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RESEARCH

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Diagnostic yield of combined ultrasound-guided fine needle aspiration and core needle biopsy versus either technique alone in peripheral lung and pleural lesions

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Abstract

Introduction Ultrasound (US) has become an integral tool for chest assessment as it provides crucial information on pleural pathologies and peripherally located lung lesions.

Aim To assess the diagnostic yield of combined fine needle aspiration (FNAB) and core needle biopsy (CNB) versus each technique ultrasound-guided in peripheral lung and pleural lesions.

Methodology The present study enrolled 30 patients presenting to Alexandria Main University Hospital, with CT scans showing undiagnosed peripheral lung or parietal pleural lesions with or without effusion. A full ultrasound chest assessment was done covering 12 regions. Assessment of the lesion of interest, vascularity was assessed via color Doppler, locating the safest entry site. Real-time US-guided FNAB was done using a spinal needle 22 gauge. Then real-time US-guided CNB using 18 gauge Trucut needle in the same setting. Duration and complications of each procedure were reported. In FNAB, three smears were prepared, fixed in alcohol, and stained with hematoxylin and eosin stain. The remaining sample was fixed in formalin and centrifuged to prepare cell blocks. On the other hand, Trucut needle biopsy specimens were fixed in formalin and processed as paraffin-embedded blocks. Immunohistochemical staining was done. The results were classified into four categories (inadequate, negative, suspicious, and positive for malignancy.

Results The diagnostic yield of combined techniques was 96.7% versus 63.3% using FNAB and 96.7% using CNB. The sensitivity of FNAB was 86% while CNB was 95%. The specificity and positive predictive value of both methods were 100%. The negative predictive value of FNAB was 57% versus 80% for CNB in peripheral lung lesions. Duration of US-guided CNB was statistically significantly longer than that of FNAB in both peripheral lung and pleural lesions. No major complications were reported using either technique.

Conclusion Combined FNAB and CNB were not superior to CNB alone regarding diagnostic yield but were superior to FNAB. Ultrasound-guided CNB has a superior diagnostic yield over FNAB, with no statistically significant difference regarding associated complications, both techniques are safe. FNAB provided sufficient material for ancillary molecular testing.

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Introduction

Ultrasound (US) has become an integral tool for chest assessment. Its use has grown among pulmonologists over the past decade as it provides valuable information in cases of pleural effusion, lung consolidation, pleural pathologies, peripherally located lung lesions, mediastinal lesions, and chest wall as well as in lymph node assessment [1]. There have been many advantages of ultrasound in pulmonary medicine compared with other radiological examinations regarding the availability, cost, time, and lack of irradiation as well as the bedside examination; facilitating the assessment, especially in emergencies [2].

For malignant lesions, thoracic ultrasound (TUS) can provide important data regarding the size, local extension, any associated atelectasis or necrosis and the vascularity surrounding the lesion denoting vascular invasion and the vascularity of the lesion itself. TUS provides information regarding pleural effusions with higher sensitivity than other radiological investigations [2]. It is superior in some aspects over chest computed tomography (CT) scans as TUS evaluates the pleuropulmonary interface and diaphragmatic movement in a real-time manner during normal respiration and cough [3].

Also, the introduction of second generation contrast material for the US has enabled the prospect of perfusion analysis of lung lesions with far fewer adverse risks compared to other contrast agents used in CT scans [4]. In patients with any contraindications for contrast administration, the use of elastography can be helpful [5, 6]. Regarding limitations, TUS assessment of peripherally located lung lesions provides data proportional to the tumor-pleura contact. In cases where the pleural abutting is small, the visualized part of the tumor is small even if the actual size is large [7]. The bony parts of the thorax can limit the visualization of some peripheral lesions, particularly those involving the paravertebral, retro scapular, parasternal, and to some extent apically located lesions [1]. Another limitation is difficulty in the presence of a chest wall pathology over the region of interest [2]. On the other hand, ultrasound-guided biopsy was effective when thoracoscopy was not feasible [8, 9]. Ultrasound offers a real-time view of the needle and a rare need for breath hold, unlike the CT-guided approach. Meta-analysis research compared the diagnostic efficacy of CT-guided lung biopsy versus ultrasound-guided lung biopsy and showed an overall diagnostic accuracy of 88.7% for ultrasound-guided biopsy, whereas CT-guided biopsy had a diagnostic accuracy of 92.1% [10].

The fine needle aspiration (FNAB) approach uses a hollow needle less than 22 gauge (G) in diameter for aspiration and only allows cytological analysis of the sample. The core needle biopsy (CNB) uses a 20G or larger diameter hollow needle, which can be used to collect tissue samples sized to allow for full histological examination [11]. FNAB-derived cell blocks (CBs) can also provide enough material for molecular profiling, such as EGFR mutation and ALK gene rearrangement tests, which are required for the therapeutic choice in lung adenocarcinoma [12]. US-guided transthoracic FNAB is an established and safe technique for diagnosing intrathoracic pathologies with a reported sensitivity of 74% to 95% and a specificity of 87% to 100% [13]. The incidence of serious complications in a previous study did not differ significantly between CNB and FNAB procedures, even though the total complication rate was much greater with CNB [14, 15].

The present study recruited patients who underwent both US-guided FNAB and CNB with comparative documentation of the different aspects of the procedures emphasizing the diagnostic yield of combined biopsies versus each technique alone.

Aim of the work

The primary objective was to assess the diagnostic yield of combined ultrasound-guided FNAB and CNB versus each technique alone in cases of peripheral lung and pleural lesions. The secondary objective was to compare the procedure time, technical complexity, and ancillary molecular tests between FNAB and CNB.

Patients

The present prospective study enrolled thirty patients presenting to Alexandria Main University Hospital (AMUH), Pulmonology Department with chest CT scans showing an undiagnosed peripheral lung lesion and parietal pleural thickening with or without pleural effusion. The timeframe that started on the 1st of May 2021 till the 1st of October of the same year. We enrolled patients with undiagnosed pleural-based lung nodules, patients with undiagnosed peripheral lung masses, patients with undiagnosed pleural thickening failed to be diagnosed by thoracocentesis (in cases with associated effusion), age 18 years or older. We excluded patients with centrally located masses and patients with a low platelet count of 1.5. Patients with respiratory failure or skin lesions at the site of needle introduction.

Methods

The present prospective study enrolled 30 patients presenting to Alexandria Main University Hospital (AMUH), Pulmonology Department. The study was accepted by the local ethical committee of Alexandria Faculty of Medicine (available from www.med.alex.edu.eg/wp-consent/uploads/2012/04/.pdf). Patients enrolled in the study were expected to come for two visits.

