

# Diagnostic Role of Video-Assisted Thoracoscopy in the Management of Indeterminate Pleural Effusion

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**ABSTRACT**

**Background:** The management of pleural effusion usually involves the drainage of the effusion, identification, and treatment of the underlying cause (s). Studies have shown that the initial diagnostic techniques do not give conclusive diagnosis in some cases of pleural effusion. This group of patients described as patients with indeterminate or undiagnosed pleural effusion constitutes a significant proportion of patients with pleural effusion in clinical practice. In this study, we examined the role of video-assisted thoracoscopy (VAT) in the diagnostic work-up of these patients. **Aim:** To determine the diagnostic outcome of VAT in the management of indeterminate pleural effusion in our center. **Patients and Methods:** Consecutive patients who presented with pleural effusions and who met the inclusion criteria had video-assisted thoracoscopy for diagnostic purposes. Outcome measures including the diagnostic yield, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of VAT in patients with indeterminate pleural effusion, duration of the procedure, duration of hospitalization after the procedure, and complications for all the patients were documented and analyzed. **Results:** Of the 22 patients with indeterminate pleural effusion, conclusive diagnosis was obtained in 18 (81.8%) with a sensitivity of 91.7% [95% confidence interval (CI); 61.5–99.8%], specificity of 100% (95% CI; 69.1–100%), PPV of 100% (95% CI; 0–100%), and NPV of 90.9% (95% CI; 60.5–98.5%) for malignancy and a sensitivity of 78% (95% CI; 40–97%), a specificity of 100% (95% CI; 75.3–100%), PPV of 100% (95% CI; 0–100%), and NPV of 86.7% (95% CI; 65.7–95.7%) for tuberculosis. **Conclusion:** Our results show that video-assisted thoracoscopy plays a useful role in our center in obtaining diagnosis in patients with indeterminate pleural effusion.

**KEYWORDS:** *Diagnosis, pleural effusion, video-assisted thoracoscopy (VAT)*

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## INTRODUCTION

Collection of a significant amount of serous fluid in the pleural space is a frequent clinical problem that requires evaluation and drainage for both diagnostic and therapeutic purposes. Although there are no comprehensive data on the incidence of this condition in Nigeria, it is a major cause of morbidity and mortality in our environment. It usually occurs as a complication of a wide range of underlying pathologies which may be thoracic or systemic.<sup>[1]</sup>

The diagnosis of the cause of pleural effusions is obtained in a large proportion of cases by thoracentesis

and analysis of the pleural fluid, percutaneous needle biopsy of the pleura, and bronchoscopy. However, in about 37.5% of cases, these techniques do not give conclusive diagnosis.<sup>[2,3]</sup> When the diagnosis is not known, it is usually difficult to institute effective treatment, thus resulting in prolonged hospital stay and an increased cost of treatment.

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Video-assisted thoracoscopy (VAT) plays an important role in establishing the diagnosis of malignancy<sup>[4-9]</sup> and tuberculosis<sup>[7-13]</sup> in the management of pleural and lung diseases. This role is particularly important among patients with indeterminate or undiagnosed etiology of pleural effusion where thoracentesis and pleural fluid analysis and blind pleural biopsy did not give conclusive diagnosis. As a result of potential negative implication of undiagnosed infectious and malignant effusions, prompt diagnosis is important. According to the British Thoracic Society guidelines, thoracoscopy is the investigation of choice in exudative pleural effusion when diagnostic thoracentesis is inconclusive and malignancy is suspected.<sup>[14]</sup> Also, Nosotti *et al.*<sup>[15]</sup> in their review article concluded that pleural biopsy, performed through pleuroscopy or VAT, remains the gold standard for the diagnosis of malignant pleural effusion.

However, this role has not been demonstrated in our center. Also, the diagnostic outcome of VAT in management of indeterminate pleural effusion has not been established in our center, necessitating the need for this study.

## METHODS

This was a prospective study that aimed at determining the diagnostic outcome of VAT in the management of patients with indeterminate pleural effusion at the University of Calabar Teaching Hospital, Calabar Nigeria. Ethical approval for the study was obtained from the Human Research Ethics Committee of our hospital before the commencement of the study.

All consecutive consenting patients, males and females,  $\geq 18$  years with indeterminate pleural effusion presenting at the cardiothoracic and vascular surgery division of the Department of Surgery of our hospital between October 2016 and September 2017 were recruited into the study. Indeterminate pleural effusion in this study refers to patients who had thoracentesis with pleural fluid analysis at least twice and blind pleural biopsy at least once without any conclusive diagnosis. Patients with bleeding abnormalities and any other co-morbid condition that precludes general anesthesia or those who did not give consent were excluded from the study.

