Section: Respiratory Medicine

Original Research Article

COMPARISON BETWEEN MEDICAL THORACOSCOPIC PLEURAL BIOPSY AND PLEURAL BRUSH CYTOLOGY IN UNDIAGNOSED EXUDATIVE PLEURAL EFFUSIONS – A PROSPECTIVE STUDY

A Ramasamy[1], M.Mathiyalagan[2]

[1]Assistant Professor, Department of Respiratory Medicine, Thanjavur medical College and Hospital, Tamilnadu, India
[2]Assistant Professor, Department of Respiratory Medicine, Government Medical College and Hospital, Pudukottai, Tamilnadu, India.

Received : 27/07/2024
Received in revised form : 17/09/2024
Accepted : 02/10/2024

Keywords:
Undiagnosed exudative pleural effusion, Medical thoracoscopy, Pleural biopsy, Pleural brush cytology, Diagnostic yield.

Corresponding Author:
Dr. M.Mathiyalagan,
Email: aadhiran511@gmail.com.

DOI: 10.47009/jamp.2024.6.5.74

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (5); 398-403

Abstract

Background: Medical thoracoscopy is a valuable diagnostic and therapeutic procedure for undiagnosed exudative pleural effusion. This study aimed to compare medical thoracoscopic pleural biopsy and pleural brush cytology in undiagnosed exudative pleural effusions and compare the yield of thoracoscopic pleural biopsy and thoracoscopic pleural brush cytology in undiagnosed exudative pleural effusions. **Materials and Methods:** This prospective study included 100 inpatients with undiagnosed exudative pleural effusion at Stanley Medical College and the Government Hospital of Thoracic Medicine between August 2018 and August 2019. Blood tests, pleural fluid analysis, chest USG, and CT to assess thoracoscopy. Medical thoracoscopy was performed under local anaesthesia, conscious sedation, and analgesia using a single puncture with semirigid thoracoscopy. Pleural specimens were obtained using brush and forceps biopsy, followed by chest tube placement, and major or minor complications were recorded. **Results:** The most common thoracoscopic findings were nodules in the parietal and visceral pleura (47.5%), adhesions (37.5%), and loculations (7.5%). Haemorrhagic pleural effusion was observed in 32.5% of the patients. Thoracoscopic pleural brushing revealed granulomas in 32% and malignancies in 45% of patients, while combined pleural biopsy and brush cytology confirmed malignancy in 52.5% and tuberculosis in 35%. The diagnostic yield was 87.5% when both techniques were used together, compared with 80% for pleural brush alone and 85% for pleural biopsy alone. The most common complications were pain (22.5%), fever (20%) and subcutaneous emphysema (10%). **Conclusion:** This study demonstrated that combining thoracoscopic pleural biopsy and pleural brush cytology improves the diagnostic yield of undiagnosed exudative pleural effusions, with an acceptable complication rate.

INTRODUCTION

Medical thoracoscopy (or pleuroscopy) involves passing an endoscope through the thoracic cage and allows for direct visualisation and biopsies from the pleura. It is both a diagnostic and a therapeutic procedure.[1,2] Pleural fluid analysis, blind pleural biopsy, and transthoracic needle aspiration cannot always achieve a diagnosis in all cases. Medical pleuroscopy or thoracoscopy is useful because pleurae can be visualised, and adequate sampling can be performed.[3]

Exudative pleural effusion is most observed in cancer, tuberculosis (TB), and parapneumonic effusion.4 Accurate diagnosis of pleural effusion remains a challenging clinical problem because even after thoracentesis and closed pleural biopsy, 15-20% of pleural effusions remain undiagnosed.[5] Several techniques are used to obtain a pleural biopsy to diagnose undiagnosed pleural effusion, including percutaneous needle pleural biopsy, CT-guided pleural biopsy, medical thoracoscopy, video-assisted thoracoscopy, and open thoracotomy.[6]

