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Literature Review

Differentiating Pleural Fluid Cytology, Abrams Biopsy, and Pleuroscopy In Malignant Pleural Effusion

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ABSTRACT

Introduction: Malignant pleural effusion (MPE) frequently occurs in advanced-stage malignancies and is typically associated with symptoms such as dyspnea and thoracic pain. Accurate diagnosis is essential for establishing prognosis and directing suitable oncological treatment. **Objective:** This literature review aims to compare pleural fluid cytology, Abrams needle biopsy, and pleuroscopy for diagnosing malignant pleural effusion, focusing on diagnostic sensitivity, advantages, limitations, and clinical applications. **Methods:** This study involved a narrative literature review of published research assessing the diagnostic efficacy of pleural fluid cytology, closed pleural biopsy with the Abrams needle, and medical thoracoscopy (pleuroscopy) in patients with suspected malignant pleural effusion. **Results:** Pleural fluid cytology exhibited a diagnostic sensitivity that varied between approximately 40% and 70%, showing increased yields in adenocarcinoma and reduced sensitivity in mesothelioma. Abrams needle biopsy demonstrated a moderate sensitivity ranging from 60% to 80%, especially when conducted with image guidance. Pleuroscopy demonstrated the highest diagnostic yield, surpassing 90%, owing to direct visualization of the pleura and the capacity to acquire targeted biopsies. **Conclusion:** Pleuroscopy provides the highest diagnostic accuracy for malignant pleural effusion when resources and expertise are accessible. Pleural fluid cytology and Abrams needle biopsy are important diagnostic methods, particularly in resource-constrained environments.

Keywords: Biopsy, Cytology, Effusion, Malignant, Pleura, Pleuroscopy

1. Introduction

The pleura is a mesothelial membrane that encases the thoracic cavity and creates a sealed pleural gap between the visceral and parietal layers, typically containing around 0.26 mL/kg of fluid. Malignant pleural effusion (MPE) is defined by the buildup of pleural fluid resulting from the infiltration of neoplastic cells into the pleura and is a prevalent consequence of advanced-stage malignancy. Clinically, malignant pleural effusion can induce dyspnea, thoracic discomfort, cachexia, and diminished physical activity, so substantially compromising quality of life. Epidemiological data reveal that around 50,000 new cases of malignant pleural effusion are reported each year in the UK, whereas internationally, MPE affects around 20% of patients with advanced cancer, with an estimated incidence of 70 per 100,000 individuals. The existence of MPE indicates the systemic dissemination of the disease and aligns with stage M1a as per the TNM classification. Given the restricted sensitivity of initial pleural fluid aspiration, histological validation through pleural biopsy is frequently essential for establishing a conclusive diagnosis and directing oncological treatment [1,2].

2. Methods

Malignant pleural effusion (MPE) frequently occurs as a complication in cases of advanced malignancy globally. MPE may affect up to 20% of patients with cancer and is associated with a poor prognosis, with median survival ranging from approximately 3 to 12 months after diagnosis. In Western countries, including the United States and Europe, approximately 500,000 new cases of MPE are reported annually. Lung cancer represents the most common underlying malignancy, with ipsilateral pleural involvement observed in approximately 90% of cases and contralateral effusion occurring in about 10% [3,4,5,6].

In breast cancer, malignant pleural effusion occurs in approximately 2–11% of patients, primarily through lymphatic dissemination. In ovarian cancer, pleural effusion may indicate FIGO stage IVa disease and can be associated with a comparatively more favorable prognosis. Approximately 15% of patients present with pleural effusion as the initial manifestation of malignancy [3,4,5,6].

Malignant pleural mesothelioma continues to constitute a significant global disease burden and is closely linked to asbestos exposure, particularly in settings where asbestos use has not been fully eliminated and regulatory oversight remains inadequate. The World Health Organization highlights that ongoing asbestos exposure contributes to the persistence of mesothelioma worldwide, with incidence rates remaining high as a consequence of the extended latency between initial exposure and the onset of clinical disease [7].