The first visit included detailed history taking; including age, gender, occupation, marital status, and medical and surgical history as well as history of previously diagnosed malignancies or chronic lung diseases. Physical examination included general examination, local chest examination, oxygen saturation assessment, blood pressure, heart rate, and respiratory rate recording and review of the patient's chest CT scans that were available with or without IV contrast.

A full ultrasound chest assessment was done covering 12 imaging regions, 6 on each side. Vascularity was assessed via color Doppler flow, locating the safest site and trajectory for biopsy [16]. A routine blood workup was ordered and coagulation profile; prothrombin time, activity, and INR. Patients who were currently on therapeutic or prophylactic anticoagulation were instructed to stop the drug before the next visit for a duration dependent on the drug's half-life. Bridging therapy for patients on warfarin was done [17]. The second visit included checking the laboratory workup for any exclusion criteria and reviewing and signing the consent. The ultrasound machine used was Sonoscape M22 EXP and the probe used was the curved array transducer. Equipment was prepared including sterile gloves, povidone-iodine 10%, normal saline, two sterile containers containing 10% formalin and another container containing sterile saline (for samples collected for microbiological analysis), six glass slides sprayed with ethanol, one spinal needle 22G, one Trucut needle size 18 15 cm in length, different size syringes, an insulin syringe, one stainless steel blade, and lidocaine 2%.

Ultrasound reassessment was done and the duration of the procedure was recorded. According to the location of the pathology, the patient's position was either lateral decubitus, prone, supine, or sitting position with his/her chest and arms supported. Real-time US guided (FNAB) was done using a spinal needle 22 gauge, 3–5 passes with different angulations to cover different areas in the lesion. After US-guided FNAB was done, US assessment for pleural sliding and absence of any bleeding or pneumothorax was confirmed using the M-mode and visualization of the "sea shore" sign. In the FNAB specimen, two or three smears were prepared, fixed in alcohol, and stained with hematoxylin and eosin (H&E) stain. The remaining sample was fixed in formalin and centrifuged to prepare cell blocks for paraffin embedding. Cytological diagnosis was based on the cytomorphologic features of the smears and cell block preparations and the results of immunocytochemical stains on cell blocks [18].

Then a very small incision using the stainless-steel blade was done to facilitate the Trucut needle entry; a real-time US-guided CNB using an 18-gauge Trucut needle of 15 cm length was done. Four to six samples were taken; one sample was placed in a sterile container for microbiological examination and the remaining were placed in 10% formalin for histopathological examination. Again, excluding any bleeding or pneumothorax was done using M-Mode. CNB specimens were fixed in formalin and processed as paraffin-embedded blocks. Diagnosis of CNB was based on histomorphology and immunohistochemical staining. After the procedure, the patients were admitted for 4 h and a chest X-ray was ordered to exclude the occurrence of any complication, after which the patient was discharged. The results were classified into four categories (inadequate, negative, suspicious, and positive for malignancy) [19]. Malignant cases were reported according to new criteria implied in the 2021 WHO classification for lung cancer diagnosis.

Immune staining was done using Dako autostainer for TTF-1 primary antibody while Ventana benchmark X was used for p63 whenever needed in both cell blocks and CNB to reach a final diagnosis. Furthermore, immunoreactivity for EGFR was assessed whenever possible on both cell blocks and CNB in case of adenocarcinomas and scored based on membranous and/or cytoplasmic staining [20]. Undiagnosed patients underwent further investigations as thoracoscopy or bronchoscopy till a final diagnosis was reached.

Results

The present study enrolled thirty patients presenting to Alexandria Main University Hospital (AMUH), Pulmonology Department with radiographic features of peripheral lung or pleural lesions on chest CT scans that were done either with or without contrast in the timeframe that started on the 1st of May 2021 till the 1st of December of the same year.

Nighty percent of the patients were males, presenting 91.3% among the malignant group and 85.7% among the benign group. The mean age was 57.60 ± 13.26 years (ranging from 20 to 80 years old). Forty percent were in the age group between 61 and 70 years old. The prevalence of smokers was 70%; 23.3% of the studied patients suffered from COPD.

The most common presenting complaint among the studied patients was cough (80%), followed by chest pain and dyspnea (each representing 73.3% of the studied patients). Nearly 78% of patients presenting with chest pain in our study were diagnosed with malignancy. Weight loss was observed in 70%. Night fever in 16.7% and finally hemoptysis in 6.7%.

Among the studied patients, 76.7% were finally diagnosed with malignant lesions, while 23.3% were diagnosed with benign lesions (Table 1). Comparison between both groups showed no statistically significant difference regarding gender, but statistically significant

Table 1 Diagnostic yield of combined CNB and FNAB versus FNAB or CNB in the studied patients ($n=30$)

	Final diagnosis		Diagnostic yield of combined FNAB and CNB		FNAB		CNB		c2(FEp)
	No.	%	No.	%	No.	%	No.	%	
All	**30**	**100.0**	**30**	**100.0**	**30**	**100.0**	**30**	**100.0**	–
Malignant lesions	**23**	**76.7**	**22**	**73.3**	**18**	**60.0**	**22**	**73.3**	3.067 (0.187)
Lung carcinoma									
Small cell carcinoma	1	3.3	0	0.0	0	0.0	0	**0.0**	–
Adenocarcinoma	10	33.3	10	33.3	9	30.0	10	**33.3**	0.077 (0.781)
Squamous cell carcinoma	5	16.7	5	16.7	4	13.3	5	**16.7**	0.131 (1.000)
Undifferentiated carcinoma	4	13.3	4	13.3	2	6.7	4	**13.3**	0.741 (0.671)
Mesothelioma	1	3.3	1	3.3	0	0.0	1	**3.3**	2.0 (1.000)
Others									
Metastatic adenocarcinoma (colon)	1	3.3	1	3.3	1	3.3	1	**3.3**	0.0 (1.000)
Metastatic adenocarcinoma (unknown primary)	1	3.3	1	3.3	1	3.3	1	**3.3**	0.0 (1.000)
Benign lesions	**7**	**23.3**	**7**	**23.3**	**1**	3.3	**7**	**23.3**	10.50*(0.005*)
Dense fibrous tissue	3	10.0	3	10.0	0	0.0	3	**10.0**	6.0 (0.100)
Necrotizing granuloma	3	10.0	3	10.0	0	0.0	3	**10.0**	6.0 (0.100)
Lipoid pneumonia	1	3.3	1	3.3	1	3.3	1	**3.3**	–
Undiagnosed	**0**	**0.0**	**1**	**3.3**	**11**	36.7	**1**	**3.3**	
Undiagnosed	0	0.0	1	3.3	**11**	36.7	**1**	**3.3**	10.417*(0.001*)

χ^2 Chi square test, *FE* Fisher exact, *p P* value for comparing between FNAB and CNB

* Statistically significant at $p \leq 0.05$

differences regarding the mean age with p value of 0.002. The mean age in the benign versus the malignant group was 45 ± 14.49 years old versus 61.43 ± 10.40 years, no statistically significant difference regarding the smoking status, with a p value of 0.554.

