

Ultrasound-guided pleural cutting needle biopsy: accuracy and factors influencing diagnostic yield

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Background: The aim of this study was to retrospectively investigate the diagnostic accuracy of ultrasound-guided pleural cutting needle biopsy (US-guided PCNB) and the potential factors influencing diagnostic yield.

Methods: From July 2014 to June 2016, a total of 147 percutaneous US-guided PCNBs in 144 patients were retrospectively reviewed. The final diagnosis was confirmed by histopathological analysis and follow-up. We calculated diagnostic accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) and divided all cases into group of correct diagnoses (true-positive and true-negative cases) and group of incorrect diagnoses (false-positive, false-negative, and inconclusive cases). Univariate and multivariate logistic regression analyses were performed to analyze the differences of influencing factors (patient, pleura, and biopsy-associated factors) in the between the two groups.

Results: Seven patients were excluded because of loss to follow-up. A total of 140 cases were ultimately included (105 males and 35 females). There were 105 cases in the correct diagnosis group, and 35 cases in the incorrect diagnosis group. The overall accuracy of US-PCNB was 75.0% and the sensitivity, specificity, PPV, NPV in malignant diagnosis were 58.1%, 99.0%, 96.2%, and 84.2%, respectively. On univariate analysis, variables affecting diagnostic accuracy of US-PCNB were the pleural thickness (<3 mm in thickness 61.0%, ≥3 mm in thickness 85.2%; $P=0.001$), morphology (non-nodular pleura 71.4%, nodular pleura 95.2%; $P=0.026$), and needle size (18 G 69.1%, 16 G 87.0%; $P=0.022$). Finally multivariate logistic regression demonstrated that pleural thickness [odds ratio (OR): 0.278, $P=0.003$] and needle size (OR: 0.291, $P=0.018$) independently predicted diagnostic accuracy.

Conclusions: Pleural thickness and the size of the biopsy needle were significantly correlated with the diagnostic yield.

Keywords: Ultrasound-guided pleural biopsy; cutting needle; influencing factors; diagnostic accuracy; retrospective study

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Introduction

Pleural effusion (PE) is a common medical problem with more than 50 recognized causes (1). Approximately 3,000 new cases of PE per 1,000,000 of the population are recorded annually in industrialized countries (2). Most exudative PEs are malignant, tuberculous, or parapneumonic (3,4).

It is difficult to determine the cause of PE, particularly malignant PE, via thoracentesis alone; the diagnostic accuracy is relatively low (2,5,6). Pleural biopsy (PB) followed by histological evaluation is important when diagnosing PE. Diagnostic tissue can be acquired using several procedures, such as blind PB, local anaesthetic thoracoscopy (LAT), VATS, or image-guided biopsy (4,7,8). Medical thoracoscopic, VATS, and image-guided pleural biopsies are more sensitive than blind PB (5,9,10). However, medical thoracoscopy (MT) and VATS require a degree of expertise, anesthesia, and the use of an operating theater (10,11). Image-guided biopsies lack these shortcomings and are clearly better than blind PB, particularly if malignant PE is suspected (9). The reported sensitivities range from 61% to 94%, and a few studies have reported 100% specificity (9,12-17).

The ultrasound and CT seem to exhibit similar diagnostic yields (18). However, ultrasound (US)-guided biopsy is particularly rapid and inexpensive and is associated with a low incidence of post-procedure pneumothorax (19). The method allows real-time visualization of the biopsy needle without exposing patients or doctors to radiation. Heavy or rapid breathing of dyspneic patients can be accommodated via real-time ultrasonic guidance. The literature indicates that the diagnostic accuracy of US-guided percutaneous needle biopsy (PCNB) is 62.9% to 94% (12-15). Because of its advantages, US is commonly used to guide biopsy in clinical practice. However, to the best of our knowledge, few reports have explored factors influencing the diagnostic yield of US-guided PCNB. Here we retrospectively analyze a large number of cases.

Methods

Patients

We conducted a retrospective study at Guangzhou Institute of Respiratory Disease. This study was approved by the Scientific Research Ethics Review Committee of the First Affiliated Hospital of Guangzhou Medical University. We retrospectively analyzed data from 147 percutaneous

US-PCNBs performed on 144 patients between July 2014 and June 2016. The inclusion criteria were (I) undiagnosed and untreated PE, (II) a unilateral transudate evident on clinical images that did not resolve on treatment, and (III) age >18 years. The exclusion criteria were (I) insufficient bleeding diathesis to allow for pleural aspiration and biopsy, (II) patient inability to provide written informed consent, or (III) non-malignant and unclearly diagnosed cases were followed up for less than 12 months or lost to follow-up.

