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Research Article

Diagnostic Yield of Percutaneous Ultrasound Guided Biopsy of Peripheral Lung Lesions

Medhat Fahmy Negam[1], Nashwa Mohammad Emara[2], Shaimaa Magdy Abo Youssef[1]* and Mostafa Mohammad Shalaby[1]

[1]Department of Chest Diseases and Tuberculosis, Faculty of Medicine, Benha University, Egypt

[2]Department of Pathology, Faculty of Medicine, Benha University, Egypt

***Corresponding Author:** Shaimaa Magdy Abo Youssef, Department of Chest Diseases and Tuberculosis, Faculty of Medicine, Benha University, Egypt.

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Abstract

Background: Trans-thoracic Ultrasonography is a well-known technique in the evaluation of thoracic disorders especially peripheral lung lesions. This study aimed at assessing the diagnostic yield of percutaneous ultrasound-guided biopsy in the diagnosis of peripheral lung lesions.

Patients and Methods: A 50 patients (38 males, 12 females) all have peripheral lung lesion underwent US-guided core biopsy using 3.5 - 5Hz Curvilinear probe to allow the availability of histopathological findings.

Results: Final diagnosis was 34 malignant cases and 15 cases with non-malignant lesions and 1 case with no diagnosis. US examination showed hypoechoic lesions in 38 cases (76%) which formed 91% of malignant cases and also revealed 29 cases (58%) with lesions with internal echoes inside, which constituted 100% of non-malignant cases with significant difference between malignant and non-malignant. US-guided biopsy was diagnostic in 48 patients out of 50 (96%). Two cases only complicated with pneumothorax (4%), one case of moderate hemoptysis, and other non-serious complications like chest pain and mild self-limited hemoptysis were found in11 cases.

Conclusion: Ultrasonography is a non- invasive, and promising bedside diagnostic tool for examination of patients with peripheral lung lesions and weak role in deeper lung lesion.

Keywords: *Trans-Thoracic US; Percutaneous Ultrasound-Guided Biopsy; Peripheral Lung Lesions*

Introduction

Thoracic lesions have broad differential diagnosis including malignant, benign, and inflammatory lesions, which may be parenchymal, pleural, or mediastinal. Tissue pathology is the gold standard for all of these lesions obtained either by open lung biopsy, mediastinoscopy, or video-assisted thoracic surgery (VATS). CT guided biopsy is also a known method for transthoracic biopsies, but its cost, radiation exposure, and patient shifting are the main drawbacks of this technique [1]. Transthoracic ultrasonography is a well-known technique in the evaluation of thoracic disorders [2]. Curiosity in transthoracic ultrasound (US) increased after the availability of portable settings that can be done by trained physician with an immediate application at the point of care, low cost, and lack of radiation [3].

Transthoracic ultrasound facilitates the differentiation of primary cancer from distant metastasis or infective and inflammatory lesions, which is crucial for the correct management of lung lesions [4]. Initially, large vessels and aerated lung parenchyma can easily be detected

with ultrasound. Secondly, it can be done as a bedside causing no or minimal distress even in patients with poor general conditions, and lastly, the integration of ultrasound into "low-tech" methods by pulmonologists can reduce the need for more expensive radiological or surgical biopsy [5]. This study aimed to assess the diagnostic yield of percutaneous ultrasound-guided biopsy in the diagnosis of peripheral lung lesions.

Materials and Methods

A prospective randomized study was performed in Chest Department, Benha University Hospital, during the period between November 2017 and December 2018. The study included 50 patients (38 males, 12 females) all have peripheral lung lesion. Institutional ethical committee has approved this study and informed written consent from all participated patients was obtained.

Inclusion criteria: Patients who were diagnosed to have peripheral pulmonary lesions in contact with the chest wall using plain chest radiograph and CT chest and are candidates for US-guided core biopsy to allow the availability of histopathological findings.

Exclusion criteria: Patients with deep pulmonary lesions away from the chest wall, Small lesions less than 3 cm in diameter and Patients who are not a candidate for transthoracic biopsy; patients with abnormal coagulation profile (INR more than 1.5 or aPTT more than 1.5 times the control value) and abnormal clotting function or thrombocytopenia (platelets < 50,000/µl) [6], emphysematous patients with a high risk of pneumothorax, suspected hydatid cyst or arterio-venous malformation, Patients on mechanical ventilation, inability of a patient to co-operate during the procedure or to suspend respiration on request or control cough and unique functional lung [7].

