

Diagnostic yield of ultrasound-guided transthoracic biopsy in peripheral lung lesions

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Background Ultrasonography (US) guidance of transthoracic needle biopsy of peripheral lung lesions is a useful diagnostic technique. It is a relatively easy and safe procedure under real-time US guidance and may give enough tissue sampling of lesions for histopathological examination. The aim of this study was to determine the diagnostic accuracy and safety of this technique in the diagnosis of peripheral lung lesions.

Patients and methods A total of 60 patients underwent US-guided percutaneous needle biopsy of peripheral lung lesions from November 2017 to October 2018 in the Chest Department. The age of patients ranged from 27 to 79 years, with mean age of 58.4 years. Overall, 48 (80%) patients of the studied group were males, whereas 12 (20%) patients were females.

Results According to the final diagnoses, 48 (80%) cases were malignant and 12 (20%) cases were benign. Diagnostic accuracy was 90%, sensitivity was 96%, both specificity and positive predictive value were 100%, and the negative

predictive value was 60%. Pneumothorax and hemoptysis occurred in two (3.33%) patients each.

Conclusion Chest US-guided biopsy in the diagnosis of peripheral lung lesions is a safe and fast procedure with high diagnostic yield and fewer complications.

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Introduction

Peripheral pulmonary lesions (PPLs) are very common, with an increase in frequency of its identification in recent years. PPLs are outlined as lesions adjacent to the pleura and having an accessible window for the ultrasound (US). PPLs are solid or fatty solid nodule present beyond the visible range of flexible bronchoscopy, detected by chest radiography and computed tomography (CT), which may be arising from lung, pleura, chest wall, or mediastinum [1,2].

Chest US is an effective and safe method for evaluation of lesions in the lung periphery, the chest wall, pleural cavity, and mediastinum. US guidance of needle biopsy to obtain specimens for histopathological examination provides real-time imaging of the procedure. US-guided percutaneous transthoracic needle biopsy has many advantages over other imaging techniques such as less exposure of the patient to radiation, acceptability, rapid, inexpensive, and bedside procedure. US-guided techniques are especially suitable for individuals who are more susceptible to injury from radiation, such as infants and pregnant women, and for patients who are difficult to move [3].

Percutaneous transthoracic needle biopsy is a well-established diagnostic procedure. It has been identified as playing a crucial role in diagnosing many pulmonary lesions [4].

The purpose of our study was to evaluate the safety and diagnostic accuracy of transthoracic US-guided needle biopsy in the diagnosis of PPLs.

Patients and methods

The study was carried out at Chest Department during the period from November 2017 to October 2018. It included 60 patients with undiagnosed PPLs as evidenced by chest radiography (posteroanterior and lateral views) and recent contrast-enhanced chest CT. All patients underwent real-time US before biopsy to detect its diagnostic outcome. The study was approved by the local ethical committee of our university to evaluate and publish information. After explaining the study details to the patients, written or verbal consent was taken from all patients.

Inclusion criteria

Patients were selected upon the presence of a mass on the chest radiograph with accessible US window (not under rib or retrosternal) and no intervening normal parenchymal tissue between pleural surface and lesion. All patients would have to be fully conscious and fit for the procedure.

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Exclusion criteria

The following were the exclusion criteria: (a) Bleeding diseases (activated partial thromboplastin time ratio or international normalized ratio more than 1.3 or platelet count less than 50 000/mm³); (b) cardiovascular instability, such as uncontrolled severe hypertension; (c) lack of patient cooperation, for example, altered consciousness; (d) contralateral pneumonectomy; (e) borderline respiratory failure (SaO₂, 85–90%) and patient on mechanical ventilation; (f) hypervascular lesion or aneurysm; (g) severe chronic obstructive pulmonary disease (forced expiratory volume in 1 s <1 l or <35% predicted); (h) pyogenic cutaneous lesion (pyoderma); and (i) patient refusal.

Methods

All patients underwent the following: (a) history taking and clinical examination; (b) chest radiograph (posteroanterior and lateral views) before and after the maneuver; (c) recent CT chest with nonionic contrast media before the biopsy; (d) laboratory studies, such as complete liver functions, kidney functions, complete blood count, erythrocyte sedimentation rate, and blood sugar; (e) preprocedural evaluation, such as pulmonary function tests, arterial blood gases, ECG, and coagulation profile (including bleeding and clotting times, prothrombin time and activity, and activated partial thromboplastin time) with the consideration that oral anticoagulants were stopped before the procedure for at least 48 h; (f) chest US for all patients using high-resolution real-time US; (g) color Doppler US by the same device in suspected vascular lesions; (h) clinical and radiological follow-up of patients over 1 week after the procedure to detect the occurrence of any complications; and (i) histopathological examination of biopsy samples.