The distribution of the studied patients according to the site of pathology as defined by CT chest was as follows: the most commonly affected lobe was the left upper lobe (30%), followed by the right upper lobe, right lower lobe, left lower lobe, and the middle lobe of the right lung in 23.3%, 16.7%, 10%, and 3.3%, respectively. The size of peripheral lung lesions ranged from 1.25 × 3.31 cm to 12.21 × 9.90 cm in maximum dimensions, with a mean of 5.70 cm ± 2.42 cm. Patients with pleural thickening from which biopsies were taken were 16.7% of the patients. The left side was the side involved in 80% and the right side in 20%. Figure 1 shows a chest CT scan and ultrasound of a patient presenting with a left upper lobe lung mass.

Our study enrolled 30 patients who underwent both procedures sequentially (FNAB and CNB). Comparison between both techniques regarding different aspects showed the following: the difference in duration of the procedure between the FNAB and CNB in cases of lung biopsy was statistically significant (mean of 10.30 ± 1.68 versus 11.96 ± 2.13 min, respectively) with a p value less than 0.0001. The difference in duration between the FNAB and CNB in cases of parietal pleural biopsy was statistically significant as well (mean of 12 ± 2.12 versus 15 ± 3.08 min, respectively, a p value less than 0.0230.

The overall yield of the combined procedures FNAB and CNB was 96.6% diagnostic, diagnosing 29 patients out of all 30 studied patients. FNAB was diagnostic in 18 patients of the malignant group ($n=23$) and 1 patient of the benign group ($n=7$). CNB successfully diagnosed 22 patients out of 23 patients of the malignant group; CNB only failed to diagnose 1 case with small cell lung cancer and was diagnosed with other means. CNB successfully diagnosed all benign patients (7/7) with very good accuracy. Combined FNAB and CNB were not superior to CNB alone regarding diagnostic yield but were superior to FNAB. The diagnostic yield of combined techniques was 96.7% versus 63.3% using FNAB and 96.7% using CNB (Table 1).

In the 5 patients that presented with parietal pleural thickening on a CT scan of the chest, the FNAB failed to successfully reach a diagnosis in any of them, whereas CNB was diagnostic in all cases. In one case, the biopsy was inadequate and the CNB diagnosed this patient as NSCLC—adenocarcinoma. Another case was diagnosed with mesothelioma using CNB; the FNAB only showed rare suspicious atypical mesothelium cells but was not

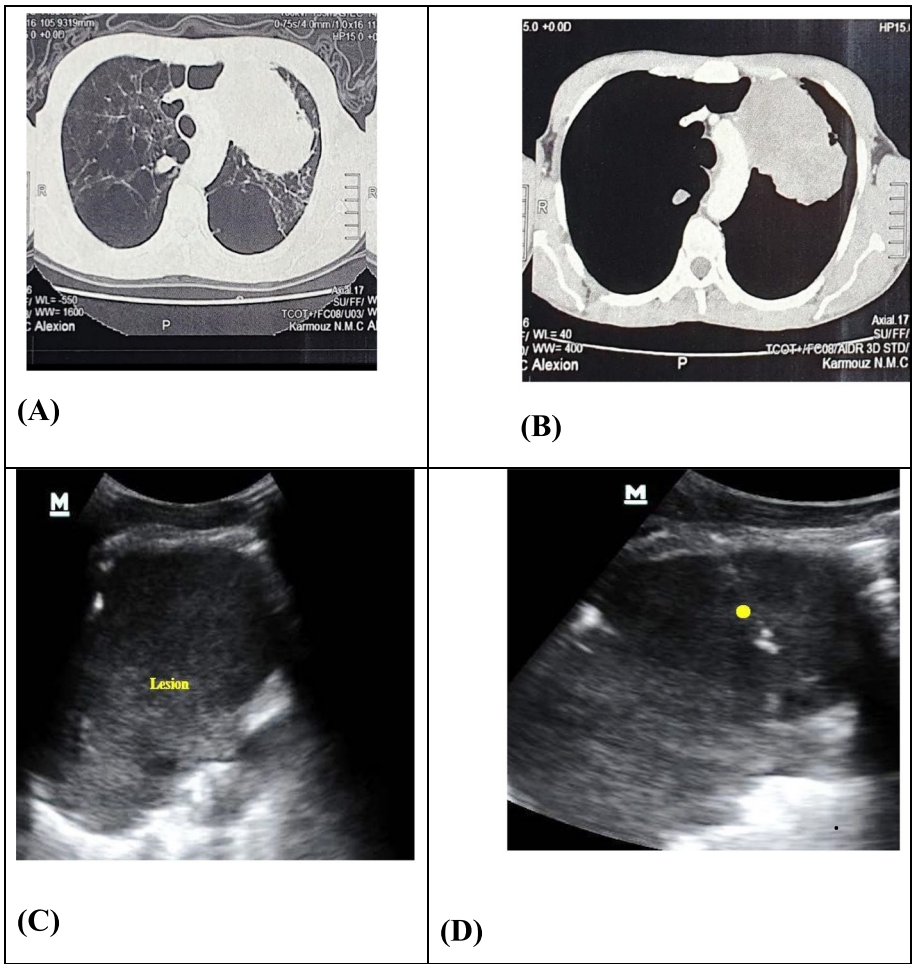

Fig. 1 Chest CT scan and ultrasound of a patient presenting with left upper lobe lung mass. **A** Lung window showing Left upper lobe soft tissue lesion and bilateral upper lobe emphysematous bullae. **B** Mediastinal window showing Left upper lobe heterogeneous lesion with rib erosion. **C** Ultrasound (US) assessment of lesion showing heterogeneous echogenicity with central breakdown and air foci. Irregular pleural line with area of rib erosion. **D** During US-guided FNAB. Yellow star shows the spinal needle intralesional

enough to diagnose the patient as mesothelioma, nor enough for IHC staining. A third case was diagnosed with pleural fibrosis following long-standing pleural infection via CNB and the remaining 2 cases were diagnosed with necrotizing granulomatous inflammation by CNB, and the FNAB was inconclusive showing nonspecific chronic inflammatory cells; microbiological examination of these cases were positive for tuberculosis.