Patients with malignant pleural effusion typically present with subacute dyspnea and chest pain. Ferrer et al. evaluated a set of clinical features in a cohort of 93 patients referred for thoracoscopy. Patients fulfilling at least four criteria were classified as having malignant pleural effusion, whereas those meeting one or none were considered to have benign pleural effusion. The assessed clinical features included dyspnea, chest pain, constitutional symptoms, symptom duration exceeding one month, absence of fever, hemorrhagic pleural fluid, and a clinical suspicion of malignancy based on comprehensive assessment [8].

Radiological evaluation represents the next step in the diagnostic workup of pleural effusion in patients with suspected malignancy. Posteroanterior chest radiography is typically the initial imaging modality used to detect pleural effusion in oncologic settings. An effusion generally becomes visible on a posteroanterior chest radiograph when the pleural fluid volume reaches approximately 200 mL, whereas as little as 50 mL can be detected on a lateral view. Blunting of the costophrenic angle usually occurs with an estimated fluid volume of about 175 mL. Pleural effusions measuring less than 500 mL, which account for approximately 10–15% of cases, are often asymptomatic [3].

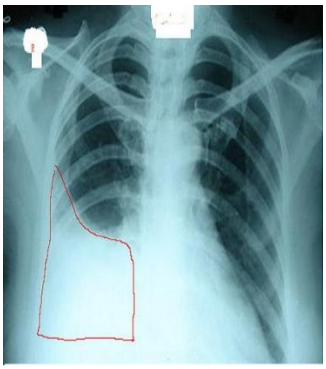

Figure 1. Right Lung Pleural Effusion Radiograph, Posteroanterior. This upright posteroanterior chest x-ray reveals a pleural effusion of the right lung [9]

Chest ultrasound is advised for the assessment of pleural effusion (PE) and serves as a reliable measure of PE volume and depth, contralateral PE presence, echogenicity, compartmentalization, intracavitary effusion, pleural thickening and nodules, as well as diaphragm position and motion. Metastatic pleural tumors exhibit characteristic ultrasound findings, including relatively small hypoechoic crystalloid-like masses, blunt chest wall margins, and masses or nodules with complex echogenic intensity [10,11].

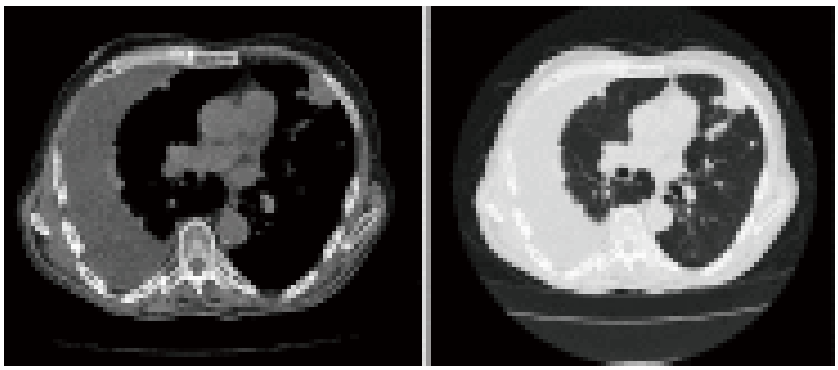

Figure 2. CT scan of the chest showing large right-sided pleural effusion with pleural and parenchymal nodularity. CT, computed tomography [11]

In standard chest radiographs, MPE is frequently unilateral; however, bilateral effusions are observed in approximately 11% of cases. Over fifty percent of MPEs are significant, occupying more than two-thirds of a hemithorax, or are categorized as large.Chest CT is effective in identifying both benign and malignant pleural conditions, as evidenced by characteristics such as pleural wall thickening or mediastinal pleura measuring over 1 cm. Irregular pleural cavities and pleural nodules suggest a considerable probability of malignant pleural effusion (MPE), characterized by high specificity (88–94%) and low sensitivity (36–51%). A chest CT must be performed before the complete drainage of the fluid. Mediastinal and pleural thickening, in conjunction with pleural nodules, suggest the possibility of a malignant pleural effusion (MPE) [11,13].