Results

This study included 60 patients with peripheral lung lesions; of them, 48 (80%) patients were males, whereas 12 (20%) patients were female. Their age ranged from 27 to 79 years, with a mean age of 57.7 years. The smoking status among patients was 73.3% smokers and 26.7% nonsmokers (Table 1). The maximum number of patients were with a lesion on right upper zone, and next came left upper zone. The mean size of the lesions was 5.90±1.4 cm (3–8 cm) (Table 1).

Most of the patients presented with chest pain (80%) and hemoptysis (73.3%), which is indicative of the lesion to be peripheral, close to the chest wall (Table 2).

Conclusive diagnosis with an initial biopsy was obtained in 54 (90%) of 60 procedures. Biopsies

Table 1 Sociodemographic characteristics among patients, size, and location of the lesion and complication (N=60)

Age (years)	
Mean±SD	58.4±13.4
Range	68.2 (27–79)
Age groups (years) [n (%)]	
20–30	4 (6.7)
31–40	4 (6.7)
41–50	8 (13.3)
51–60	12 (20.0)
61–70	24 (40.0)
71–80	8 (13.3)
Sex [n (%)]	
Male	48 (80.0)
Female	12 (20.0)
Smoking [n (%)]	
Smoker	44 (73.3)
Nonsmoker	16 (26.7)
Size of lesion [n (%)]	
3–4	6 (10)
4–5	8 (13.4)
5–6	14 (23.3)
6–7	18 (30)
7–8	14 (23.3)
Mean±SD (range)	5.90±1.41 (3–8)
Radiological site [n (%)]	
RT upper zone	20 (33.3)
RT middle zone	4 (6.6)
RT lower zone	8 (13.3)
LT upper zone	16 (26.8)
LT middle zone	6 (10)
LT lower zone	6 (10)
Complication [n (%)]	
Pneumothorax	2 (3.3)
Hemoptysis	2 (3.3)

LT, left; RT, right.

Table 2 Presenting symptoms of patients

Symptoms	n (%)
Dyspnea	30 (50)
Cough	26 (43.3)
Expectoration	22 (36.6)
Chest pain	48 (80)
Hemoptysis	44 (73.3)
Toxic manifestation	14 (23.3)

were successfully performed in all patients. The most frequent diagnosis was adenocarcinoma in 20 (33.3%) patients. Regarding the final diagnosis, the percentage of malignant lesions was as follows: adenocarcinoma in 20 (33.3%) patients, squamous cell carcinoma in 14 (23.3%) patients, undifferentiated nonsmall cell carcinoma in 12 (20%) patients, and small-cell carcinoma in two (3.3%) patients. Percentage of benign lesions was as follows: tuberculosis in four (6.7%) patients, organizing pneumonia in six (10%) patients, and thymoma in two (3.3%) patients (Table 3).

Six (10%) patients in whom the specimen obtained by US was nondiagnostic underwent alternative diagnostic procedures (CT-guided needle biopsy). These cases required a second biopsy to get a definite opinion. Five cases were described as nonspecific inflammatory cells in the first biopsies and underwent second biopsies, where two cases were documented to be squamous cell carcinoma, third and fourth cases were documented to be undifferentiated nonsmall cell carcinoma, and the fifth case was documented to be small-cell carcinoma. As for the remaining one, an initial report was that of the proteinaceous cast with no viable tissue, and a repeat biopsy was demanded, on which conclusive report of thymoma was obtained.

Table 3 Final histopathological diagnosis of biopsy

Final diagnosis	n (%)	Diagnostic accuracy of initial biopsy [N/n (%)]
Undifferentiated nonsmall cell	12 (20)	10/12 (83.3)
Adenocarcinoma	20 (33.3)	20/20 (100)
Squamous cell carcinoma	14 (23.3)	12/14(85.7)
Small-cell carcinoma	2 (3.3)	1/2 (50)
Thymoma	2 (3.3)	1/2 (50)
Tuberculosis	4 (6.7)	4/4 (100)
Organizing pneumonia	6 (10)	6/6 (100)
Total	60 (100)	56/60 (90)

Table 4 Histopathological results in relation to smoking

Diagnosis	Cell type	Smoker	Nonsmoker	P value
Malignant	Undifferentiated nonsmall cell	12	0	0.003**
	Adenocarcinoma	6	14	
	Squamous cell carcinoma	14	0	
	Small-cell carcinoma	2	0	
Total		34	14	
Benign	Thymoma	0	2	0.049*
	Tuberculosis	4	0	
	Organizing pneumonia	6	0	
Total		10	2	

*P value is statistically significant. **P value is statistically highly significant.

