoracoscopic setting.[25] When frozen section examination is not available, as is the case in our institution, one might consider proceeding with pleurodesis in patients where variable sized nodules are seen on thoracoscopic examination. Similarly, anti-tuberculosis therapy can be started in a high tuberculosis prevalence setting in the presence of diffuse, small sized nodules.

Finally, our study has a few limitations including a small sample size and the involvement of a single center. Due to the small sample size, there is a possibility of error caused by a higher number of failed pleuroscopies in the semirigid arm. Hence, a larger trial is required to assess the usefulness of the two procedures. We did not verify the results of the non-diagnostic thoracoscopy (nonspecific inflammation/fibrinous pleuritis) by using a reference standard of diagnosis, such as thoracotomy or VATS although we did follow these patients for at least six months. The duration of the procedure was longer than reported elsewhere.[14] The reasons included performance of adhesiolysis in the rigid arm, and difficulty in obtaining pleural biopsy in the semirigid arm. Also, the operators included fellows with variable amounts of experience with the instruments, which caused some bias even though the procedures were supervised by one of the consultants. However, this allowed us to compare the performance of the two instruments in a real-life situation where multiple operators with variable experience might be performing the procedures.

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CONCLUSIONS

In conclusion, the study found a higher diagnostic yield with rigid thoracoscopy on an intention-to-treat analysis. The yield was similar, wherever a biopsy could be performed with the semirigid device. It may be better to resort to the rigid device if adhesions are present or suspected. Due to the small sample size, a larger study is required to define the usefulness of the two procedures, and the choice of a particular thoracoscope in different subset of patients.

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LEGEND TO FIGURES

Figure 1: Flow diagram (CONSORT figure) depicting the study protocol and the participant inclusion process (* of the five patients, four are crossed over from the semirigid arm)

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Table 1. Baseline characteristics of study population

	Rigid thoracoscopy (n=45)	Semirigid thoracoscopy (n=45)	Total (n=90)	P value
Age (years)	54.2 ± 14.9	48.8 ± 13.3	51.5 ± 14.3	0.08
Sex (male: female)	31:14	31:14	62:28	1.00
History of tobacco smoking, No. (%)	9 (20.0)	8 (17.8)	17 (18.9)	1.00
Duration of symptoms (days)	26.9 ± 10.2	27.9 ± 13.1	27.5 ± 11.7	0.68
Comorbidities				
Hypertension	14 (31.1)	17 (37.8)	31 (34.4)	0.66
Diabetes mellitus	13 (28.9)	9 (20.0)	22 (24.4)	0.46
Chronic kidney disease	7 (15.6)	10 (22.2)	17 (18.9)	0.59
Pre-procedure diagnosis				
Malignancy	22 (48.9)	18 (40.0)	40 (44.4)	0.53
Tuberculosis	23 (51.1)	27 (60.0)	50 (55.6)	
Pleural fluid investigations				
Total leucocyte count, cells/µL	1040 ± 1852	812 ± 926	926 ± 1461	0.46
Protein, gm/dL	4.63 ± 1.15	4.98 ± 1.26	4.81 ± 1.21	0.16
Glucose, mg/dL	104.6 ± 67.9	99.2 ± 34.5	101.9 ± 53.7	0.63
Adenosine deaminase, U/L	26.9 ± 18.9	30.3 ± 18	28.7 ± 18.4	0.39
Amount of pleural effusion				
Small	7 (15.6)	9 (20.0)	16 (17.8)	0.58
Moderate	19 (42.4)	23 (51.1)	42 (46.7)	0.40
Large	4 (8.9)	6 (13.3)	10 (11.1)	0.50
Massive	15 (33.3)	7 (15.6)	22 (24.4)	0.09
Presence of loculations, n/N (%)				
Chest radiograph	9/45 (20.0)	6/45 (13.3)	15/90 (16.7)	0.57
Computed tomography chest	9/37 (24.3)	10/35 (28.6)	19/72 (26.4)	0.79
Thoracic ultrasound	4/11 (31.4)	5/24 (20.8)	9/35 (25.7)	0.42
By any technique	11/45 (24.4)	13/45 (28.9)	24/90 (26.7)	0.81

All values are expressed as mean ± SD or number (percentage) unless otherwise stated

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Table 2. Primary and secondary outcomes of the study