Undiagnosed patients underwent further investigations as thoracoscopy or bronchoscopy till a final diagnosis was reached. Among all patients, 73.3% were diagnosed with malignancy and 23.3% were diagnosed with benign lesions. The difference in the diagnostic yield between the FNAB and CNB in the benign group was statistically significant with a p value of 0.005. FNAB failed to accurately diagnose 11 patients of the 30 studied patients that were then diagnosed using further investigations such as thoracoscopy or bronchoscopy while CNB failed to diagnose only one case, the difference in performance was statistically significant with a p-value < 0.001.

Comparing the sensitivity and specificity of both techniques among patients with parenchymal lung lesions showed the following: sensitivity of FNAB was 86% while CNB was 95%. The specificity and PPV of both methods were shown to be 100%. The NPV of FNAB was 57% while the NPV of CNB was 80%. The accuracy calculated for FNAB was 88% and 96% for CNB (Table 2). The difference in pathologic diagnosis of different patients using FNAB and CNB is shown in Fig. 2.

The procedure was shown to be safe. Only three patients experienced minor complications. One patient had mild wound bleeding, another patient complained of transient hemoptysis after finishing the procedure, and the third patient complained of chest pain during biopsy

Table 2 Agreement (sensitivity, specificity, and accuracy) for diagnostic performance of FNAB and CNB for peripheral lung lesions

	Sensitivity	Specificity	PPV	NPV	Accuracy
FNAB	86%	100%	100%	57%	88%
CNB	95%	100%	100%	80%	96%

PPV Positive predictive value, *NPV* Negative predictive value

using a Trucut needle, he was finally diagnosed with mesothelioma.

Pathology reports of CNB and FNAB as written by the pathologist (blinded from the sample) along with the results of the immunohistochemistry and microbiological tests are available as Supplementary material, Table 1.

Discussion

As lung cancer is the leading cause of cancer-related deaths worldwide in both genders, timely assessment and diagnosis of the peripheral lung lesion is of crucial importance particularly as the rate of 5-year survival drops from 82% for stage IA to 6% for stage IV [21]. Ultrasound assessment of peripheral lung lesions and pleural thickening provides paramount information about the nature of the pathology and possible diagnostic means.

In the present study, 30 patients were enrolled. Ninety percent of the patients were males. With further stratification of the studied group to malignant and benign groups as regards the final diagnosis, male predominates as well presenting 91.3% among the malignant group and 85.7% among the benign group. The male-to-female ratio in this study was higher than in other comparable studies [22, 23]. Yet another study conducted in Egypt showed an analogous male-predominant percentage as stated by Kawshty et al. where males represented 80% of the patients [24]. The ratio in the current study reflects the current status in Egypt due to the higher incidence of smoking among men as well as exposure to other noxious particles and higher-risk occupations increasing the incidence of lung diseases in general and malignancies in particular.

The mean age of the patients enrolled in the current study was 57.60 ± 13.26 years old, and the mean age for patients that were diagnosed with malignancy was 61.43 ± 10.40 years old versus 45.0 ± 14.49 years old in benign disease. The difference in mean age between the benign and malignant groups was statistically significant, with a p value of 0.002. This indicates a higher probability of malignant nature in peripheral lung and pleural lesions among the elderly population. Concerning comorbidities among the studied patients, 23.3% of the studied patients suffered from COPD. These patients were all diagnosed with malignancy. Similar findings were observed by Lee et al. [9]. This finding further emphasizes the association between COPD and lung cancer. Nearly 78% of patients presenting with chest pain in our study were diagnosed with malignancy. This can be attributed to the fact that peripheral lung and pleural lesions irritate the parietal pleural layer so pleuritic chest pain should not be underestimated in the high-risk, smoker, and elderly populations [25].

The most affected lung lobe in our study was the upper lobe (52.3%). The size of peripheral lung lesions ranged from 1.25 × 3.31 cm to 12.21 × 9.90 cm in maximum dimensions, with a mean of 5.70 cm ± 2.42cm, matching with the mean size reported by Kawshty et al. [24] and Diacon et al. [26] Other studies showed smaller mean sizes of lesions as shown by Lee et al. [9] with a mean of 3.55 cm ± 2.19 cm. Larger lesions were associated with more necrosis as evident in the US view and necrotic areas with air foci were avoided during the biopsy.

On comparing the duration of CNB to that of FNAB in both peripheral lung mass biopsies and pleural biopsies, limited data was published. In our study, the duration of CNB was longer with a statistically significant difference, and this is explained by the fact that the CNB is wider and longer and more injuries to the surrounding tissue are possible, requiring more time and precision during needle entry and as it pierces the chest wall layers as well as during the firing phase. Also, in cases with pleural thickening, the needle was inclined as soon as the parietal pleural layer was pierced with view optimization to avoid any injury to the underlying visceral pleural, such procedure was not done using the fine needle aspiration. The previous factors contributed to the longer duration of the CNB and also to the higher pain score found using the CNB. It was noticed that the smaller the lesion, the longer the procedure and the more technically challenging it was. In our study, the duration of pleural biopsy was significantly longer and required more technical skill than cases with peripheral lung mass.