Table 5 Histopathological results in relation to age

Diagnosis	Cell type	<50 years	≥50 years	P value
Malignant	Undifferentiated nonsmall cell	2	10	0.005**
	Adenocarcinoma	2	18	
	Squamous cell carcinoma	2	12	
	Small-cell carcinoma	0	2	
Total		6	42	
Benign	Thymoma	2	0	0.548
	Tuberculosis	4	0	
	Organizing pneumonia	4	2	
Total		10	2	

**P value is statistically highly significant.

There was a highly significant association between smoking and malignant lesions ($P<0.03$) (Table 4). In addition, there was a highly significant association between age more than or equal to 50 years and malignant lesions, whereas no significant association was detected between the two age groups (<50 years and ≥50 years) and benign lesions. This means that smoking and aging are risk factors for malignancy (Table 5). This also indicated that the probability of the lesions to be malignant was increased if the patient is smoker and old and the probability of the lesions to be benign was increased if the patient is a nonsmoker and young.

Regarding the final diagnosis, diagnostic accuracy was 90% (27/30), sensitivity was 96%, both specificity and positive predictive value were 100%, and the negative predictive value was 60% (Table 6). Complication reported in four (6.66%) patients in the form of hemoptysis and pneumothorax (two for each). The hemoptysis stopped spontaneously without specific treatment, and pneumothorax was small, which did not require intercostal tube drainage and improved spontaneously (Table 1).

Statistical analysis

The data were collected, tabulated, and statistically analyzed using Stata, version 7.0 software (Stata Corp.,

College Station, Texas, USA). Enumeration data were presented as mean±SD and were analyzed with an

Table 6 Diagnostic yield of ultrasound-guided needle biopsy

Variables	%
Sensitivity	88
Specificity	100
PPV	100
NPV	62.5
Accuracy	90

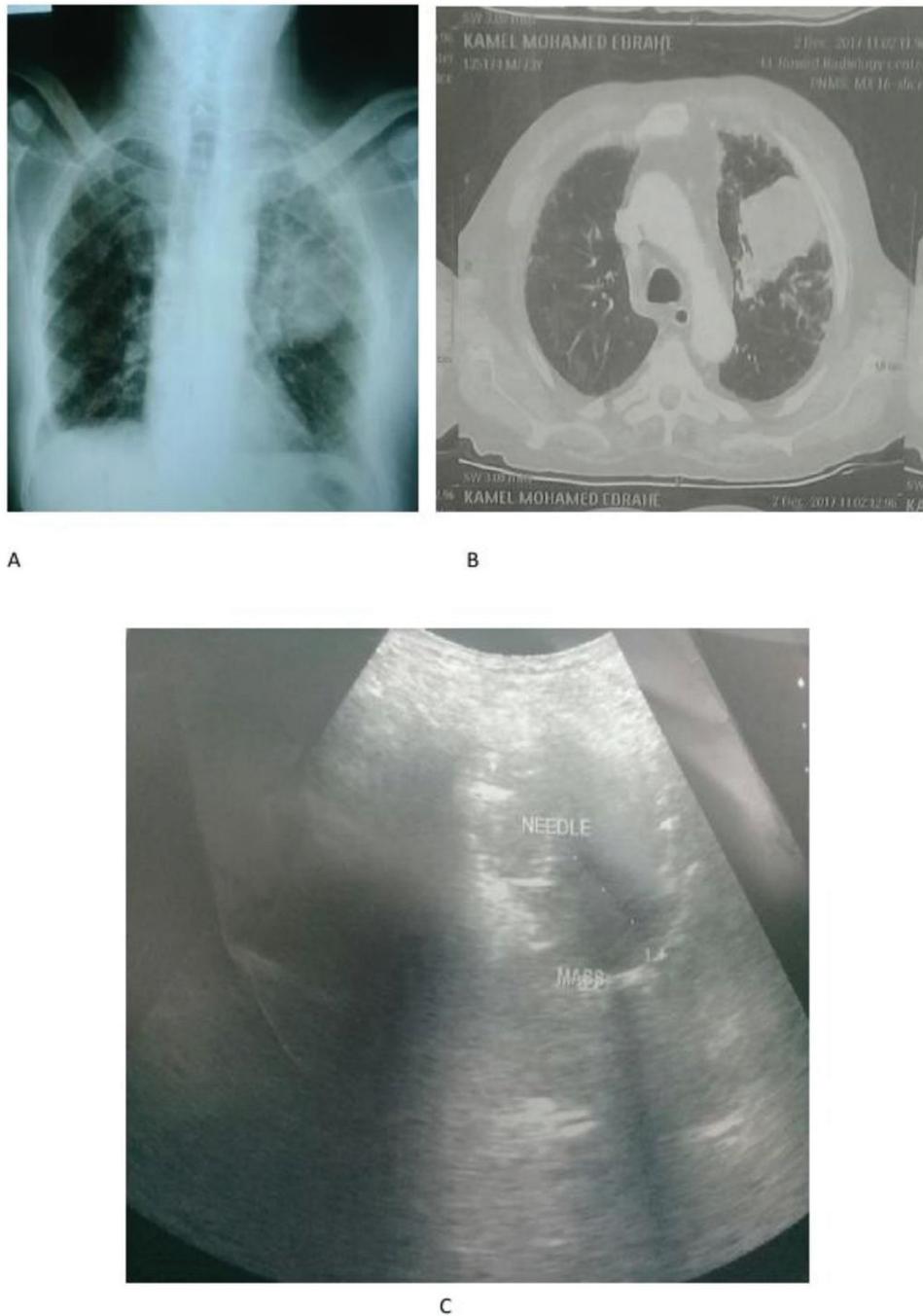
NPV, negative predictive value; PPV, positive predictive value.