A forceps biopsy is the most commonly used instrument to obtain thoracoscopic specimens from suspected pleural lesions.[7] However, it may be associated with bleeding that hinders further biopsy, and the decision to perform a biopsy could be difficult, especially when the targeted lesions are on the visceral pleura or near the vascular structure.8 In

contrast, a pleural brush can be used to obtain pleural specimens through medical thoracoscopy from suspected areas, either in the parietal or visceral pleura or near the vascular structure.[1]

Aim

This study aimed to compare medical thoracoscopic pleural biopsy and pleural brush cytology in undiagnosed exudative pleural effusions and compare the yield of thoracoscopic pleural biopsy and thoracoscopic pleural brush cytology in undiagnosed exudative pleural effusions.

MATERIALS AND METHODS

This prospective study included 100 inpatients with undiagnosed exudative pleural effusion in the Department of Respiratory Medicine of Stanley Medical College and Government Hospital of Thoracic Medicine, Tambaram for 1 year, from August 2018 to August 2019. This study was approved by the Institutional Ethics Committee before initiation, and informed consent was obtained from all patients.

Inclusion Criteria

All inpatients with undiagnosed exudative pleural effusions were included in this study.

Exclusion Criteria

Patients with transudative effusion, neutrophilic effusion, pyothorax, hemothorax, patients < 12 years of age, pregnant and lactating mothers, patients with blood coagulation disorder, comorbid conditions such as coronary artery disease, and cerebrovascular disease who were not willing to provide consent for thoracoscopy were excluded from this study.

Methods

Blood and pleural fluid analyses were also performed. Chest ultrasonography and computed tomography (CT) were performed to assess the feasibility of thoracoscopy. In addition, patients with bleeding diathesis, hemodynamic instability, arrhythmias, or intractable cough are ineligible for thoracoscopy. Medical thoracoscopy was performed with complete aseptic precautions under local anaesthesia, conscious sedation, and potent analgesia.

The procedures must be performed using a single-puncture technique with a semi-rigid thoracoscope. The patients were placed in the lateral decubitus position with the affected side upward. The patient's blood pressure, pulse rate, and oxygen saturation level were monitored continuously. Supplemental oxygen was provided to maintain oxygen saturation, and lidocaine 2% (10–20 ml) was used for local anaesthesia. Conscious sedation may be achieved with intravenous midazolam (0.05 mg/kg body weight) administered for analgesia before the commencement of the procedure.

After local anaesthesia was administered, a small skin incision was made in the mid-axillary line, either in the fifth or sixth intercostal space. The skin incision was followed by the introduction of a 10-mm blunt trocar with a cannula into the thoracic cavity. After the trocar was removed, all fluid was suctioned, and the thoracoscope was introduced into the pleural cavity, where the parietal and visceral pleura were successively inspected.

A pleural brush was used first, followed by a forceps biopsy, to obtain pleural specimens from suspected areas under visual control. The procedure was followed by the placement of a 24F standard chest tube. A chest radiograph was obtained after the procedure and histopathological results were obtained. Major and minor complications were recorded routinely. Major complications were retrospectively defined as events requiring active medical management during hospital stay. Minor complications are events that require medical supervision only.

All the data are presented as frequencies and percentages. The study calculated the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of both diagnostic methods.

RESULTS

Most patients were aged between 41-50 years (27.5%), followed by the 60-70 years age group (25%), and 51-60 years (22.5%) age groups. Only 2.5% of the patients were in the youngest (21-30 years) and oldest (70-80 years) age groups. Most patients were male (67.5%), with a number being smokers (60%). In laterality, right-sided involvement was the most common, affecting 52.5% of patients, with 42.5% having left-sided pleural effusion and 5% experiencing bilateral effusions. Right massive pleural effusion was the most frequent (52.5%), followed by left massive pleural effusion (40%), with only 2.5% presenting with moderate left pleural effusion and 5% with bilateral pleural effusion. CBNAAT results were negative in 87.5% of cases and positive in 12.5% of cases. Pleural protein levels were recorded at an average of 4.96±0.83, adenosine deaminase (ADA) levels averaged 40.5±11.1, and the median value of LDH was 476. [Table 1]