The diagnostic criteria for malignant pleural effusion (MPE) include the identification of cancer cells through pleural fluid cytology or pleural biopsy. Cytological diagnosis serves as a conventional diagnostic method; nevertheless, its sensitivity is limited when tumor cell quantity is sparse. Numerous studies indicate that the sensitivity of pleural fluid cytology ranges from around 40% to 87%, exhibiting modest positive rates. The volume of cytological fluid obtained during diagnostic thoracentesis remains contentious, with certain studies indicating that a minimum of 75 mL of pleural fluid is necessary for cytopathological diagnosis [11].

A pleural biopsy is the definitive method for diagnosing malignant pleural effusion (MPE). CT-guided or ultrasound-guided biopsies can be conducted to obtain pleural tissue for diagnostic purposes, with a sensitivity of 76–88% and a specificity of up to 100% for the detection of malignant pleural effusion (MPE). In cases of malignant pleural effusion (MPE) where pleural thickness exceeds 1 cm, the diagnostic sensitivity of CT-guided pleural biopsy is similar to that of thoracoscopy (96% versus 95%). A pleural biopsy, in conjunction with pleural fluid cytology, can enhance the diagnostic sensitivity for malignant pleural effusion (MPE) by 7–27% [10].

The pleura is histologically lined with mesothelium, an epithelium originating from the mesoderm. It consists of a single layer of cells supported by a stroma that contains fibroblasts, endothelial cells, immune cells, and extracellular matrix. The visceral pleura comprises the following sequential layers: a delicate layer of mesothelial cells, an underlying fibro-collagenous tissue, an external elastic lamina, a loose connective tissue containing vessels and nerve fibers, and an internal elastic lamina; the latter two layers are continuous with the underlying interlobular connective tissue and the elastic layer of the alveoli, facilitating the distribution of mechanical forces during respiration. The parietal pleura possesses a comparable structure and is situated atop a layer of adipose tissue, which rests on fibrocollagenous tissue affixed to the thoracic cage [1].

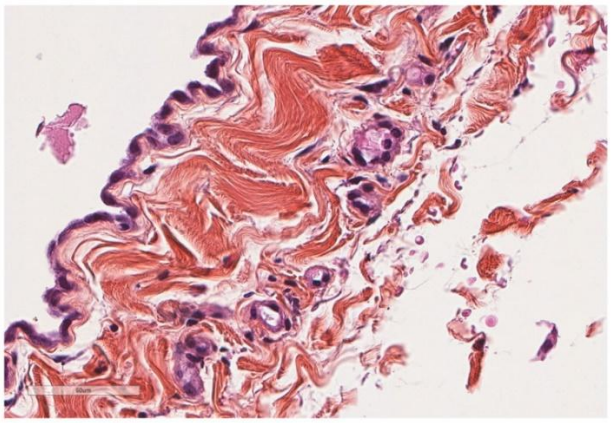

Figure 3. Normal parietal pleura microscopy. A thin connective tissue outline a single mesothelial cell layer. Haematoxylin, eosin, saffron (x400) [1]

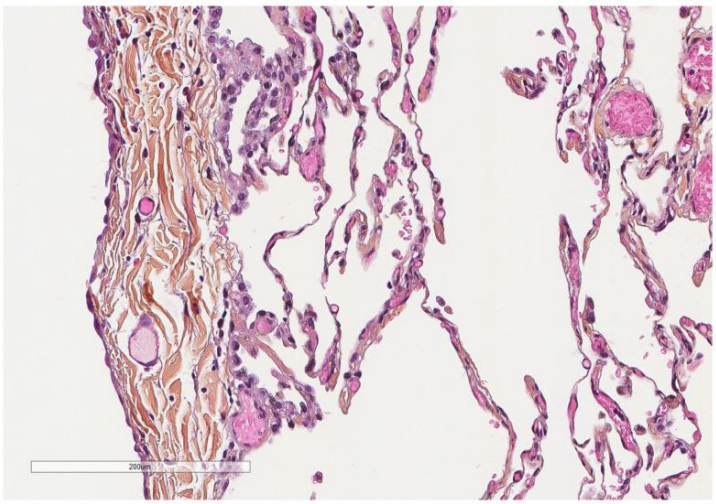

Figure 4. Microscopic examination of the visceral pleura enveloping the underlying alveoli. Hematoxylin, eosin, and saffron staining (×200) [1]