unpaired *t* test. Categorical variables were analyzed with Pearson's χ^2 and Fisher exact tests. *P* value less than 0.05 was statistically considered significant (Figs 1–6).

Discussion

Transthoracic ultrasound allows thoracic lesion visualization and their structural characterization; moreover, the internal echotexture of the lesion can be evaluated with the help of color Doppler, allowing precise targeting of central necrosis in large masses [5].

Figure 1



(a) Chest radiograph of a 63-year-old man showing upper left lobe opacity; (b) CT chest showing upper lobe mass of 5×4.5 cm; (c) US image showing TNB entering the mass. CT, computed tomography; TNB, transthoracic needle biopsy; US, ultrasound.

Figure 2



Photograph showing 18 Gx20 cm Tru-cut needle biopsy 46026-Quistello (MN) (Italy).

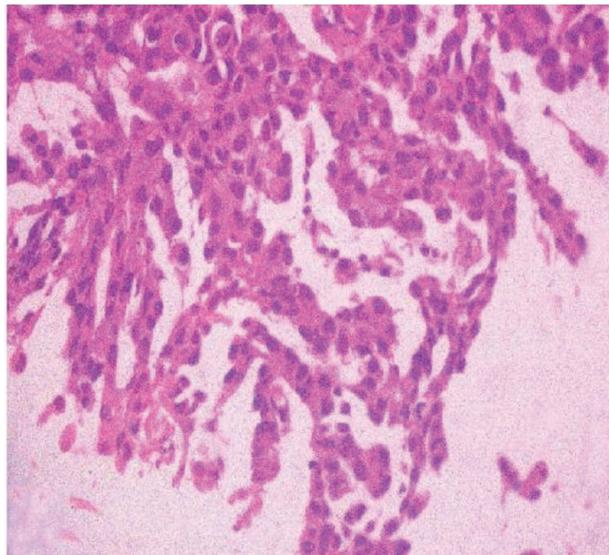
Figure 3



Photograph showing ultrasound Siemens Acuson, x300.