US-guided CNB and FNAB in both peripheral lung and pleural lesions is a safe procedure and was proved to be even safer than CT-guided biopsies [9]. In this study, the overall incidence of complications was significantly low with no occurrence of any pneumothorax, hemothorax, or pulmonary hemorrhage. This matches with other studies as the study conducted by Schubert et al. [27] that showed no major complication occurrence. Another study reported the incidence of pneumothorax as high as 15.4% with CNB and 10.8% with FNAB [28]. Some showed controversial data where the incidence of pneumothorax was higher using FNAB compared to CNB (the incidence of pneumothorax was up to 35.1% in FNAB versus 15.9% in CNB) in a study by Anderson et al. [29] yet this study was conducted via CT guidance

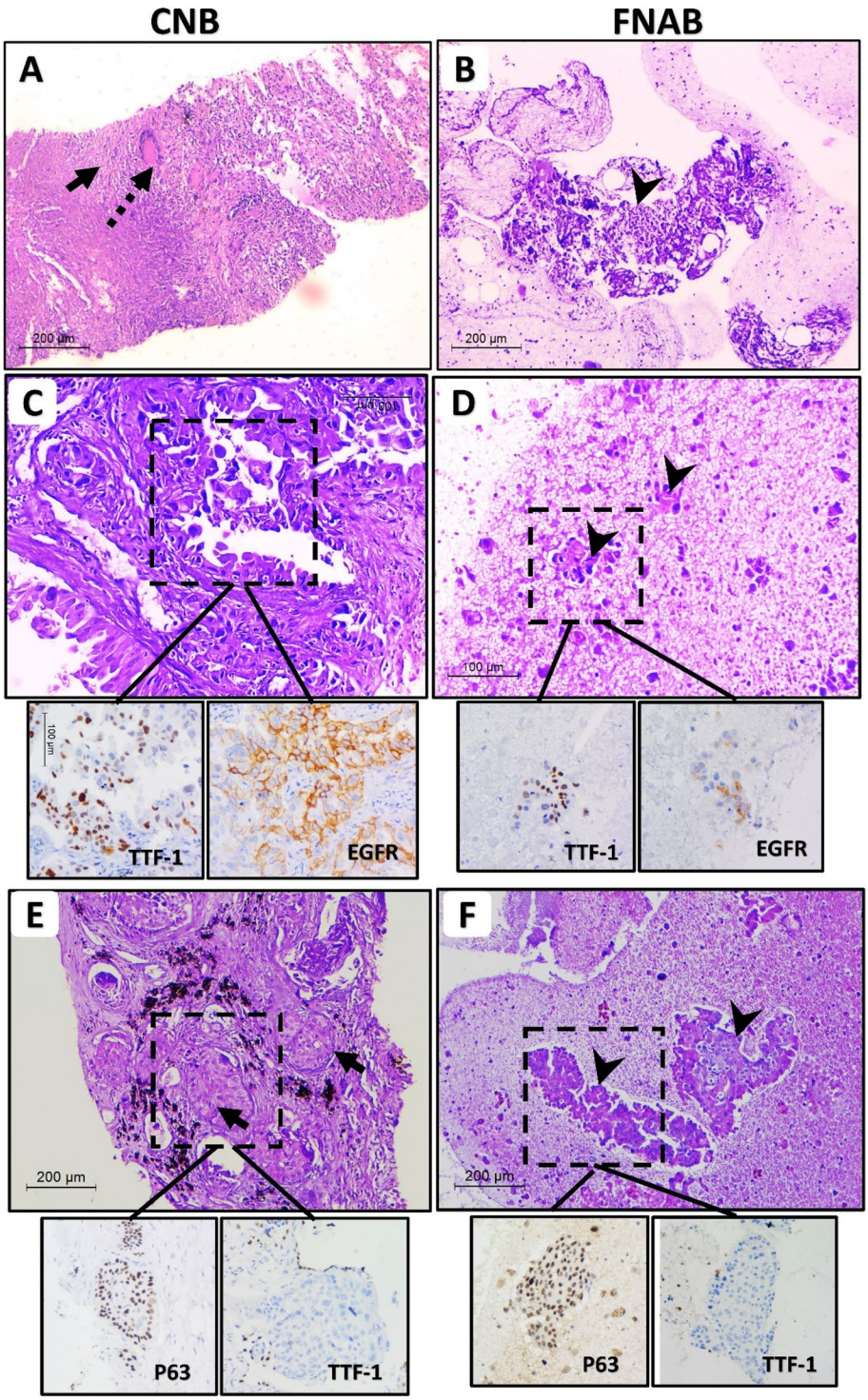

Fig. 2 Pathologic diagnosis of three different patients. **A**, **B** A case of pleural tuberculosis. **A** CNB showing multiple granulomas (arrow) with Langhans giant cell (dashed arrow) (H&E, ×100). **B** FNAB showing necrotic background (arrowhead) incorporating few macrophages and mixed inflammatory cells (failed to diagnose the case). **C**, **D** A case of lung adenocarcinoma. **C** CNB showing multiple large glands lined by atypical cells (arrows) (H&E, ×200). Insets show positive TTF-1 nuclear stain and score 3 EGFR membranous stain. **D** FNAB showing clusters of malignant cells with vague attempts of acinar formation (arrow heads). Insets show positive TTF-1 and score 3 EGFR (concordant with CNB). **E**, **F** A case of squamous cell carcinoma. **E** CNB showing nest of cohesive malignant cells with ample eosinophilic cytoplasm (arrows). (H&E, ×100) Insets show positive P63 nuclear stain and negative TTF-1 confirming diagnosis of SCC. **F** FNAB shows sheets of atypical cells with eosinophilic cytoplasm (arrow heads). Insets reveal positive P63 and negative TTF-1 (concordant with CNB). (H&E, ×100). Insets (IHC, ×100). CNB core needle biopsy, FNAB fine needle biopsy, TTF-1 thyroid transcription factor-1, EGFR epidermal growth factor receptor, SCC squamous cell carcinoma

which does not allow real-time biopsy. In our study, only three patients showed minor complications after Trucut biopsy. One patient (3.3%) (who underwent peripheral lung lesion biopsy) had a mild attack of hemoptysis that resolved spontaneously. The incidence of hemoptysis was reported to be higher in CNB compared to FNAB (4.1% versus 2.4%, respectively) in the study by Lauren et al. [30] Moulton et al. [31] reported the incidence of self-limited hemoptysis or perilesional hemorrhage as 2.6%. One patient had excessive wound bleeding (perilesional bleeding) and it was attributed to the dilated chest veins as this patient presented with superior vena cava (SVC) syndrome with dilated chest veins, congested nonpulsatile neck veins, and erythema of the head and neck and upper chest. This patient was diagnosed with NSCLC-squamous cell carcinoma. Although SVC syndrome is not a contraindication for transthoracic biopsy, the risk versus benefit should be considered before diagnostic interventions. The absolute contraindications of image-guided transthoracic biopsy include bleeding diathesis and anticoagulation treatment, deep parenchymal lesions in patients with pulmonary hypertension, severe emphysematous disease, and large bullae in the biopsy path [32]. Only one patient had a high pain score during CNB of the parietal pleura and was diagnosed with mesothelioma. The incidence of malignancy was very high among the studied population (76.7%) reflecting the importance of biopsies in peripheral lung masses and parietal pleural thickening especially in old, smoker males. Although pulmonary metastasis is the most common malignant tumor in the lungs [33], in our study, primary lung cancers were more common than metastatic lesions. This could be explained by the age of the patients, the size of the lesion as well as the high prevalence of smoking and high PYI in addition to preexisting COPD in many patients. The most common malignancies diagnosed in our study were NSCLC constituting 82.6% of malignant lesions diagnosed; the most common NSCLC diagnosed was adenocarcinoma, (33.3%). These results match the literature as NSCLC represents around 80% of primary lung cancers and adenocarcinoma constitutes around 40% of all lung cancers and 60% of NSCLC [34].