Procedure

All procedures were similar, with patients placed in either the sitting, prone, supine, or lateral decubitus position. First, US (Esaote Mylab 90, Italy) using a low-frequency (2–5 MHz) convex transducer was used to collect information on the PE, the pleura, and blood flow. To maximize accuracy, the thickest point of the pleura or a focally thickened region was chosen for biopsy on the premise of security. If such an area was not available, the entry points were selected to be as close to the diaphragm as possible. If patients had undergone prior chest computed tomography (CT), the CT scans were also examined. Next, both low-frequency (2–5 MHz) and high-frequency (5–10 MHz) probes were alternately used to guide the PB, which was performed by two operators. The biopsy plan was decided by the operators in consultation. Operator 1 was a sonographer who assessed the condition of the pleura and also provided the guidance. Operator 2 used an 18 or 16 G automated cutting needle with a specimen notch of 20 mm (MC1816, Bard Max. Core, Bard Inc., USA) to perform the biopsy with the patient under local anesthesia with 2% lidocaine. The tip of the cutting needle was inserted through the guide channel into the pleural superstratum. We found it wise to program a launch distance ≥ 22 mm to avoid lung damage. The number of punctures depended on the quality of the specimens and the patient's tolerance. All specimens were immediately fixed in 10% formalin and sent for histopathological examination. All US procedures, including pleural ultrasonic examination and real-time guidance, were performed by two experienced interventional sonographers (DZ Zhou and XH Zhou). All biopsies were performed by these sonographers or an experienced pulmonologist (JL Wang).

Prior to PB, thoracentesis was used to obtain PE samples from all patients for biochemical and microbiological analysis. The Abrams biopsy was performed

in cases of moderate and large effusion after US-guided PB. We routinely used US to check whether a pneumothorax and/or active intrathoracic bleeding was present. If a pneumothorax or a related symptom was suggested, we scheduled further radiological examination.

Diagnostic assessment

Diagnoses were classified as malignant, specifically benign [e.g., benign mesothelioma, tuberculosis (TB) and eosinophilic infection], nonspecifically benign (e.g., nonspecific inflammation), or inconclusive. Malignancy and specifically benign disease were considered positive findings, and nonspecific benign disease was considered a negative finding. An inconclusive diagnosis indicated that the biopsy had not been completed because of complications and the pathological results were not definitive (e.g., granulomatous inflammation).

A definitively positive diagnosis, including malignancy or specifically benign disease, was made via histopathological analysis of the US-PCNB samples or if other sites revealed the same histological characteristics, metastasis was identified, followed by surgery or clinical treatment. A definitively negative diagnosis was made by histopathological analysis, if the PE subsequently disappeared, or if follow-up chest radiographs or CT scans showed that the PE remained stable for ≥ 12 months after corresponding treatment. True-positive and true-negative cases belong to correct diagnoses. False-positive, false-negative, and inconclusive cases belong to incorrect diagnoses.

Variables

Variables were classified into three categories: patient, pleural, and biopsy-related factors. Patient factors included patient age and sex. Pleural factors included pleural thickness and morphology. Pleural thickness was the thickness of the parietal pleura along the path of the needle as measured using US and was divided into thickness < 3 mm and ≥ 3 mm. Pleural morphology was divided into the presence of pleural nodules/masses (Figure 1) and a non-nodular pleura. Biopsy factors included use of contrast agent, number of punctures, needle size, needle insertion angle (Figure 2), region of insertion, and precise location. The region reflected the distance from the diaphragm. If the distance from the costophrenic angle was < 25 mm, we recorded biopsy at that angle. Location was divided into left or right thorax.

Statistical analysis

Statistical analyses were performed using SPSS version 17.0 (IBM, Armonk, NY, USA). We calculated diagnostic accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). True-positive and true-negative cases were correct diagnoses. False-positive, false-negative, and inconclusive cases were incorrect diagnoses. Continuous variables were expressed as means with standard deviations, and categorical variables were expressed as frequencies or percentages. In univariate analyses, independent two-samples *t*-tests and the chi-square or Fisher's exact test were used, as appropriate, to compare differences between groups. Multivariate logistic regression analysis was used to identify significant predictors of diagnostic success. $P < 0.05$ was considered statistically significant.

Results

We performed 147 biopsies on 144 patients; seven patients were excluded because of loss to follow-up. Three patients underwent two procedures. Each biopsy procedure was recorded as an individual case. A total of 140 cases were ultimately included (105 males and 35 females). The average patient age was 55.3 years (range, 22–86 years).

The 140 pathological results of US-guided PCNBs revealed 26 malignant lesions, three cases of benign mesothelioma, specific infectious disease in 28 cases (27 cases of tuberculosis and one case of eosinophilic infection), 79 nonspecifically benign cases, and four cases for whom diagnosis failed (four cases of granulomatous inflammation). However the final diagnostic results were 43 malignant lesions (38 malignant metastatic tumors, five cases of malignant mesothelioma), five cases of benign mesothelioma, 40 cases of specific infectious disease (39 cases of tuberculosis and one case of eosinophilic infection), 49 nonspecifically benign cases, and three cases of granulomas that failed to resolve in terms of the final pathological inflammation. The pathological characteristics of initial US-guided PCNBs and final diagnoses are shown in Table 1.