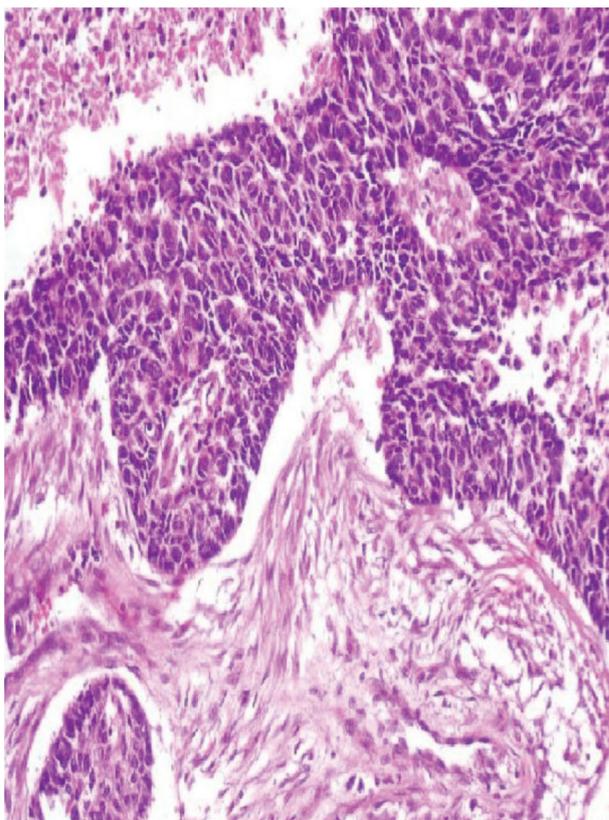
In addition, the US allows percutaneous-guided biopsies with lower risks compared with the other radiological guiding methods such as CT. The US has several advantages: no radiation exposure, accessibility, real-time monitoring, lower costs, and shorter biopsy time [6].

Figure 4



A biopsy specimen was taken from a lung mass showing moderately differentiated adenocarcinoma (hematoxylin and eosin stain, x400).

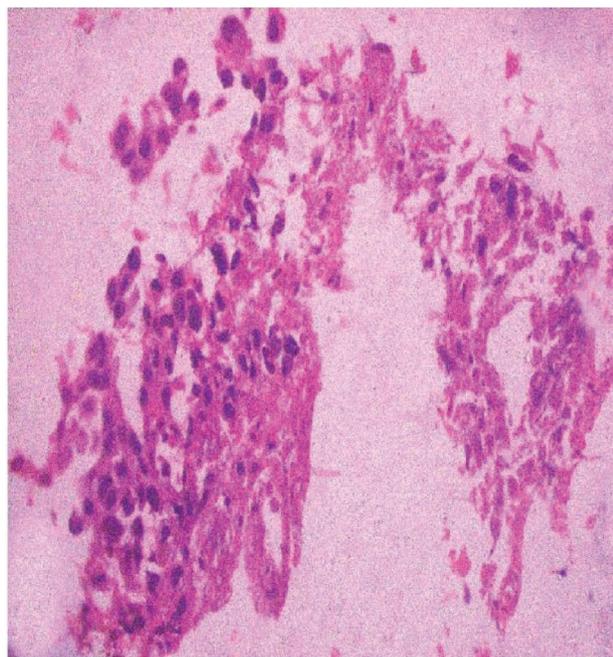
Figure 5



A biopsy specimen was taken from a lung mass showing poorly differentiated squamous cell carcinoma (hematoxylin and eosin stain, x200).

However, there are some limiting factors that prohibit sonographic evaluation of the chest, which are dependent on the physical limitations of the US beam [7]. Its limitations are obscurement of lesions by aerated lungs and smaller, deep seated, and

Figure 6



A biopsy specimen was taken from a lung mass showing small-cell carcinoma (hematoxylin and eosin stain, x400).

cavitary lesions. Sonography is employed for guidance in lung, and for pleural or mediastinal lesions in contact with the chest wall and CT for those not approachable by US. CT scan depicts clear anatomical details and provides access to any space of the body. It is, however, overpriced and therefore the needle is not passed in real time. CT has, among its blessings, clear depiction of anatomical details and access to any area of the body. It, however, is expensive, takes a long time to perform, and includes radiation exposure [8].

US is often as effective as CT for the guidance of thoracic biopsy of peripheral thoracic lesions. CT guidance was necessary only in cases of deeper or smaller nodules, or where the nodules were situated close to the heart and great vessels [9].

Imaging-guided transthoracic needle biopsy is a well-established and safe method for procurement of tissue from lung lesions, with high diagnostic accuracy, sensitivity, and specificity. With recent refinements in sonographic techniques, sonography can be as effective as CT for guiding transthoracic biopsy of peripheral chest lesions [10,11].

The results of the present study showed that there were 54 (90%) patients out of 60 patients accurately diagnosed by US transthoracic true-cut needle biopsy. In agreement with our study, Yuan *et al.*

[12] reported a study including 30 patients with very small pulmonary peripheral lesions with a success rate of 90%. Moreover, this result was in agreement with El-Shimya *et al.* [13] who showed that the diagnostic yield of sonographic examination in PPLs was 90.3%. This result was in accordance with Garcia-Ortega *et al.* [3]. They documented that the diagnostic accuracy of percutaneous US-guided biopsies of peripheral thoracic lesions was 90.4%. This result is also consistent with a study conducted by Blank [14] who reported that the diagnostic yield exceeds 90%. This result is similar to the studies by Jeon *et al.* [15] and Cao *et al.* [16] which founded that diagnostic accuracy of US-guided lung core biopsy was 89.6%.