Outcome	Rigid thoracoscopy	Semirigid thoracoscopy	Total	P value
PRIMARY OUTCOME				
Diagnostic yield				
Intention-to-treat	44/45 (97.8)	33/45 (73.3)		**0.002**
In those with successful biopsy	47/47 (100)	33/35 (94.3)		0.18
SECONDARY OUTCOMES	(N=44)	(N=35)		
Doses of sedatives/analgesics				
Midazolam, in mg	5.1 ± 2.3	3. 9 ± 1.3	4.5 ± 1.9	**0.009**
Pentazocine, in mg	45 ± 16.5	39 ± 13.2	42.3 ± 15.3	0.08
Tramadol, in mg	68.8 ± 30.6	50.1 ± 31.9	60.5 ± 32.3	**0.01**
Scar size, in mm	23.1 ± 4	18.7 ± 3.2	21.2 ± 4.3	**0.0001**
Biopsy size, in mm	13.9 ± 4.4	4.4 ± 1.4	9.2 ± 5.8	**0.001**
Duration of procedure (minutes)	58.6 ± 13.9	53.4 ± 10.8	56.3 ± 12.8	0.07
Duration of post-procedure intercostal tube drainage (days)	5.6 ± 5.8	5.5 ± 7.5	5.6 ± 6.6	0.95
Operator rated characteristics on visual analog scale (0-100 mm)				
Quality of image	88 ± 7	92 ± 5		**0.002**
Ease of maneuvering	85 ±14	84 ± 12		0.87
Ease of taking a biopsy	86 ± 12	79 ± 12		**0.01**
Expectation that biopsy will reveal a definitive histological diagnosis	86 ± 17	83 ± 19		0.41

All values are expressed as mean ± SD or number (percentage) unless otherwise stated

All secondary outcomes are reported after excluding the procedures that were either converted or abandoned

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Table 3. Thoracoscopic findings, histopathological diagnosis and final diagnosis of study patients

	Rigid thoracoscopy	Semirigid thoracoscopy	Total	P value
Thoracoscopic findings				
Presence of adhesions	28/45 (62.2)	25/45 (55.6)	53/90 (58.9)	0.67
Few	12/28 (42.9)	12/25 (48.0)	24/53 (45.3)	0.79
Extensive	16/28 (57.1)	13/25 (52.0)	29/53 (54.7)	
Thin	7/28 (25.0)	10/25 (40.0)	17/53 (32.1)	0.24
Thick	11/28 (39.3)	9/25 (36.0)	20/53 (37.7)	0.81
Both	10/28 (35.7)	6/25 (24.0)	16/53 (30.2)	0.35
Presence of nodules	31/47 (66.0)	23/35 (65.7)	54/82 (65.9)	1.00
Focal	15/31 (48.4)	11/23 (47.8)	26/54 (48.1)	1.00
Diffuse	16/31 (51.6)	12/23 (52.2)	28/54 (51.9)	
Uniform sized	13/31 (41.9)	12/23 (51.2)	25/54 (46.3)	0.58
Variable sized	18/31 (58.1)	11/23 (47.8)	29/54 (53.7)	
Histopathological diagnosis, n (%)	N=47	N=35	N=82	
Malignancy	19 (40.4)	7 (20)	26 (31.7)	0.08
Tuberculosis	12 (25.5)	9 (25.7)	21 (25.6)	0.98
Nonspecific inflammation/ Fibrinous pleuritis	15 (31.9)	17 (48.6)	32 (39.0)	0.49
Sarcoidosis	1 (2.1)	0	1 (1.2)	-
Aspergillosis	0	1 (2.9)	1 (1.2)	-
Rheumatoid nodule	0	1 (2.9)	1 (1.2)	-

All values are expressed as n/N (%) unless otherwise stated

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Table 4. Association of gross thoracoscopic findings and probability of histological diagnosis

Thoracoscopic findings	Histological diagnosis	Odds ratio (95% confidence intervals)
Presence of nodules	Definitive diagnosis*	**6.66 (2.43-18.26)**
Size of nodules		
Presence of variable sized nodules	Malignancy	**9.21 (3.18-26.63)**
Presence of uniform sized nodules	Tuberculosis	**4.92 (1.71-14.20)**
Distribution of nodules		
Diffuse nodules	Malignancy	2.14 (0.82-5.62)
Diffuse nodules	Tuberculosis	**3.75 (1.33-10.56)**

*A definitive diagnosis implies a histological diagnosis of malignancy, tuberculosis etc and excludes non-specific inflammation or fibrinous pleuritis

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Table 5. Follow-up of 32 patients with nonspecific inflammation/fibrinous pleuritis

	No. of patients/ duration of followup	Follow up
Inadequately treated parapneumonic effusion	11/10-14	Antituberculous therapy was stopped; patients were treated with prolonged course of broad-spectrum antibiotics
Uremic pleuritis	9/8-12	Given renal replacement therapy; pleural effusion decreased in all these patients with dialysis. Five of them underwent renal transplantation
Idiopathic pleuritis	10/10-12	All treatment stopped after biopsy. Followup showed no recurrence of effusion
Tuberculous pleural effusion	2/4-6	Lack of response to antibiotics, and response to anti-tuberculosis therapy; transbronchial lung biopsy revealing necrotic granulomas in one subject