The most common thoracoscopic finding was the presence of multiple nodules in 40% of patients, followed by multiple adhesions (37.5%). Straw-coloured pleural effusion was more frequent (65.5%) than haemorrhagic (32.5%). Adhesions were present in 37.5% of the cases, while nodules were identified in 47.5% of the patients. Malignancy was confirmed in 52.5% of patients, with adenocarcinoma being the most common (27.5%), followed by tuberculosis (35%), and squamous cell carcinoma (12.5%). Granulomas were found in 32.5% of pleural brush reports, whereas 10% showed necrotic material. Inconclusive findings occurred in 15% of biopsy reports and 10% of pleural brush reports. Thoracoscopic complications were primarily pain (22.5%), fever (20%),

ISSN (O): 2687-5365; ISSN (P): 2753-6556

subcutaneous emphysema (10%), and hypoxia (2.5%). Most reports yielded a definitive diagnosis (87.5%), with 35% of the patients diagnosed with tuberculosis. [Table 2]

In thoracoscopy, brush samples demonstrated accuracy when compared to biopsy results. The sensitivity of the thoracoscopy brush technique for detecting malignancy was 95.2%, indicating that it correctly identified 95.2% of the cases with malignancy. The specificity was 100%, indicating that it perfectly identified patients without malignancies. The positive predictive value (PPV) was 100%, indicating that all positive thoracoscopy brush results were true malignancies. The negative predictive value (NPV) was 95%, indicating that 95% of the patients with a negative brush result did not have malignancy. [Table 3]

In thoracoscopy, the brush test showed moderate diagnostic accuracy compared with the biopsy results. The sensitivity was 76.47%, indicating that the brush test correctly identified 76.47% of true-positive cases of malignancy. The specificity was 91.6%, indicating that 91.6% of the patients without malignancy were correctly identified. The positive predictive value (PPV) was 96.6%, showing that nearly all patients who tested positive on the thoracoscopy brush test were confirmed to have malignancy. However, the negative predictive value (NPV) was lower at 57.89%, meaning that only 57.89% of the negative brush results were truly negative, indicating a higher chance of missing some malignancies. Although the test is highly reliable for confirming malignancy, it has limitations in ruling out malignancy when the result is negative. [Table 4]

Pleural biopsy sensitivity was 91.85%, pleural brush cytology sensitivity was 76.47%, and combined pleural biopsy and pleural brush cytology augmented the diagnostic procedure yield. [Table 5]

The diagnostic yield revealed that pleural biopsy alone had a high success rate of 81.6%, indicating that it correctly identified cases in 81.6% of the patients. The yield of pleural brush cytology was slightly lower (69.7%), indicating that brush cytology alone was less effective than biopsy cytology for identifying cases. However, when both procedures were combined, the yield increased significantly to 90%, showing that using both methods together enhanced the diagnostic accuracy and increased the chances of obtaining a definitive diagnosis. [Table 6]

Table 1: Demographic details and clinical characteristics

		Frequency (%)
Age (years)	21-30	1 (2.5%)
	31-40	8 (20%)
	41-50	11 (27.5%)
	51-60	9 (22.5%)
	60-70	10 (25%)
	70-80	1 (2.5%)
Gender	Male	27 (67.5%)
	Female	13 (32.5%)
Smoking	Yes	24 (60%)
	No	16 (40%)
Laterality	Right	21 (52.5%)
	Left	17 (42.5%)
	Bilateral	2 (5%)
Laterality & severity	Right massive	21 (52.5%)
	Left massive	16 (40%)
	Left moderate	1 (2.5%)
	Bilateral	2 (5%)
CBNAAT results	Positive	5 (12.5%)
	Negative	35 (87.5%)
Levels of pleural and serum parameters	Protein	4.96±0.83
	ADA	40.5±11.1
	LDH	476 (145-2314)