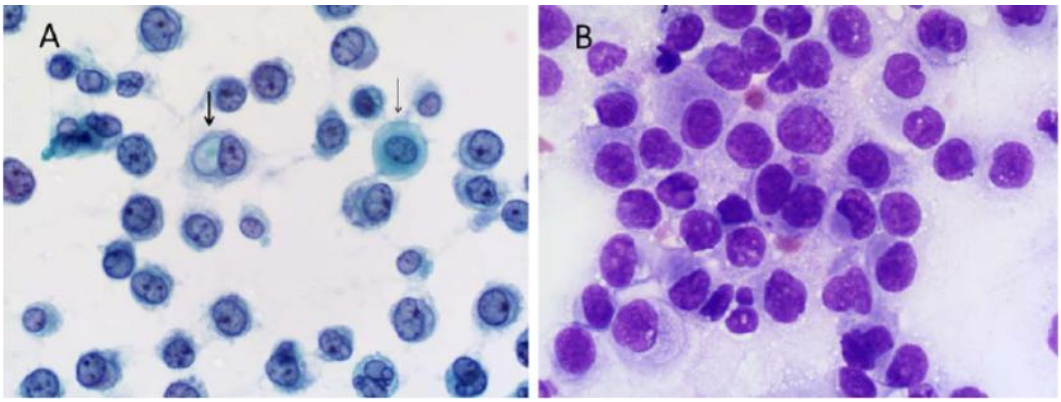

Figure 5. Metastatic lung cancer identified in a pleural effusion specimen. The malignant cells were disseminated, homogeneous, and comparable in size to mesothelial cells (arrow). Observe the targetoid cytoplasmic vacuole [13]

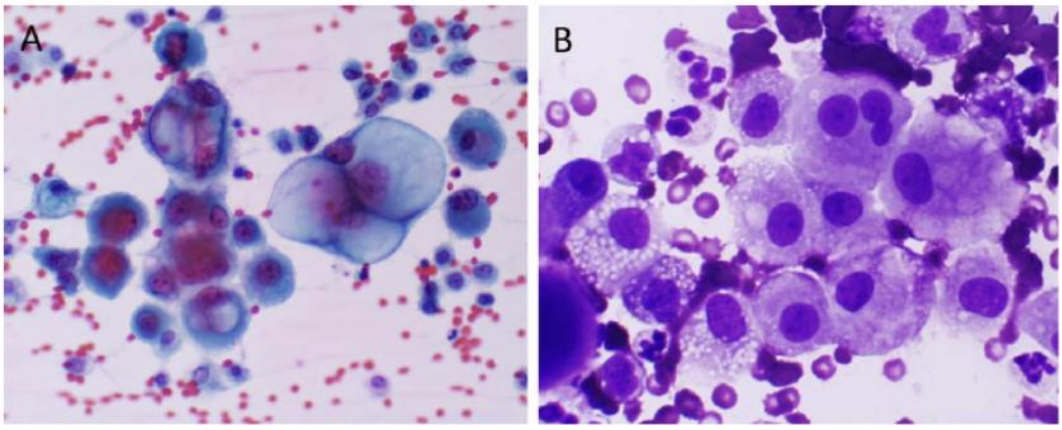

Figure 6. Mesothelioma identified in a pleural fluid specimen. Atypical mesothelial cells were organized individually and in tiny, loose clusters. Several significantly expanded cells containing cytoplasmic vacuoles were seen [13].