All patients were subjected to the following: History taking and physical examination, Laboratory investigations (CBC, LFTs, KFTs, bleeding profile, ESR), CXR and CT chest, Ultrasonography was done with 3.5 - 5Hz Curvilinear probe (Figure 1). The site, size, echogenicity, borders, internal echoes, and vascularities of each lesion were noted; Lesions were biopsied by Fine core needle 16F or 18F, and 4 - 6 biopsies were performed with different depths (Figure 2). Biopsy samples were saved in formalin jar and sent for histopathology and Patients were observed after procedure for complications, and post-procedure CXR was done. All data were collected, tabulated, and statistically analyzed.

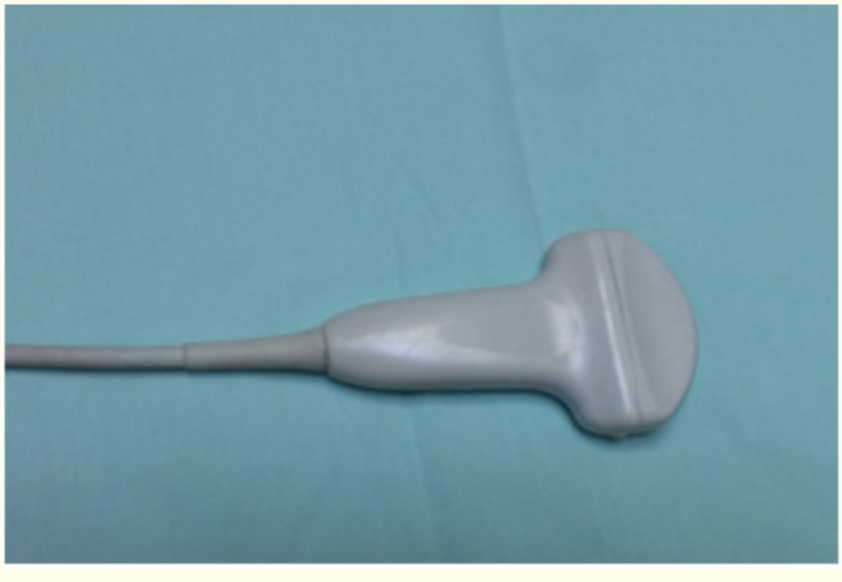

Figure 1: *Curvilinear probe, 3.5 - 5Hz.*

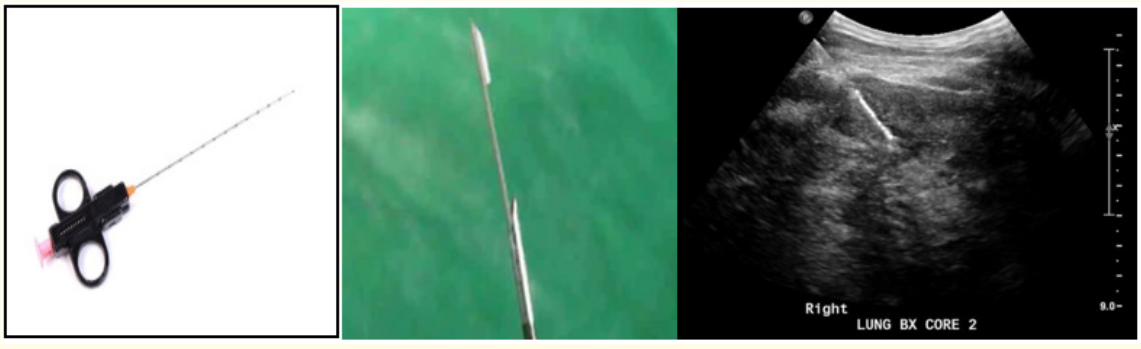

Figure 2: *Fine core needle 16F or 18F.*

Statistical analysis

Data analysis was done using SPSS vs.25 (IBM, Armonk, New York, United States). Numerical data were summarized as means and standard deviations or median and range. Categorical data performed as numbers and percentages and compared using the Chi-square test or Fisher's exact test when appropriate. Comparisons between malignant and non-malignant lesions were performed using the Mann Whitney U test for numerical data. All P values were two-sided. P values less than 0.05 were considered significant.

Results

This study included 50 patients; 38 males and 12 females, their ages ranged from 13 to 84 years old with Mean ± SD 54 ± 17.