Table 2: Thoracoscopic findings, effusion characteristics, and diagnostic outcomes in patients undergoing thoracoscopy

		Frequency (%)
Thoracoscopy morphology	Blackish pigmentation all over the pleura	1 (2.5%)
	Glistening pleura	1 (2.5%)
	Multiple nodules	16 (40%)
	Nodular lesions over the parietal pleura and visceral pleura	3 (7.5%)
	Multiple adhesions	15 (37.5%)
	Multiple loculation	1 (2.5%)
	Normal pleura	3 (7.5%)
Colour of pleural effusion	Haemorrhagic effusion	13 (32.55)
	Straw colour effusion	27 (65.5%)
Adhesion	Yes	15 (37.5%)
	No	25 (57.5%)
Nodules	Yes	19 (47.5%)

ISSN (O): 2687-5365; ISSN (P): 2753-6556

	No	21 (52.5%)
Thoracoscopy pleural brush report	Positive for malignancy	11 (25%)
	Adenocarcinoma	6 (15%)
	Malignant melanoma	1 (2.5%)
	Granuloma	13 (32.5%)
	Necrotic material	4 (10%)
	Squamous cell carcinoma	1 (2.5%)
	Inconclusive	4 (10%)
Thoracoscopy pleura biopsy histopathology report	Malignant melanoma	1 (2.5%)
	Adenocarcinoma	11 (27.5%)
	Mesothelioma	1 (2.5%)
	Small cell lung carcinoma	1 (2.5%)
	Tuberculosis	14 (35%)
	Osteosarcoma secondary's	1 (2.5%)
	Squamous cell carcinoma	5 (12.5%)
	Inconclusive	6 (15%)
Malignancy	Yes	21 (52.5%)
	No	19 (47.5%)
Tuberculosis	Yes	14 (35%)
	No	26 (65%)
Inconclusive report	Inconclusive	5 (12.5%)
	Definitive diagnosis	35 (87.5%)
Thoracoscopy complication	Subcutaneous emphysema	4 (10%)
	Fever	8 (20%)
	Hypoxia	1 (2.5%)
	Pain	9 (22.5%)

Table 3: Thoracoscopic pleural biopsy sensitivity in malignant pleural effusion

Thoracoscopy brush	**Biopsy**	
	Malignancy	**Others**
Malignancy	20%	0%
Other diagnosis	1%	19%
	Diagnostic accuracy	
Sensitivity	95.2% (88.6%-100%)	
Specificity	100% (100%-100%)	
Positive predictive value	100% (100%-100%)	
Negative predictive value	95% (88.3%-100%)	

Table 4: Thoracoscopic pleural brush cytology sensitivity

Thoracoscopy brush	**Biopsy**	
	Positive	**Negative**
Positive	26%	5%
Negative	8%	19%
	Diagnostic accuracy	
Sensitivity	76.47% (58.83%-89.25%)	
Specificity	91.6% (61.52%-99.79%)	
Positive predictive value	96.6% (90.9%-100%)	
Negative predictive value	57.89% (42.29%-72%)	

Table 5: Sensitivity and specificity of medical thoracoscopy pleural biopsy and pleural brush cytology

	Pleural biopsy	**Pleural brush**
Sensitivity	91.85%	76.47%
Specificity	100%	91.6%
Positive predictive value	100%	96.6%
Negative predictive value	66.6%	57.89%
Accuracy	96%	76%

Table 6: Combined pleural biopsy and pleural brush cytology augment the yield of medical thoracoscopy diagnostic procedure

Yield of pleural biopsy	**Yield of pleural brush cytology**	**The yield of the combined procedure**
81.60%	69.70%	90%