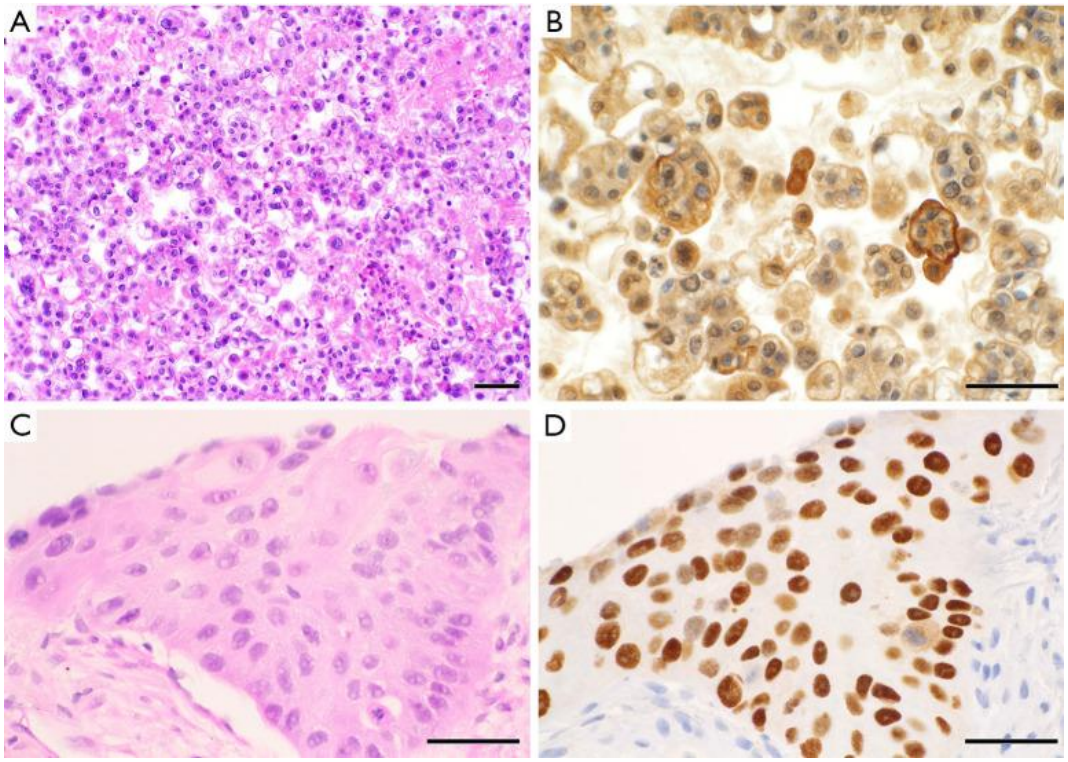

Figure 7. Cytological examination of representative malignant pleural effusion: (A) Adenocarcinoma H&E.(B) Adenocarcinoma H&E in a cell block stained with CK7 immunohistochemical stain.(C) Squamous cell carcinoma in a cell block, stained with hematoxylin and eosin (H&E). (D) Squamous cell carcinoma exhibiting p63 immunohistochemical staining [14]. These findings illustrate the diagnostic value of pleural fluid cytology combined with cell block preparation and immunohistochemistry in improving diagnostic accuracy and facilitating tumor subtyping in malignant pleural effusion

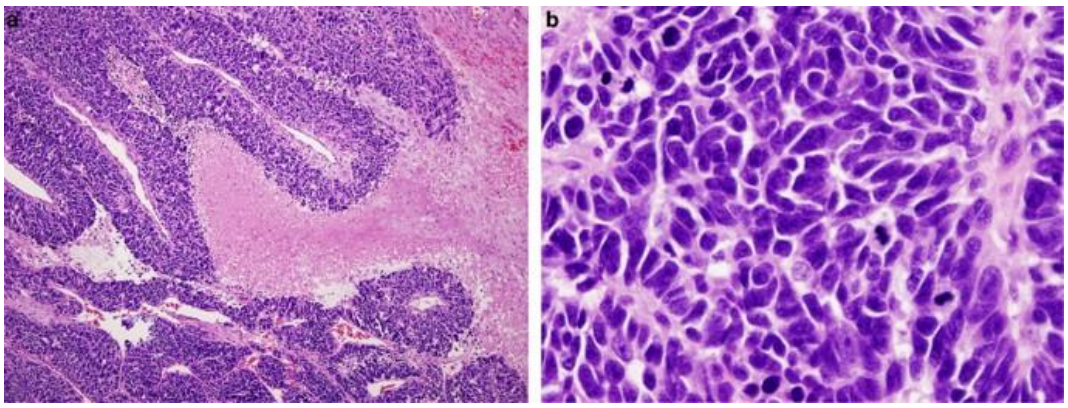

Figure 8. Small cell carcinoma. This neoplasm comprises extensive arrays of tiny malignant cells. Significant necrosis is evident. The tumor has dense aggregates of tiny cells characterized by little cytoplasm, coarsely granular nuclear chromatin, frequent mitotic activity, and inconspicuous or nonexistent nucleoli [15].