Laboratory data	Mean ± SD
ESR	100 ± 27
INR	1.23 ± 0.32
Hemoglobin	11.9 ± 1.5
Total leucocyte count	12.1 ± 5.6
Platelets	286 ± 96
AST	41 ± 16
ALT	37 ± 11
Creatinine	1 ± 0.6

Table 1: *Descriptive analysis of studied group as regarding their laboratory data.*

X-ray, CT findings	n.	%
Lung mass	45	90
Consolidation	16	32
Cavitation	7	14
Pleural effusion	14	28

Table 2: *Descriptive analysis of the studied group regarding their X-ray and CT findings.*

US findings		n.	%
Echogenicity	Anechoic	1	2
	Hyper-echoic	3	6
	Hypo-echoic	38	76
	Hypo-echoic and hyper-echoic	1	2
	Iso-echoic	7	14
Internal echoes	Present	29	58
Internal vascularity	Present	14	28
Well defined borders	Present	32	64
Pleural based	Present	36	72

Table 3: *Descriptive analysis of the studied group regarding their Ultrasound findings.*

Result of US-guided biopsy	n.	%
Adenocarcinoma	12	24
Pneumonia	8	16
Squamous cell carcinoma	8	16
Lung abscess	3	6
Hodgkin lymphoma	2	4
Non-Hodgkin lymphoma	2	4
Round cell tumor	2	4
Small cell carcinoma	2	4
Undifferentiated carcinoma	2	4
Not conclusive	2	4
Acinar carcinoma	1	2
Adenosquamous carcinoma	1	2
Interstitial pulmonary disease	1	2
Metastatic carcinoma	1	2
Myo-fibroblastic tumor	1	2
Sclerosing mediastinitis	1	2
Pulmonary tuberculosis	1	2

Table 4: *Descriptive analysis of the studied group regarding their US-guided biopsies results.*

		Malignant (n = 34)	Non-malignant (n = 15)	P value
ESR	Mean ± SD	111 ± 21	78 ± 27	< 0.001
INR	Mean ± SD	1.26 ± 0.32	1.18 ± 0.34	0.269
Hemoglobin	Mean ± SD	11.6 ± 1.5	12.6 ± 1.3	0.015
Total leucocyte count	Mean ± SD	10.4 ± 5.3	15.8 ± 4.7	0.001
Platelets	Mean ± SD	281 ± 101	286 ± 79	0.991
AST	Mean ± SD	41 ± 14	42 ± 18	0.862
ALT	Mean ± SD	38 ± 11	33 ± 10	0.204
Creatinine	Mean ± SD	1.1 ± 0.7	0.9 ± 0.3	0.305

Table 5: *Descriptive analysis of the studied group as regarding the laboratory data in relation to the pathological results. (Mann Whitney U test was used).*

		Malignant (n = 34)	Non-malignant (n = 15)	P value
Lung mass	n (%)	33 (97.1)	11 (73.3)	0.026
Consolidation	n (%)	5 (14.7)	10 (66.7)	< 0.001
Cavitation	n (%)	3 (8.8)	4 (26.7)	0.179
Pleural effusion	n (%)	11 (32.4)	2 (13.3)	0.165

Table 6: *Descriptive analysis of the studied group as regard the CXR and CT chest findings to the pathological results.*

			Malignant (n = 34)	Non-malignant (n = 15)	P value
Echogenicity	Anechoic	N (%)	1 (2.9)	0 (0.0)	< 0.001
	Hyper-echoic	N (%)	0 (0.0)	2 (13.3)	
	Hypo-echoic	N (%)	31 (91.2)	7 (46.7)	
	Mixed	N (%)	1 (2.9)	0 (0.0)	
	Iso-echoic	N (%)	1 (2.9)	6 (40.0)	
Internal echoes	present	N (%)	13 (38.2)	15 (100.0)	< 0.001
Internal vascularity	Present	N (%)	10 (29.4)	4 (26.7)	0.845
Well defined borders	Present	N (%)	30 (88.2)	2 (13.3)	< 0.001
Pleural based	Present	N (%)	27 (79.4)	8 (53.3)	0.063

Table 7: *Descriptive analysis of the studied group regarding the US findings to the pathological results.*

Complications	N	%
Mild hemoptysis	7	14.0
Chest pain	4	8.0
Pneumothorax	2	4.0
Moderate hemoptysis	1	2.0
No complications	36	72.0

Table 8: *Descriptive analysis of the studied group regarding their complications.*