The present study showed that combined sequential FNAB and CNB were superior to FNAB alone but not to CNB. A previous study aimed to assess the diagnostic accuracy of same-session sequential computed tomography (CT)-guided percutaneous fine-needle aspiration (FNA) and core-needle biopsy (CNB) in comparison with FNA and CNB performed separately for diagnosing intrathoracic lesions. Sequential FNA and CNB improve the diagnostic accuracy of percutaneous CT-guided procedures in malignant lesions. There was only mild improvement, which was not statistically significant, for the diagnosis of benign specific lesions by the sequential procedures compared with the yield of CNB alone. This could be explained by the fact that, due to the non-specific cytopathological appearance of benign disease, a specific benign diagnosis (e.g., granuloma, hamartoma) can be achieved by FNA in only a low percent of the cases [35]. Another recent retrospective study [36] aimed to evaluate the practice of using combined FNA/CNB for patients with a solitary lung nodule. The adequacy of FNA specimens was assessed immediately by a cytopathologist. The rate of diagnostic consistency between FNA and CNB was 83.4%, and the rate of diagnostic accuracy for malignancy was 98.5% for combined FNA/CNB. Combined FNA/CNB showed high diagnostic efficacy for malignancy (sensitivity, 97.6%; specificity, 100%) and had a lower false-negative rate for malignancy (2.2%) than either FNA (7.2%) or CNB (6.2%) alone. Furthermore, the immediate evaluation of FNA specimen adequacy was useful not only for determining whether sufficient tissue was obtained but also to guide radiologists in determining the best CNB location.

Comparing the diagnostic yield of FNAB versus CNB in our study, there was a statistically significant difference showing CNB superiority in the overall diagnostic yield reporting only one undiagnosed case using CNB versus 11 undiagnosed cases using FNAB (two biopsies were inadequate for processing and six biopsies were eventually diagnosed as a benign etiology). The overall sensitivity, specificity, PPV, NPV, and accuracy of CNB versus FNAB in cases of peripheral lung lesion biopsies were 95%, 100%, 100%, 80%, and 96% versus 86%, 100%, 100%, 57%, and 88%, respectively. These results were coherent with other studies, a recent study compared both techniques showed conformity between FNAB and CNB assisted by ultrasound [37] and another study presented by Gong et al., where CNB was superior to FNAB regarding the diagnostic yield in both malignant (86.7%% versus 85.1, respectively) and benign lesions (92% versus 40%, respectively). Also, the study conducted by Diacon et al. showed that CNB showed superior diagnostic performance compared to FNAB in non-carcinomatous and benign lesions [26]. In contrast to our findings, [21], Sagar et al. [38] reported superior diagnostic performance of FNAB versus CNB in peripheral lung lesions sized 3–10 cm. He reported that FNAB sensitivity, specificity, and accuracy were 82.6%, 57.1%, and 76.7%, respectively, versus CNB sensitivity, specificity, and accuracy as 56.5%, 100%, and 66.7%. Similar results were found by Kim et al. [28] who showed superior performance of FNAB over CNB in benign lesions only. This was explained by the fact that during FNAB the spinal needle can be angulated to cover different areas of the lesion unlike in CNB where

a single trajectory is used which might result in low yield due to necrosis.

The superiority of CNB diagnostic yield in our study in benign lesions rather than in malignant lesions is most likely explained by the larger tissue sample and better preserving of tissue architecture. Benign etiologies require detailed tissue architecture to reach a final diagnosis. The FNAB samples contained cells and fragments that showed inflammatory changes and cellular infiltrations but not enough tissue to reach a histological diagnosis as evident in the patients finally diagnosed with tuberculosis. In patients diagnosed with TB, FNAB samples showed inflammatory cells and tissue infiltrations but not the caseating granulomas required for the diagnosis of tuberculous infection (supplemented by the positive TB culture), which was not the case for CNB. Pathology statements in cases of TB showed a significant discrepancy between CNB and FNAB as shown in one of our cases, where pathology report of the CNB samples showed "Lung tissue featuring poorly formed granulomata formed of epithelioid cells with indistinct cytoplasm and slender nuclei. Scattered Langerhans-type giant cells are noted as well as wide areas of necrosis. The alveolar spaces show pneumocytic hyperplasia of the lining and neutrophils within the lumen". On the other hand, the FNAB report of a case finally diagnosed as TB showed "Scattered histocytes, lymphocytes, and neutrophils as well as epithelioid cells. Inconclusive".

All the studies that showed higher FNAB sensitivity and/or accuracy over CNB used rapid on-site evaluation (ROSE) for FNAB samples which might have contributed to these results. In these studies, the ROSE technique was only applied to FNAB samples and guided further needle passes according to the presence or absence of malignant cells.

The high diagnostic performance reported in our study is likely related to the size of lesions as the mean size of masses in the recruited patients was 5.70 cm ± 2.42 cm although there were more necrotic areas, there was enough space for needle entry and manipulation in different areas in the mass rather than single trajectory. This matches the results of other studies with CNB accuracy of 97–98% in lesions larger than 5 cm [9, 11].