### Study procedure

Patients who met the inclusion criteria and who do not possess any of the exclusion criteria had VAT. All patients had detailed clinical evaluation with history and clinical examination. Complete blood count with clotting profile and urinalysis were performed. All patients had postero-anterior and lateral erect chest radiographs taken in deep inspiration. This was also repeated after the procedure. Not all patients had computed tomography (CT) scan because of the high cost of the

study and for the fact that no financial assistance was obtained for this study.

After general anesthesia and double lumen endotracheal intubation, patients were placed in the lateral decubitus position. The patient's arms were placed at 90 degrees with the elbows flexed in a praying position and with two pillows between the arms. A pad was placed between the arm board and elbow to minimize the risk of compression and damage to the ulnar nerve. The operating table was flexed with the patient's anterior-superior iliac crest positioned over the flexion of the table. This opens the rib spaces and shifts the hip out of the way, so it does not interfere with the movement of the thoracoscope. The monitor was placed above the head end of the table to enable the surgeon and all assistants have an unobstructed view of the monitor. The surgeon stood in front of the patient. The chest was prepared and draped. A size 5 mm (Medicon 51.13.10 Germany) or 10 mm (Medicon 91.10.00 Germany) thoracoscope with a 30 or 0 degree viewing angle (as found appropriate) was used. The site was chosen depending on the position of the pathology and the intended procedure. Either single or multiple ports were used. The ipsilateral lung was collapsed for unimpaired visibility of the intra-thoracic structures using one lung ventilation. Initial thoracoscopic exploration of the pleural cavity was performed sometimes using the initial chest tube wound (when the chest tube wound was less than 3 days to reduce chances of introducing infection into the chest cavity), and if there was a need for further inter-costal access for instrumentation, it was created. Any residual pleural fluid was drained by controlled suction, and biopsy was taken from suspicious areas on the pleura and lung surfaces for histologic diagnosis.

At the completion of the procedure, a single chest tube was placed in the pleural space and connected to a single chamber underwater seal drainage bottle.

The specimen for histology was preserved in 10% formalin solution, properly labeled, and sent for histopathologic analysis. Pleurodesis was performed later in the ward by the patient bedside after full lung expansion was achieved and after confirmation of diagnosis and fulfillment of criteria for pleurodesis.

After collecting relevant data, a spreadsheet of data obtained was prepared. Statistical analysis using statistical package for social sciences (SPSS) IBM version 20.0 was used to analyze the data. Continuous variables were presented as means and standard deviation and also as median and inter-quartile ranges where applicable, whereas categorical variables were presented as percentages. Presentation of data in tables and

histogram was performed where necessary. Appropriate test of significance using the *P* value was performed.

**RESULTS**

A total of 22 patients who had pleural effusions of undiagnosed etiology were recruited into the study consisting of 15 (69.2%) males and 7 (30.8%) females giving a male: female ratio of 2.25: 1. The median age (inter-quartile range = IQR) of the study participants was 42.5 (22) years with those aged 41–50 accounting for 7 (31.8%) of study participants. Table 1 shows the socio-demographic characteristic of study participants.

Prior to VAT, 16 (72.7%) of the patients had thoracentesis at least twice with about the same proportion with 19 (86.3%) having had needle biopsy at least once. The average number of thoracentesis was 2, whereas the average number of needle biopsy was 1.18.

Eighteen of the 22 patients with indeterminate pleural effusion who had VAT for diagnostic purposes had conclusive diagnosis, whereas the remaining four had additional thoracotomy for the purpose of decortication in order to enhance lung re-expansion and for biopsy. Thus, the percentage success achieved with the use of VAT was 81.8%. Eleven patients out of the 18 had malignancy, and seven had tuberculosis. Seven of the 11 patients with malignancy had previously diagnosed cancer (four patients had breast cancer, two patients had lymphoma, and one patient had prostate cancer) before undergoing VAT. Four patients had no known malignant disease before VAT. There was no previous diagnosis of tuberculosis among the seven patients diagnosed with tuberculosis following VAT.

The histologic diagnosis made from tissue samples collected from the study participants is shown in Figure 1. Most of the patients were diagnosed as either Adenocarcinoma 7 (31.8%) or Tuberculosis 7 (31.8%).