Discussion

What makes Ultrasonography so accessible in the diagnosis of pulmonary conditions in recent years is that the ability to perform diagnostic procedures in real-time and does not expose the patient or the physician to radiation. The safety and efficacy of thoracic ultra-sonography have been established in many diagnostic methods, including the thoracocentesis site, insertion of a chest tube, transthoracic fine-needle aspiration biopsy [2]. Furthermore, peripheral lung lesions with no air trapped between the chest wall and the lesion can easily be identified using ultra-sonography. Many methods could be used to diagnose such lesions as; fluoroscopy, computed tomography, fiberoptic bronchoscopy, electromagnetic navigation bronchoscopy, virtual bronchoscopic navigation, and surgical biopsy. However, these techniques are inferior to ultrasound-guided biopsy because some are expensive, some require advanced expertise and experience, some are more invasive, and some involve radiation exposure [8].

Trans-thoracic ultrasound-guided biopsy is readily accessible and cheap, can be done bedside in normal situations and in emergency and critical care settings with high diagnostic accuracy. It doesn't involve radiation exposure, is less invasive, doesn't require general anesthesia or sedation, supports procedures in real-time, and is associated with low morbidity and mortality [9]. Many studies show that

ultrasound-guided biopsies done by radiologist have comparable diagnostic yield with the CT scan guided procedures, ultrasound-guided biopsies can be done by the pulmonologist and this will not only save the time of the patient but also help in early diagnosis [10].

This study included 50 patients; 38 males and 12 females, their ages ranged from 13 to 84 years old. Malignant cases have higher age group with mean 58 compared to 44 in the non-malignant group. All cases have performed laboratory investigations including CBC, liver, and kidney function tests, ESR and INR, malignant patients obviously show higher values of ESR (mean = 111) compared to (mean = 78) in non-malignant lesions (p-value < 0.001) (Table 1 and 5) which coincide with Zhang., *et al*. [11], that showed that ESR levels were significantly higher in the lung cancer group compared to that in the chronic respiratory diseases group with (p-value < 0.001).

In this study, TLC is significantly higher in non-malignant group than malignant group (15.8, 10.4) 10^3 cell/dl respectively, this is due to that non-malignant lesions were mainly infections (12 case: 8 pneumonia, 3 lung abscess, and 1 tuberculosis) so infections make 80% of non-malignant lung lesions and, Hemoglobin and serum creatinine show lower values in the malignant group.

Chest X-ray is considered the first step in the diagnosis of pneumonia; however, it has several limitations and is not sensitive or specific 100%. During the last decade, CT is considered the primary imaging tool for the accurate diagnosis of pneumonia. Although CT could be regarded as the "gold standard" technique in the diagnosis of pneumonia, it cannot be used usually as a first-radiological step in all patients with suspected pneumonia [12]. Computed tomography of the chest can identify specific features in lung nodules and other lung lesions that are diagnostic. High resolution scanning further refines its diagnostic ability. The ability of computed tomography scanning to evaluate the entire thorax at the time of localized lesion assessment is of further benefit [13]. All patients in this study had chest X rays, CT chest, and chest ultrasound, then ultrasound-guided biopsies were taken from them. Findings of CXR, CT chest and chest ultrasound are illustrated in table 2 and 3. This study showed that 45 cases (90%) diagnosed as lung masses by chest x-ray and CT chest, while 16 cases (32%) showed consolidations, 7 cases (14%) showed cavitary lesions, and 14 cases (28%) showed pleural effusion in their chest x-ray and CT chest (Table 2 and 6). These findings didn't coincide with Abo Youssef., *et al*. [14], which performed their study on 31 cases and showed 14 cases (45%) diagnosed as lung masses and 14 cases were diagnosed as consolidation by CT chest.

In this study, Ultrasound examination showed hypoechoic lesions in 38 cases (76%) which formed 91% of malignant cases and also revealed 29 cases (58%) with lesions with internal echoes inside, which constituted 100% of non-malignant cases, these results showed significant difference between two groups (Table 3 and 7). While in Abo Youssef., *et al*. [14], Ultrasound has diagnosed only 3 cases (9.7%) with internal echoes and 11 cases (35.5%) with hypoechoic lesions with no significance.