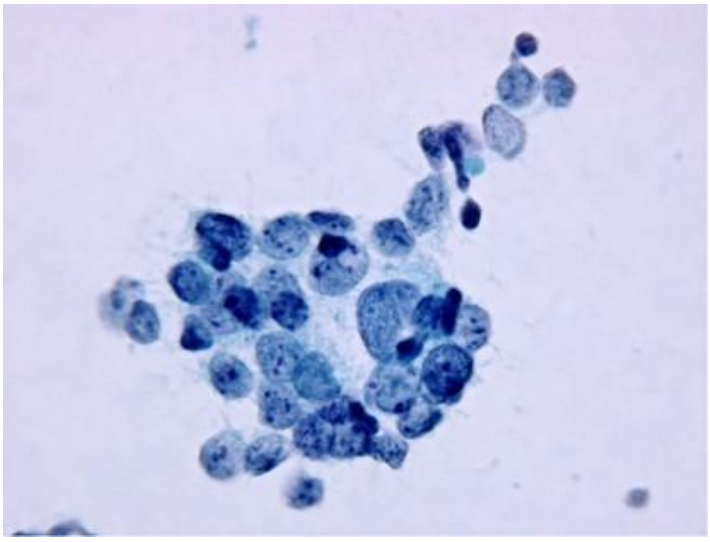

Figure 9. Cytology of small cell cancer. This aggregation of neoplastic cells is densely arranged with minimal cytoplasm, exhibiting coarsely granular nuclear chromatin, and the absence of nucleoli [15].

3. Results and Discussion

The diagnosis of malignant pleural effusion via pleural fluid sampling is definite alone when cytology reveals malignant cells. Porcel and colleagues determined that the yield of the initial PF cytology specimen in MPE was 51% from a contemporary series of over 3,000 PF aspirations, which increased to merely 59% when included second and third cytological specimens in the overall MPE patient sample. The seemingly modest 8% incremental yield undermines the value of conducting serial PF cytological testing. Submitting large PF aliquots (i.e., >250 ml) does not seem to enhance the cytological yield for malignancy diagnosis. The overall detection rate stabilizes at a volume of 75 ml; however, a minimum of 150 ml may be necessary to optimize the efficacy of the cell block preparation. Increased volumes may provide additional benefit when comprehensive immunohistochemistry testing or molecular genetic analysis of the fluid is expected.Four The American College of Physicians Health and Public Policy Committee asserted in a position paper that a diagnostic thoracentesis necessitates only 50–100 mL of fluid [16].

A meta-analysis included thirty-six studies involving 6057 patients with malignant pleural effusion (MPE). The sensitivity of pleural fluid cytology for diagnosing malignant pleural effusion (MPE) is 58.2%. Various significant complications may arise from pleural interventions. A large case series indicates that pneumothorax formation is the most common iatrogenic complication. Clinicians must identify a persistently bubbling chest drain as an indication of an ongoing air leak, whether in cases of spontaneous pneumothorax or after pleural intervention. Reexpansion pulmonary oedema (RPO) is an uncommon yet potentially fatal complication associated with pleural interventions. Iatrogenic intrapleural haemorrhage is a significant

complication linked to pleural interventions, often resulting from injury to the underlying viscera or, more frequently, the intercostal vessels. The occurrence of metastatic malignancy at sites of prior pleural intervention is a rare yet acknowledged issue [17].

The Abrams and Tru-Cut biopsy needles are the predominant instruments utilized for closed pleural biopsy. The treatment is generally conducted under local anesthetic. The patient is positioned either sitting upright or in a lateral decubitus position to facilitate access to the pleural space. Upon site identification, the skin is sterilized, and a local anesthetic is injected to induce numbness in the area. The Abrams needle comprises three distinct components: two concentric tubes and a stylet. The outer tube features a trocar point, sufficiently enough to penetrate the chest wall without perforating the lung in the absence of pleural effusion. Upon penetrating the parietal pleura, the notch is opened, the needle is angled vertically at 45°, and subsequently retracted until pleural tissue is secured within the notch. The inner tube's sharp cutting cylinder is subsequently rotated, severing the tissue akin to a guillotine and holding the excised part within the notch. The needle is subsequently advanced, straightened, and retracted, severing any residual adhering tissue. The inner stylet effectively inhibits air or fluid leakage and can be retracted to verify the position within the pleural space or to aspirate fluid for analysis. The Abrams needle features an indication that shows the alignment of the cutting edge. Precautions must be observed to prevent damage to the neurovascular bundle located on the inferior aspect of the superior rib at the 12 o'clock position relative to the needle, ideally sampling successively between the 3 and 9 o'clock locations [18,19].