For the remaining four patients (18.2%), who had no previous diagnosis of cancer at any other part of the body and in which diagnosis was not conclusive using

VAT, thoracotomy was performed for the purpose of decortication and for biopsy. Two (50%) of them were diagnosed as having tuberculosis, one (25%) patient had adenocarcinoma, and one (25%) patient remained inconclusive. Thus, a total of 12 (54.5%) had malignancy, nine (41%) had tuberculosis, and one (4.5%) remained inconclusive.

The comparison of diagnostic yield of VAT and the final diagnosis after thoracotomy for patients with cancer is shown in Table 2. In 11 cases, VAT correctly diagnosed patients that had cancer, giving it a sensitivity of 91.7% (95% CI 61.5–99.8%), whereas all the cases

**Table 1: Socio-demographic characteristics of patients that had VAT for diagnostic purposes**

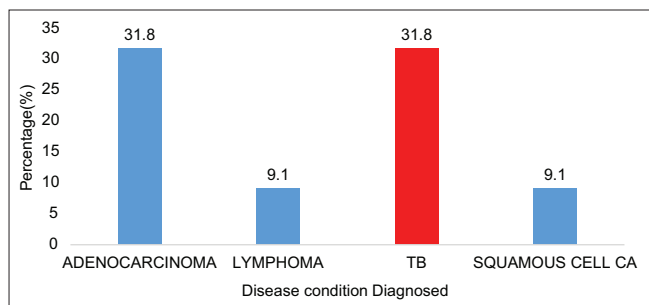
Variable	Frequency (n=22)	Percentage
Age (Years)		
<20	2	9.3
21-30	4	18.1
31-40	4	18.1
41-50	7	31.8
>50	5	22.7
Median age (IQR)	42.5 (22)	
Gender		
Male	15	69.2
Female	7	30.8

IQR=Inter-quartile range

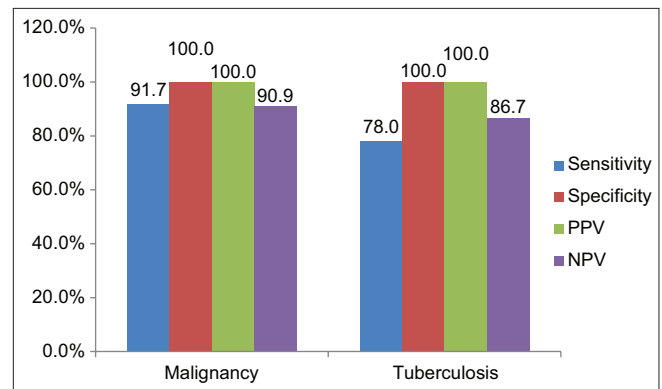
**Table 2: Comparison of diagnostic yield of VAT versus final diagnosis after thoracotomy in cancer patients**

VAT Diagnosis	Definitiv Confirmed presence of disease	Diagnosis Confirmed absence of disease	Total
Disease present	11	0	11
Disease not present	1	10	11
Total	12	10	22

Sensitivity 91.7% (95% CI 61.5-99.8%); specificity 100.0% (95% CI 69.1-100.0%); PPV 100.0% (95%CI 0.0-100.0%); NPV 90.9% (95% CI; 60.5-98.5%)



**Figure 1: Diagnosis made among study participants with indeterminate pleural effusion using VAT (n = 18)**



**Figure 2: Comparison of the diagnostic accuracy of VAT in the diagnosis of cancers compared to tuberculosis in the graphical form**

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without cancer were correctly ruled out using VAT as not having cancer, giving a specificity of 100% (95% CI 69.1–100.0%). The use of VAT in correctly diagnosing or ruling out tuberculosis showed a sensitivity of 78% (95% CI 39.9–97.2%) and a specificity of 100% (95% CI 75.3–100.0%) as seen in Table 3. Figure 2 shows a comparison of the diagnostic accuracy of VAT in diagnosing cancers versus tuberculosis and shows that VAT has higher sensitivity and a negative predictive value in cancer patients compared to those with tuberculosis.

The majority of all the patients with indeterminate pleural effusion 9 (42.9%) had non-specific pleural changes, followed by those with thick pleura 7 (33.3%) and the least proportion being those with thick pleura and nodules 5 (23.8%).