DISCUSSION

In our study, patients were aged between 41-50 years (27.5%), followed by the 60-70 years age group (25%), and 51-60 years (22.5%) age groups. Only 2.5% of the patients were in the youngest (21-30 years) and oldest (70-80 years) age groups. Most patients were male (67.5%), with a number being smokers (60%). In laterality, right-sided involvement was the most common, affecting 52.5% of patients, with 42.5% having left-sided pleural effusion and 5% experiencing bilateral effusions. Right massive pleural effusion was the most frequent (52.5%), followed by left massive pleural

ISSN (O): 2687-5365; ISSN (P): 2753-6556

effusion (40%), with only 2.5% presenting with moderate left pleural effusion and 5% with bilateral pleural effusion. CBNAAT results were negative in 87.5% of cases and positive in 12.5% of cases. Pleural protein levels were recorded at an average of 4.96±0.83, and the adenosine deaminase (ADA) level averaged 40.5±11.[1]

The most common thoracoscopic finding was the presence of multiple nodules in 40% of patients, followed by multiple adhesions (37.5%). Straw-coloured pleural effusion was more frequent (65.5%) than haemorrhagic (32.5%). Adhesions were present in 37.5% of the cases, while nodules were identified in 47.5% of the patients. Khanduri et al. study presented the data of 45 patients. The mean age was 59.68 years. Nodules were the most common finding on the thoracoscopic examination. Pleural brush cytology was positive in 26 patients with malignancy, 13 with infection, and six with inadequate cytology. However, forceps biopsy was positive in 42 of 45 cases (93.3%) in detecting malignancy and infectious diseases, and semi-rigid thoracoscopy LTF type 160 was used, but rigid thoracoscopy was used. Semi-rigid thoracoscopy is a safe and efficacious procedure for patients with undiagnosed pleural effusion. It is easy to manipulate, such as a bronchoscopy procedure in the pleural cavity, with fewer complications when combined with a pleural brush and biopsy. Pleural brushing can be performed even in difficult areas to obtain a biopsy and even in normal pleural space.[8]

In our study, forceps and brushes were used in the same patient, and 52.5% of undiagnosed pleural effusion cases confirmed malignancy. Inconclusive findings occurred in 15% of biopsy reports and 10% of pleural brush reports. Thoracoscopic complications were primarily pain (22.5%), fever (20%), subcutaneous emphysema (10%), and hypoxia (2.5%). Most reports have yielded a definitive diagnosis (87.5%), with 35% of patients diagnosed with tuberculosis. Mohamed et al. combined thoracoscopic pleural specimens for diagnosis in 24 patients (96%), all of whom were malignant. Forceps biopsy was positive in 23 patients (92%), whereas pleural brush and pleural lavage were positive in 18 patients (72%) and 15 patients (60%), respectively. A pleural brush was the only diagnostic modality in one patient. Minimal complications were recorded.[9]

In our study, a pleural fluid cartridge-based nucleic acid amplification test diagnosed five patients with tuberculosis and positive findings on biopsy 35 (87.5%), and in brush 32(80%) and malignant pleural effusion with a sensitivity of 95.2%, specificity of 100, positive predictive value of 100, and negative predictive value of 95. In a study by Mohamed et al., the diagnostic procedure showed positive findings in 23 (93%) biopsies and 18 (72%) brushes, with a sensitivity of 95.8% and specificity of 100%. The positive predictive value (PPV) is 100%, meaning that every positive result is a true positive, the negative predictive value (NPV) is 50%, and negative results are true negatives in biopsy methods. In the brush method, the sensitivity is lower at 75%, indicating that it detects 75% of the true positives. The biopsy showed a specificity of 100%, indicating no false positives. The PPV was 100%, indicating that all positive results were accurate. However, the NPV is only 14.3%, indicating that most negative results are false negatives, which reduces its reliability.[9]