he diagnostic sensitivity for malignant disease, when conducted as a traditional "blind" procedure, varies between 40% and 73%.18 Pneumothorax is the most prevalent complication, especially associated with the use of the large caliber Abrams needle. Unguided procedures were linked to a significant incidence of complications, including pneumothorax (3–15%) and hemothorax or other forms of bleeding (~2%). The complication rate for US-guided closed pleural biopsy was 3% (1% major and 2% minor complications), which is significantly lower than the 7% complication rate associated with CT-guided biopsy. The seeding of metastatic malignancy at sites of prior pleural intervention is a common complication, particularly in cases of malignant mesothelioma [18].

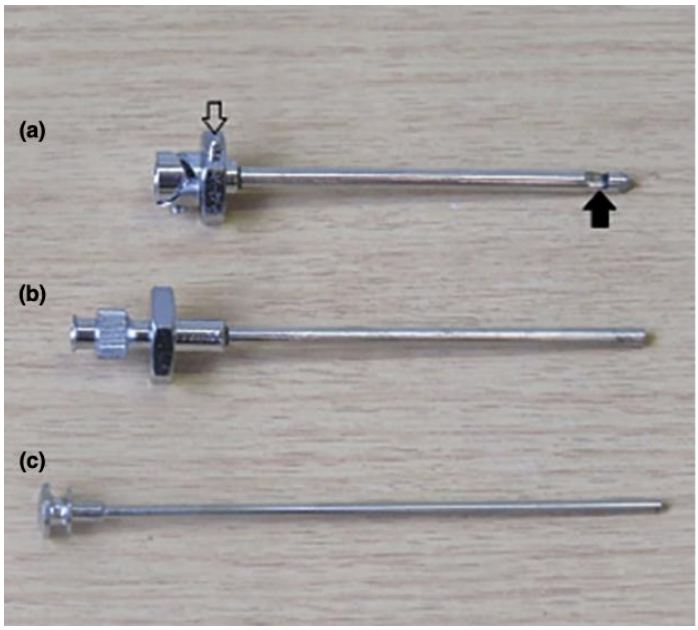

Figure 10. Abrams needle [18]

Medical thoracoscopy, or pleuroscopy, is a minimally invasive technique that involves the insertion of an endoscope through the chest wall for direct visualization of the pleural space. The primary steps involved in pleuroscopy encompass patient preparation and positioning, fluid aspiration, pneumothorax induction, administration of local anesthesia and sedation, trocar introduction, thoracic cavity assessment via pleuroscope with photographic or video documentation, collection of multiple biopsy samples, and subsequent bleeding control.19 MT demonstrates a high diagnostic yield for malignant pleural effusion, with reported rates between 86% and 100% across various studies. Thoracoscopic talc pleurodesis is the preferred method for pleurodesis in patients with malignant pleural effusion who exhibit superior performance status [20,21].

The diagnostic sensitivity of thoracentesis is approximately 60%. The yield of pleural fluid cytology from the initial specimen is 51%, with an increase of 7% from the second specimen and an additional 2% from the third. The sensitivity of pleural fluid cytology varies according to the specific primary malignancy. A study reported an overall sensitivity of pleural fluid cytologic analysis at 46%. The sensitivities for primary malignancies were 6% for mesothelioma, 40% for hematologic malignancies, 79% for lung adenocarcinoma, and as high as 95% for ovarian cancer as the primary malignancy [21].

Complications of MT can be categorized as major and minor complications. A comprehensive investigation indicated that significant problems (pneumonia, bleeding, empyema, bronchopleural fistula, port site tumor development, postoperative pneumothorax, or air leak) arose in 1.8% of cases. small problems, including fever, small bleeding, subcutaneous emphysema, operational skin site infection, atrial fibrillation, or hypotension during the procedure, occurred in 7.3% of instances [21].