**Table 3: Comparison of diagnostic yield of VAT versus final diagnosis after thoracotomy in patients with tuberculosis**

VAT Diagnosis	Definitive Confirmed Presence of Disease	Diagnosis Confirmed Absence of Disease	Total
Predicts Disease present	7	0	7
Predicts Disease absent	2	13	15
Total	9	13	22

Sensitivity 78.0% (95% CI 40.0-97.2%); specificity 100.0% (95% CI 75.3-100.0%); PPV 100.0% (95% CI 0-100.0%); NPV 86.7% (95% CI 65.7-95.7%)

**Table 4: Relationship between gross findings and definitive diagnosis in patients with pleural effusion**

	Carcinoma n (%)	TB n (%)	Total	Test statistics	P
Gross findings					
Non-specific pleural changes	4 (33.3)	5 (55.6)	9 (42.9)	1.193*	0.551
Thick pleura	5 (41.7)	2 (22.2)	7 (33.3)		
Thick pleura and nodules	3 (25.0)	2 (22.2)	5 (23.8)		
Nodules	0 (0.0)	0 (0.0)	0 (0.0)		

\*Likelihood

**Table 5: Other measures of outcome of VAT for patients with pleural effusion**

Parameters	Pleural effusion (n=22)
Mean duration of surgical procedure±S.D (mins)	130±14.5
Minimum-maximum duration of surgical procedure (mins)	45-160
Average amount of fluid drained during VAT±S.D (mls)	638.9±491.7
Minimum-maximum amount of fluid drained during VAT	250-2600
Mean duration of chest tube drainage±S.D (days)	5.9±3.7
Minimum-maximum duration of chest tube drainage (days)	1-17
Mean total volume of chest fluid drained±S.D (ml)	1555.3±817.1
Minimum-maximum total volume of chest fluid drained (ml)	430-3500
Mean post-operative hospital stay±S.D (days)	16.2±5.5
Minimum-maximum post-operative hospital stay.	6-28
Patients with full lung re-expansion n (%)	19 (86.3)

SD=Standard deviations

Most of the patients who were diagnosed with carcinoma had nodules and thick pleura compared to those with tuberculosis (25.0% versus 22.2%). Again, a higher proportion of those diagnosed with carcinoma had thick pleura only compared to those with tuberculosis (41.7% versus 22.2%). However, higher proportions of those with non-specific pleural changes were seen in those with tuberculosis compared to those with carcinoma (55.6% versus 33.3%). These differences were not statistically significant (p = 0.551) as shown in Table 4.

Other measures of outcome including duration of the procedure, duration of the chest tube drainage post procedure, and duration of hospital stay are shown in the Table 5 below.

The common complications observed following the VAT procedure were post-operative pain in 11 (52.4%), wound infection 7 (33.3%), failure of lung expansion 3 (13.6%), prolonged air leak 2 (9.1%), and empyema 1 (4.7%). No mortality because of the procedure was recorded.

**DISCUSSION**

Indeterminate or undiagnosed pleural effusion remains a major clinical problem confronting the thoracic surgeon. The prevalence has been estimated at between 20% and 40%.<sup>[2,3]</sup> The majority of undiagnosed pleural effusion is related to malignancy or tuberculosis.<sup>[7-12]</sup>

In this study, 18 (81.8%) of the 22 patients with indeterminate pleural effusion had definitive diagnosis

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made by VAT. A similar result was obtained by Ozkaya *et al.*,<sup>[5]</sup> who evaluated the diagnostic efficacy of video-assisted thoracoscopic surgery in their patients with undiagnosed pleural effusion. On the other hand, studies by McDonald *et al.*<sup>[6]</sup> and Arkin *et al.*<sup>[8]</sup> revealed a diagnostic yield of 96% and 98%, respectively. A larger sample size and longer duration of study by these authors may be responsible for their impressive result. Also, the use of thoracic ultrasound by McDonald *et al.* may have facilitated a more precise port placement and a better yield. Out of the remaining four, three were reported as inadequate specimen and in one, a normal muscle tissue was found. These patients, who also did not have malignant disease or tuberculosis at other parts of the body, had thoracotomy. This is because at this point, diagnosis of etiology of pleural effusion was not made and there was a need to decorticate the lung to enhance its expansion and for biopsy.

Eleven patients were diagnosed as having malignant disease using VAT, and out of this number, seven patients had previously diagnosed cancer at other parts of the body. The pathologic lesions diagnosed with VAT in these patients may be secondaries from the primary disease at other parts of the body, although immuno-histochemistry would have clarified that. Four patients had no previous malignancy prior to VAT, and the pathologic lesions diagnosed with VAT are most likely primary diseases. There was no prior diagnosis of tuberculosis in seven patients who had tuberculosis following VAT.