In our study, 85% (34/40) and pleural brush cytology yielded 80% (32/40) by combining this procedure in some patients, augmenting the diagnostic yield by up to 90%. The most common complication observed was pain, occurring in nine patients (22.5%), followed by fever in eight patients (20%). Subcutaneous emphysema was reported in four patients (10%), and hypoxia was the least frequent complication, occurring in one patient (2.5%). In the study by Zamzam et al., thoracoscopic pleural biopsy was performed in 92.9% (26/28) of the patients, and pleural brush was positive in 17 out of 28 patients (60.7%). A complication of medical thoracoscopy is combining pleural biopsy and pleural brush cytology in 28 patients within 24 hours of the procedure, which is very safe when compared with pleural biopsy in difficult-to-obtain biopsy cases. The pleural brushing procedure reduces the subcutaneous emphysema events and less painful.[10]

Limitations

Pleural brush cytology was found to be more sensitive and specific than pleural biopsy. A pleural brush cannot be adapted as a single technique for diagnosing undiagnosed pleural effusion. In more than one-third of our cases, Pleural brush was found to be positive for malignancy this specific type of pathology in malignant pleural effusion the procedure does not arrive.

CONCLUSION

The study concluded that a thoracoscopic pleural brush could be performed simply, and safely, and allowed the collection of pleural cellular material, even in harmful areas, from biopsy specimens. This could augment the diagnostic yield of thoracoscopy.

REFERENCES

1. Shojaee S, Lee HJ. Thoracoscopy: medical versus surgical-in the management of pleural diseases. J Thorac Dis 2015;7: S339-51. https://doi.org/10.3978/j.issn.2072-1439.2015.11.66.
2. Loddenkemper R, Mathur PN, Lee P, Noppen M. History and clinical use of thoracoscopy/pleuroscopy in respiratory medicine. Breathe (Sheff) 2011; 8:144–55. https://doi.org/10.1183/20734735.011711.
3. Chockalingam A, Hong K. Transthoracic needle aspiration: the past, present and future. J Thorac Dis 2015;7 Suppl 4: S292-9. https://doi.org/10.3978/j.issn.2072-1439.2015.12.01.
4. Skok K, Hladnik G, Grm A, Crnjac A. Malignant pleural effusion and its current management: A review. Medicina (Kaunas) 2019;55. https://doi.org/10.3390/medicina55080490.
5. Froudarakis ME. Diagnostic work-up of pleural effusions. Respiration 2008; 75:4–13. https://doi.org/10.1159/000112221.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

6. Karkhanis VS, Joshi JM. Pleural effusion: diagnosis, treatment, and management. Open Access Emerg Med 2012; 4:31–52. https://doi.org/10.2147/OAEM.S29942.
7. Sivagnaname Y-., Radhakrishnan P, Maria Selvam A. Thoracoscopic pleural brushing - an innovative method of pleural sampling in diagnostic medical thoracoscopy. Adv Respir Med 2019; 87:257–60. https://doi.org/10.5603/ARM.2019.0046.
8. Khanduri R, Jethani V, Kumar S, Sindhwani G, Chandra S, Pant S. Efficacy of pleural brush cytology in the diagnosis of pleural diseases. Ind J Respir Care 2019; 8:76–9. https://doi.org/10.4103/ijrc.ijrc_25_18.
9. Mohamed KH, Hassan OA. Usefulness of fiberoptic pleuroscopy and brushing in patients with unknown pleural effusion. Egypt J Chest Dis Tuberc 2013; 62:111–4. https://doi.org/10.1016/j.ejcdt.2012.12.001.
10. Zamzam MA, Khames AA, El-Dahdouh SS, El-Rebey HS, Eid HA. Role of thoracoscopic pleural lavage and brush in undiagnosed exudative pleural effusion. Egypt J Chest Dis Tuberc 2015; 64:601–5. https://doi.org/10.1016/j.ejcdt.2015.05.001.

ISSN (O): 2687-5365; ISSN (P): 2753-6556