In this study, the final histopathological result of malignancy was found in 34 cases (68%), with adenocarcinoma being the most common diagnosis with percentage of 24% (Table 4), compared to Laursen., *et al*. [15], who found 99 malignant cases (60%) in 126 US-guided biopsies from peripheral lung lesions. Arslan., *et al*. [16], underwent their study upon 294 patients with different peripheral pulmonary lesions diagnosed by needle biopsy, 259 malignant lesions (88.1%) and 35 benign lesions (11.9%), Variations in results may be due to the difference in the number of the studied group. This study agreed with Lederlin., *et al*. [17], who stated that adenocarcinoma is the most prevalent diagnosis in peripheral lung lesions forming 50% of lung cancers while adenocarcinoma in this study constituted 35.2% (12/34).

In this study, US-guided biopsy was diagnostic in 48 patients out of 50 (96%), which was more than Lavinia., *et al*. [18], who performed their study on 59 patients and histopathological confirmation occurred in 54 cases with percentage of (91.52%) and more than Coskun., *et al*. [19], who have 93.8% sensitivity by diagnosing 30 from 32 cases. Moreover, this study gave results of sensitivity more than Elshimy., *et al*. [20], who published that they performed their study on 50 cases and reached histopathological confirmation in 91.7% of their cases. This study also agreed with Diacon., *et al*. [21], who reported that chest ultrasonographic guidance improves the appropriateness of needle insertion site selection and also said accuracy 86% with transthoracic ultrasonography-guided biopsy. Di Bardino., *et al*. [22], concluded that the diagnostic accuracy of ultrasound-guided transthoracic lung biopsy was 88.7%.

Regarding safety, US guidance was extremely safe with the two most common complications reported being pneumothorax, a large proportion of which can be managed conservatively with observation rather than tube thoracotomy, as well as hemorrhage. Severe complications, including hemothorax, air embolism, or cardiopulmonary arrest, are infrequent. There is a higher reported pneumothorax rate using CT guided imaging as compared to US guidance. This complication is likely secondary to the fact that US guided biopsies are only performed on nodules and masses that are directly abutting the pleura [22]. This study showed 2 cases who were complicated with pneumothorax (4%), one case of moderate hemoptysis, and other non-serious complications like chest pain and mild self-limited hemoptysis were found in11 cases (Table 8). while in Lavinia., *et al*. [18], 4 cases out of 59 were complicated with pneumothorax (6.7%), and in Laursen., *et al*. [15], who performed their study on 126 patients; only 3 patients were complicated by pneumothorax (2.4%), and two cases of hemoptysis (1.6%). In Sconfienza., *et al*. [23], 6 cases out of 103 (5.8%) were complicated with pneumothorax, and one case (1%) was complicated with hemoptysis. In the meta-analysis from Di Bardino., *et al*. [22], US-guided biopsy was generally very well-tolerated and safe, with a pooled incidence of pneumothorax of 4.4% (22/503) in the reported papers.

There was no significant difference in complications incidence between malignant and non-malignant groups suggesting that complications are non-dependable on the pathological nature of tissues. So, this study shows that US-guided needle biopsy performed by interventional pulmonologist can be used to obtain a specific diagnosis of peripheral lung lesions in contact with the pleura in up to 96%. Not only malignant lesions could be identified, but also US-guided biopsy can establish the diagnosis of benign diseases such as infectious processes, interstitial and granulomatous lung diseases, and benign lung tumors. The safety profile of the study procedure was also excellent with low incidence of serious complications (6%), which is due to the ability of the technician to monitor biopsy taking and puncturing the lesion while visualizing the procedure in real-time, and we also state that proper training of the procedure technicians, good selection of patients and site and depth of lesion puncturing can significantly improve the efficacy and the safety of the procedure.

Conclusion

Ultrasonography is a non- invasive, and promising bedside diagnostic tool for examination of patients with peripheral lung lesions. It has an excellent diagnostic performance of most common lung pathologies (pneumonia, lung abscess, and different neoplastic lesions). Ultrasonography-assisted interventions can be performed by pulmonologists without sedation and with minimal monitoring, even outside the operating theatre with the improved outcome and decreased complications. Ultrasound-guided biopsy in peripheral lung lesion is a safe and efficient technique in obtaining tissue biopsy sufficient for histopathological analysis and diagnosis.

Recommendations

Chest ultrasound should be used routinely as a primary imaging modality, maybe before the CT scan to decrease exposure to the ionizing radiation. Ultrasound-guided biopsy should be the first choice in peripheral lung lesions superior to other modalities of imaging-guided technique. Further studies are required on a more significant number of cases on the diagnostic yield and safety of ultrasound-guided biopsy in peripheral lung lesions.

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