The duration of followup is in months and is depicted as range

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Table 6. Complications of rigid and semirigid thoracoscopy

Complication	Rigid thoracoscopy	Semirigid thoracoscopy	Total	P value
Any complication	16	9	25	0.57
Major				0.97
Empyema	3	1	4	
Major hemorrhage	0	0	0	
Persistent air leak (>3 days)	3	1	4	
Re-expansion pulmonary edema	2	1	3	
Minor				0.97
Subcutaneous emphysema	2	3	5	
Operative site infection	2	1	3	
Non-infective fever	3	1	4	
Minor hemorrhage	1	1	2	

*Crossover patients were included under rigid arm for analysis of complications

All values are expressed as numbers unless otherwise stated

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AUTHOR CONTRIBUTIONS

SD: involved in patient management and data collection, drafted the manuscript

NS: involved in patient management

ANA: involved in patient management, revised the manuscript

DG: involved in patient management, revised the manuscript

RA: conceived the idea, involved in patient management, data collection, statistical analysis, drafted and revised the manuscript for intellectual content

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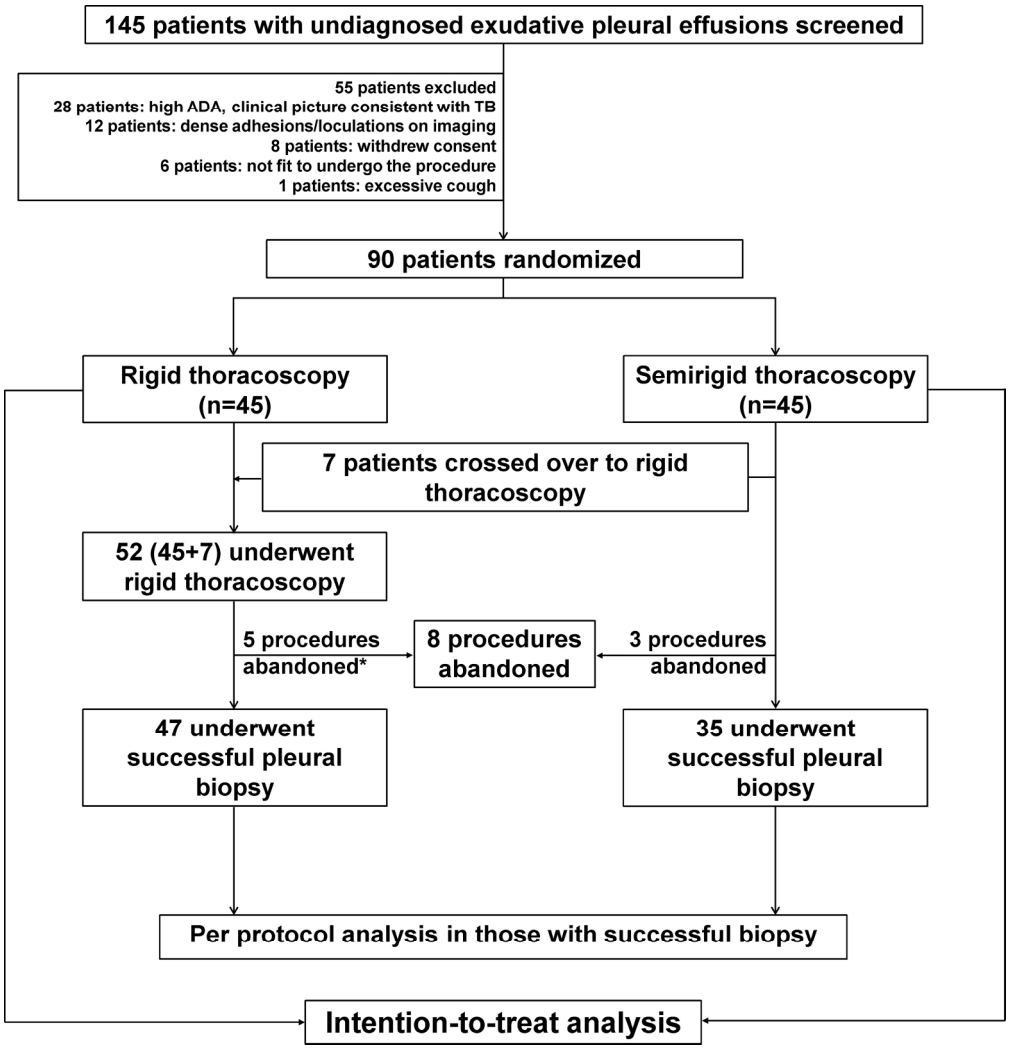

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