All patients that presented with parietal pleural thickening showed either heavily septated pleural space as viewed on US assessment or minimal encysted effusion; all impeding the possibility of medical thoracoscopy. Regarding the performance of US-guided CNB and FNAB in cases with parietal pleural thickening, in literature, FNAB has not been thoroughly studied in such cases likely due to the technique of the biopsy where the needle needs to move to and fro through the lesion under negative suction to harvest enough material for processing. In our study, the FNAB did show cells whether inflammatory or suspicious cells but they were not enough for the pathologist to reach a diagnosis or provide enough data for planning treatment in all the cases. These results need to be validated by further studies on a larger population as our study randomly recruited only a few patients with parietal pleural thickening without evident lung masses. On the contrary, US-guided CNB performance in close pleural biopsy results were satisfactory. On review of the literature, the diagnostic yield of US-guided CNB of the pleura was up to 82% and 76% in tuberculous and malignant etiologies, respectively, as shown in a systemic review and meta-analysis conducted by Mei et al. [39] Closed pleural biopsy using US has been proven superior to historically done blind pleural biopsy [40] and with comparable results to thoracoscopy [41]. Our results suggest that closed pleural biopsy using a US-guided core needle is a great diagnostic modality for undiagnosed exudate pleural effusion serving as an alternative to thoracoscopy, providing the patient with less invasive diagnostic modality as well as in generally unwell patients unfit for thoracoscopy or patients unwilling to undergo thoracoscopy as well as in patients presenting with septated, loculated, or minimal pleural effusion and also in localized pleural pathology. This does not underrate by any means the advantages of medical thoracoscopy and its almost perfect diagnostic yield as well as its dual role being therapeutic and diagnostic modality.

The advantages of our study include the comprehensive review and comparative analysis of FNAB versus CNB as regards the diagnostic yield and limitations of each technique as well as immunohistochemistry stain applied on specimens of both techniques. On the other hand, the study limitations included the lack of the ROSE technique which might have improved the yield of FNAB samples, in addition to the limited sample size enrolled.

We conclude that ultrasound-guided biopsy is a safe, reliable, and very useful tool in assessing peripheral lung and pleural lesions. No major complications were reported using either technique. Ultrasound-guided procedures both FNAB and Trucut biopsy have high sensitivity and specificity in diagnosing peripheral-located pleural-based lesions. The results of combined sequential FNAB and CNB were superior to FNAB alone but were not superior to CNB. Ultrasound-guided CNB has a superior diagnostic yield over US-guided FNAB. FNAB of peripheral lung lesions provided sufficient material for ancillary molecular testing with comparable results to CNB. FNAB was technically easier to perform compared to US-guided CNB, especially in smaller lesions. CNB of pleural thickening is a safe procedure with a high diagnostic yield and less invasive than medical thoracoscopy with great usefulness in cases with encysted, minimal, or septated pleural effusion.

Abbreviations

ALK	Anaplastic lymphoma kinase
AMUH	Alexandria Main University Hospital
CNB	Core needle biopsy
COPD	Chronic obstructive pulmonary disease
CT	Computed tomography
DM	Diabetes mellitus
DVT	Deep venous thrombosis
EGFR	Epidermal growth factor receptor
FNAB	Fine needle aspiration biopsy
IHC	Immunohistochemistry
ROSE	Rapid on-site evaluation
SpO2	Oxygen saturation via pulse oximetry
TUS	Thoracic ultrasound
US	Ultrasound

Supplementary Information

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Additional file 1: Table 1. Pathology reports of CNB and FNAB as written by the pathologist (blinded from the sample) along with the results of the immunohistochemistry and microbiological tests.

Authors' contributions

Corresponding author: Dr. Rania Ahmed Sweed directed the practical part of the research, presented the results, and wrote the manuscript. Prof. Dr. Yehya Mohamed Khalil decided the main idea of the research and the methodology and revised the whole manuscript. Mina Botros performed the practical part, statistics, and data collection. Prof. Dr. Hany Amin Sharawy guided the practical part and revised the manuscript. Dr. Eman Sheta Ali Gawdat Alsawy examined the whole specimens and wrote pathology reports.

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Availability of data and materials

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

All subjects enrolled in the study signed informed consent before participation. The study was accepted by the local ethical committee of Alexandria Faculty of Medicine (available from www.med.alexu.edu.eg/wp-content/uploads/2012/04/ethics-guide.pdf).

Competing interests

All authors have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

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References

1. Mayo PH, Copetti R, Feller-Kopman D, Mathis G, Maury E, Mongodi S et al (2019) Thoracic ultrasonography: a narrative review. Intensive Care Med 45(9):1200–1211
2. Chira RI, Chira A, Mircea PA (2017) Transthoracic ultrasonography: advantages and limitations in the assessment of lung cancer. In: Adonis M (ed) A global scientific vision: prevention, diagnosis, and treatment of lung cancer. InTech, Rijeka, pp 61–80
3. Wei H, Lu Y, Ji Q, Zhou H, Zhou X (2018) The application of conventional us and transthoracic ultrasound elastography in evaluating peripheral pulmonary lesions. Exp Ther Med 16(2):1203–1208
4. Averkiou MA, Bruce MF, Powers JE, Sheeran PS, Burns PN (2020) Imaging methods for ultrasound contrast agents. Ultrasound Med Biol 46(3):498–517
5. Lim CK, Chung CL, Lin YT, Chang CH, Lai YC, Wang HC et al (2017) Transthoracic ultrasound elastography in pulmonary lesions and diseases. Ultrasound Med Biol 43(1):145–152
6. Xu W, Wen Q, Zhang X, Pan M, Liu C, Zha L et al (2021) The application of contrast-enhanced ultrasound for core needle biopsy of subpleural pulmonary lesions: retrospective analysis in 92 patients. Ultrasound Med Biol 47(5):1253–1260
7. Sperandeo M, Rotondo A, Guglielmi G, Catalano D, Feragalli B, Trovato GM (2014) Transthoracic ultrasound in the assessment of pleural and pulmonary diseases: use and limitations. Radiol Med 119(10):729–740
8. Hallifax RJ, Corcoran JP, Ahmed A, Nagendran M, Rostom H, Hassan N et al (2014) Physician-based ultrasound-guided biopsy for diagnosing pleural disease. Chest 146(4):1001–1006
9. Lee MH, Lubner MG, Hinshaw JL, Pickhardt PJ (2018) Ultrasound guidance versus ct guidance for peripheral lung biopsy: performance according to lesion size and pleural contact. AJR Am J Roentgenol 210(3):W110–W117
10. DiBardino DM, Yarmus LB, Semaan RW (2015) Transthoracic needle biopsy of the lung. J Thorac Dis 7(Suppl 4):S304–S316
11. Anzidei M, Porfiri A, Andrani F, Di Martino M, Saba L, Catalano C et al (2017) Imaging-guided chest biopsies: techniques and clinical results. Insights Imaging 8(4):419–428
12. Cozzolino I, Ronchi A, Messina G, Montella M, Morgillo F, Vicidomini G et al (2020) Adequacy of cytologic samples by ultrasound-guided percutaneous transthoracic fine-needle aspiration cytology of peripheral pulmonary nodules for morphologic diagnosis and molecular evaluations: comparison with computed tomography-guided percutaneous transthoracic fine-needle aspiration cytology. Arch Pathol Lab Med 144(3):361–369
13. Tosi D, Mendogni P, Carrinola R, Palleschi A, Rosso L, Bonaparte E et al (2019) CT-guided fine-needle aspiration biopsy of solitary pulmonary nodules under 15 mm in diameter: time for an afterthought? J Thorac Dis 11(3):724–731
14. Heerink WJ, de Bock GH, de Jonge GJ, Groen HJ, Vliegenthart R, Oudkerk M (2017) Complication rates of CT-guided transthoracic lung biopsy: meta-analysis. Eur Radiol 27(1):138–148
15. Sangha BS, Hague CJ, Jessup J, O'Connor R, Mayo JR (2016) Transthoracic computed tomography-guided lung nodule biopsy: comparison of core needle and fine needle aspiration techniques. Can Assoc Radiol J 67(3):284–289
16. Corcoran JP, Tazi-Mezalek R, Maldonado F, Yarmus LB, Annema JT, Koegelenberg CFN et al (2017) State of the art thoracic ultrasound: intervention and therapeutics. Thorax 72(9):840–849
17. Polania Gutierrez J, Rocuts K (2020) Perioperative anticoagulation management. StatPearls Publishing, Treasure Island
18. Celik B, Bulut T, Khoor A (2019) Subtyping of non-small cell lung cancer by cytology specimens: a proposal for resource-poor hospitals. Cytojournal 16:8
19. Nicholson AG, Tsao MS, Beasley MB, Borczuk AC, Brambilla E, Cooper WA et al (2021) The 2021 WHO classification of lung tumors: impact of advances since 2015. J Thorac Oncol 2022:362–387
20. Yoshida M, Nagatomo T, Ohnishi T, Kawashima M, Naitoh A, Morii E (2017) Detection of epidermal growth factor receptor mutations in lung adenocarcinoma cytological specimens by immunocytochemistry. Mol Clin Oncol 7(6):981–987
21. Khan T, Usman Y, Abdo T, Chaudry F, Keddissi JI, Youness HA (2019) Diagnosis and management of peripheral lung nodule. Ann Transl Med 7(15):348
22. Gong Y, Sneige N, Guo M, Hicks ME, Moran CA (2006) Transthoracic fine-needle aspiration vs concurrent core needle biopsy in the diagnosis of intrathoracic lesions: a retrospective comparison of diagnostic accuracy. Am J Clin Pathol 125(3):438–444