Many authors from developed societies report high incidence of malignancy in patients with indeterminate pleural effusion and a high success rate for thoracoscopy.<sup>[4,8,9,16]</sup> However, in developing countries such as ours, the incidence of tuberculosis among patients with indeterminate pleural effusion is high.<sup>[12,17,18]</sup> In this study, 41% of patients with indeterminate pleural effusion had pulmonary tuberculosis. We believe that this is high compared to other series.<sup>[6,8,9,16]</sup> It shows that this disease is still prevalent in our environment and poses diagnostic challenges.

McDonald *et al.*<sup>[6]</sup> reported a sensitivity of 93%, a specificity of 94%, a positive predictive value of 99%, and a negative predictive value of 76% for malignancy. In this study, we recorded a sensitivity of 91.7% (95% CI 61.5–99.8%), a specificity of 100% (95% CI 69.1–100%), a positive predictive value of 100% (95% CI 0.0–100%), and a negative predictive value of 90.9% (95% CI 60.5–98.5%) for malignancy. Adenocarcinoma of the lungs was the most common histological type recorded in this study. This is similar to what was recorded by other authors.<sup>[5,11]</sup> Obviously, the global campaigns against tobacco smoking and

its negative impact may have resulted in reduced prevalence of tobacco smoking<sup>[19]</sup> and consequently the incidence of squamous cell carcinoma. It is therefore necessary to determine whether there is a genetic factor or any other factor responsible for increased incidence of adenocarcinoma. Diacon *et al.*<sup>[12]</sup> recorded a sensitivity, specificity, and negative predictive value of 100%, respectively, for tuberculosis. However, in this study, we recorded a sensitivity of 78% (95% CI 40–97.2%), a specificity of 100% (95% CI 75.3–100%), a positive predictive value of 100% (95% CI 0.0–100%), and a negative predictive value of 86.7% (95% CI 65.7–95.7%) for tuberculosis. The lower diagnostic performance of VAT seen in this study (especially the lower sensitivity for tuberculosis) when compared with the other studies cited may be because of sub-optimal exploration of the pleural cavity and inability to assess some of the lesions on the pleura and lung surfaces.

There was no correlation between the gross findings on VAT and the final diagnosis ( $P = 0.551$ ). A similar finding was noted by de Groot *et al.*,<sup>[17]</sup> who reported that most cases described as gross tumor on thoracoscopy turned out to be tuberculosis. However, this observation did not agree with Ferrer J *et al.*<sup>[20]</sup> report, which noted that pleural mass was one of the predictors that pleural malignancy would be diagnosed at thoracoscopy. It is important to note that pleural tuberculosis is known to present with nodules which could confuse with malignancy grossly. We suspect that the cause of pleural effusion in the patient who remained undiagnosed probably may be because of non-specific pleuritis or parapneumonic effusion because the symptoms did not progress during the brief period (3 weeks) before being lost to follow-up. Although some studies suggest that most patients diagnosed as non-specific pleuritis after VAT eventually have benign disease,<sup>[21,22]</sup> others show a high rate of malignancy among this group of patients.<sup>[8,23]</sup> Therefore, proper follow-up is essential to make diagnosis early and institute proper treatment.

The mean duration for the procedure in this study was  $130 \pm 14.5$  min. This is high when compared with other studies that assessed the effectiveness of VAT in the management of pleural collections<sup>[23-25]</sup> This is probably because we added anesthesia time to it. However, there was a decline in the duration of the procedure in the last 50% of the cases. Also, the mean duration of hospitalization after VAT was  $16.2 \pm 5.5$  days. This duration was slightly longer when compared with results of other investigators.<sup>[17,23,26]</sup> Some of the patients had to wait and commence definitive treatment of the pathology before being discharged, and we believe that this could be the reason. In all, 19 (86.3%) patients had full lung

re-expansion. Two patients with malignancy and one patient with tuberculosis had failure of lung re-expansion. We thought that this could be as a result of the severity of the underlying lung parenchyma disease. Also, there was a significant improvement in lung function parameters 2 weeks after the procedure in a large proportion of the patients in this study. One of our patients in this study had empyema in the early stage, and the patient responded to appropriate antibiotics without adding to morbidity. No mortality because of the procedure was recorded.

This study has demonstrated that VAT plays a significant role in the management of patients with indeterminate pleural effusion in our center, especially in making diagnosis. It is also an effective and safe diagnostic modality in the management of these patients. Patients with undiagnosed pleural effusion should be sent for VAT early to avoid delay in making diagnosis in these patients. This is a single-center study; the duration of study is short and the sample size rather small. These limitations in no doubt will affect the generalizations of the findings. A multi-center study conducted over a longer period with a larger sample size will validate the findings in this study.

#### Declaration of patient consent

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

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#### Conflicts of interest

There are no conflicts of interest.

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