Abrams needle biopsy is a semi-invasive method that entails the insertion of a needle into the pleural cavity to procure tissue specimens. Complications encompass pneumothorax, occurring in around 5–10% of instances, hemorrhage if a blood vessel is compromised, and localized discomfort at the biopsy site. Infection is uncommon yet feasible. The diagnostic sensitivity varies between 60% and 80%, which is inferior than pleuroscopy yet adequate in numerous instances. This method is straightforward, economical, and feasible in resource-constrained environments, rendering it a pragmatic option in the absence of sophisticated apparatus [18].

Pleuroscopy, also known as medical thoracoscopy, is a more intrusive procedure that necessitates an incision and the introduction of a scope into the pleural cavity under local anesthesia or sedation. The problems encompass pneumothorax, typically anticipated and addressed during the treatment, as well as infrequent instances of infection, hemorrhage, or subcutaneous emphysema. Notwithstanding these hazards, pleuroscopy exhibits a diagnostic sensitivity surpassing 90%, as it facilitates direct vision of the pleura and enables targeted biopsies. This establishes it as the benchmark for diagnosing malignant pleural effusion, especially when a definitive diagnosis is crucial. Abrams needle biopsy is generally economical, with expenses usually between $100 and $300, contingent upon the healthcare environment [20].

Pleural fluid cytology is a minimally invasive procedure that entails the aspiration of pleural fluid using thoracentesis. The related consequences are typically minimal, encompassing pneumothorax (5–15%), infection, or small hemorrhage. The diagnostic yield is inconsistent, with a sensitivity of 40–70%, contingent upon the malignancy type and tumor burden. Cytology is highly effective for diagnosing adenocarcinomas but is less dependable for identifying mesothelioma. Pleural fluid cytology is frequently the initial diagnostic procedure in suspected pleural cancer due to its simplicity and safety. Pleural fluid cytology is the most minimally intrusive and frequently the most economical method, with expenses generally between $50 and $200 [10].

Table 1. Overall Comparison for MPE Diagnosis

Aspect	Abrams Needle Biopsy	Pleuroscopy	Pleural Fluid Cytology
Invasiveness	Moderate	High	Low
Complication Rate	Moderate (pneumothorax, bleeding)	Low to moderate (air leak, bleeding)	Low to moderate (pneumothorax)
Diagnostic Yield	60–80%	>90%	40–70%
Advantages	Cost-effective, simple	High sensitivity, direct visualization	Non-invasive, simple
Limitations	Limited yield, skill-dependent	Requires expertise and equipment	Low sensitivity, sample-dependent
Price	Low ($100 to $300)	High ($1,000 to $3,000)	Low ($50 to $200)
Procedure Time	~30–60 minutes	1–2 hours	~15–30 minutes
Recovery Time	Minimal	Hours to a day	Minimal

4. Conclusion

In summary, pleuroscopy provides the highest diagnostic yield with a relatively low complication rate, making it the preferred choice for malignant pleural effusion diagnosis when resources and expertise are available. Abrams needle biopsy and pleural fluid cytology, while less sensitive, remain valuable options, particularly in resource-constrained settings or as complementary methods. pleuroscopy, also known as medical thoracoscopy, is more expensive, with costs ranging from $1,000 to $3,000, depending on the hospital and equipment used.

5. Data Availability Statement

The datasets generated and analyzed during the current study are not publicly available due to privacy and ethical considerations but are available from the corresponding author upon reasonable request.

6. Ethical Statement

Sumatera Medical Journal (SUMEJ) is a peer-reviewed electronic international journal. This statement below clarifies ethical behavior of all parties involved in the act of publishing an article in Sumatera Medical Journal (SUMEJ), including the authors, the chief editor, the Editorial Board, the peer-reviewer and the publisher (TALENTA Publisher Universitas Sumatera Utara). This statement is based on COPE's Best Practice Guidelines for Journal Editors.

7. Author Contributions

All authors made substantial contributions to the conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

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10. Conflict of Interest

The authors declare that they have no conflicts of interest or financial interest or any other conflict of interest.

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