23. Diacon AH, Theron J, Schubert P, Brundyn K, Louw M, Wright CA et al (2007) Ultrasound-assisted transthoracic biopsy: fine-needle aspiration or cutting-needle biopsy? Eur Respir J 29(2):357–362
24. Kawshty F, AbdElradi A, Ahmed A (2019) Diagnostic yield of ultrasound-guided transthoracic biopsy in peripheral lung lesions. Egypt J Bronchol 13(4):469–76
25. Walter L, Chang A, Chen P, Harper G, Rivera J, Conant R et al (2021) Current diagnosis & treatment geriatrics. McGraw Hill, London
26. Diacon AH, Schuurmans MM, Theron J, Schubert PT, Wright CA, Bolliger CT (2004) Safety and yield of ultrasound-assisted transthoracic biopsy performed by pulmonologists. Respiration 71(5):519–522
27. Schubert P, Wright CA, Louw M, Brundyn K, Theron J, Bolliger CT et al (2005) Ultrasound-assisted transthoracic biopsy: cells or sections? Diagn Cytopathol 33(4):233–237
28. Kim HK, Shin BK, Cho SJ, Moon JS, Kim MK, Kim CY et al (2002) Transthoracic fine needle aspiration and core biopsy of pulmonary lesions. A study of 296 patients. Acta Cytol 46(6):1061–8
29. Anderson JM, Murchison J, Patel D (2003) CT-guided lung biopsy: factors influencing diagnostic yield and complication rate. Clin Radiol 58(10):791–797
30. Laurent F, Latrabe V, Vergier B, Michel P (2000) Percutaneous CT-guided biopsy of the lung: comparison between aspiration and automated cutting needles using a coaxial technique. Cardiovasc Intervent Radiol 23(4):266–272
31. Moulton JS, Moore PT (1993) Coaxial percutaneous biopsy technique with automated biopsy devices: value in improving accuracy and negative predictive value. Radiology 186(2):515–522
32. Birchard KR (2011) Transthoracic needle biopsy. Semin Intervent Radiol 28(1):87–97
33. Rubin E, Reisner H (2009) Essentials of Rubin's pathology. Wolters Kluwer Health/Lippincott Williams & Wilkins, Philadelphia
34. Zheng M (2016) Classification and pathology of lung cancer. Surg Oncol Clin N Am 25(3):447–468
35. Aviram G, Greif J, Man A, Schwarz Y, Marmor S, Graif M et al (2007) Diagnosis of intrathoracic lesions: are sequential fine-needle aspiration (FNA) and core needle biopsy (CNB) combined better than either investigation alone? Clin Radiol 62(3):221–226
36. Chen L, Jing H, Gong Y, Tam AL, Stewart J et al. Diagnostic efficacy and molecular testing by combined fineneedle aspiration and core needle biopsy in patients with a lung nodule. Cancer Cytopathol. 2020;128(3):201–6.
37. Marhana IA, Widianiti K, Kusumatuti EH (2022) Conformity of fine needle aspiration biopsy (FNAB) and core needle biopsy (CNB) in peripheral lung tumor patients: a cross-sectional study. Ann Med Surg (Lond) 75:103423
38. Sagar P, Gulati M, Gupta SK, Gupta S, Shankar S, Joshi K et al (2000) Ultrasound-guided transthoracic co-axial biopsy of thoracic mass lesions. Acta Radiol 41(6):529–532
39. Mei F, Bonifazi M, Rota M, Cirilli L, Grilli M, Duranti C et al (2021) Diagnostic yield and safety of image-guided pleural biopsy: a systematic review and meta-analysis. Respiration 100(1):77–87
40. Koegelenberg CF, Diacon AH (2011) Pleural controversy: close needle pleural biopsy or thoracoscopy-which first? Respirology 16(5):738–746
41. Rajawat GS, Batra S, Takhar RP, Rathi L, Bhandari C, Gupta ML (2017) Diagnostic yield and safety of closed needle pleural biopsy in exudative pleural effusion. Avicenna J Med 7(3):121–124

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