In contrast, a study by Liao *et al.* [10] documented that correct diagnosis was obtained in 48 (96%) of the 50 patients. Yeow *et al.* [17] analyzed 631 transthoracic cutting needle lung biopsy procedures, and the results showed that the lesion size is one of the most important factors affecting diagnostic accuracy. Pulmonary lesions smaller than 1.5 cm or larger than 5 cm are associated with lower diagnostic accuracy rates. This can be explained by the fact that the presence of a higher percentage of tumor necrosis may have accounted for the lower diagnostic accuracy rate for tumors larger than 5 cm in diameter. In a study by Cao *et al.* [16], the overall diagnostic accuracy was 85.9% (104 of 121).

On the contrary, Jeon *et al.* [15] had shown that the overall diagnostic accuracy of US-guided transthoracic biopsy of PPLs was 91.8% (89/97). Liao *et al.* [10] reported diagnostic accuracy of 96% for US-guided transthoracic biopsy of peripheral thoracic lesions, which were less than 3 cm. According to Yang *et al.* [18], neither lesion location nor lesion size affected the results of US-guided needle biopsy of thoracic lesions. Muhammad *et al.* [19] and Jamakani *et al.* [20] found that the diagnostic yield of US-guided tru-cut biopsies of peripheral lesions was 98%. Moreover, Sconfienza *et al.* [21] documented that the diagnostic yield of US-guided biopsies of peripheral lesions was 97.1% (100 of 103 biopsies).

Pneumothorax is a common complication, and its rate varies from 4 to 5%. However, the problem must be considered dangerous [22]. Other complications like hemoptysis (4–5%) are found to subside without intervention. Air embolism is an extremely rare complication in transthoracic needle aspiration (TTNA). It occurs when a fistula is created between a pulmonary vein and an airway [23]. Hemoptysis and pneumothorax are the foremost frequent complications

of transthoracic biopsy and are principally delicate and self-limiting [24]. In our study, two (3.33%) patients developed pneumothorax and another two (3.33%) developed hemoptysis. Overall complications were 6.66%. Similar to our study, Cao *et al.* [16] reported that only four (3.3%) patients out of 121 patients had mild hemoptysis. This result was in agreement with Sreelatha *et al.* [25] who documented that pneumothorax and hemoptysis occurred in 4% (one patient out of 22 patients for each one).

This result is closely consistent with the studies conducted by El-Shimya *et al.* [13], Diacon *et al.* [26], and Chira *et al.* [7], who reported that incidence of pneumothorax was 4% for US-assisted transthoracic biopsy.

In contrast, Jamakani *et al.* [20] founded that incidence of pneumothorax was 9% (five out of 55 patients) after US-guided biopsies. However, Jeon *et al.* [15] reported that post-procedural pneumothorax and hemoptysis occurred in two patients [two (2.1%) out of 97 patients]. In addition, Grasso *et al.* [27] mentioned that two (2.4%) patients showed two episodes of massive pneumothorax and four (4.8%) patients experience low-grade hemoptysis. Sconfienza *et al.* [21] provided that postbiopsy pneumothorax was observed in six (5.8%) of 103 US-guided procedures and hemorrhage occurred in one (1.0%) of 103 US-guided procedures.

Our study has several limitations. First, the number of the patients was small despite the observable variations regarding diagnosis, lesion size, and location. So, larger studies are required to identify the role of US in the diagnosis of PPLs of different etiologies. Second, there was a selection bias because only lesions that were in contact with pleural tissue were selected for biopsy. Further future study can be done on a large number of patients with peripheral lung lesions comparing the tru-cut needle with other types of needles. The last limitation to our study is the absence of a pathologist capable of making an on-the-spot cytology evaluation of the lesion during the biopsy procedure.

Conclusion

The US is an effective method with high diagnostic yield for the diagnosis of any PPLs. It has many advantages such as no radiation exposure, real-time monitoring, accessibility, inexpensive, short time of biopsy, and few complications. Transthoracic needle biopsy under US guidance was a very efficient, safe, and

less invasive diagnostic method for obtaining histopathological diagnosis avoiding unnecessary surgical procedures.

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Conflicts of interest

There are no conflicts of interest.

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