Of the 140 biopsies, 56 (40.0%) were true positives, 49 (35.0%) true negatives, 31 (22.1%) false negatives, 1 (0.7%) false positive, and 3 (2.1%) inconclusive. The only false-positive case was suspected squamous cell carcinoma on initial US-PCNB. However, the patient was eventually diagnosed thoracoscopically with tuberculous pleurisy. After antituberculosis treatment, the pleural fluid level in

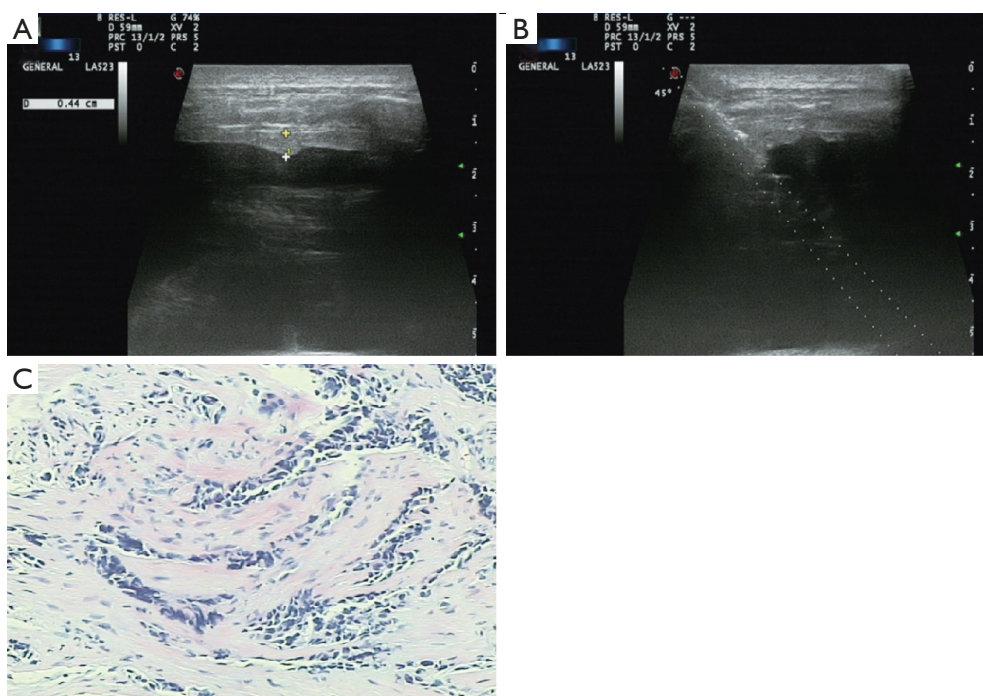


Figure 1 A 46-year-old man with pleural nodule undergoing US-guided cutting biopsy. (A) Thoracic Ultrasound detected a nodule in the left thoracic parietal pleura and the thickness of nodule was measured to be 4.4 mm; (B) specimen of pleural nodule was acquired by real-time ultrasound-guided cutting needle biopsy through the guide channel; (C) histopathology of specimen showed adenocarcinoma metastasized from lung.

this patient did not increase during 12 months of follow-up. This case, false positive in terms of malignancy and false negative in terms of tuberculosis, was deemed to be a false-positive case overall. The 31 false-negative cases included 18 malignancies, 11 tuberculosis cases, and two benign mesotheliomas. Of the 18 malignant false negatives, seven were confirmed via standard pleural biopsy (SPB), five by analysis of transbronchoscopic biopsy specimens, two by histopathological analysis of a lung biopsy and thoracoscopic biopsy, three as metastases of extrapulmonary malignant tumors, and one patient was diagnosed with lymphoma in another hospital and died during follow-up. Six of the 11 tuberculosis cases were confirmed via SPB, three by histopathological analysis of transbronchoscopic biopsy specimens, one via laboratory testing of *Mycobacterium tuberculosis*, and one through a positive purified protein derivative (PPD) skin test (>10 mm) and clinical signs and symptoms. Two cases of benign mesothelioma were confirmed via SPB.

The overall accuracy of US-PCNB was 75.0%. The sensitivity, specificity, PPV, NPV in terms of malignant

diagnosis were 58.1%, 99.0%, 96.2%, and 84.2%, respectively. The factors affecting diagnostic yield are shown in Table 2. On univariate analysis, variables affecting diagnostic accuracy of US-PCNB were the pleural thickness, morphology and needle size. Firstly, in the thickness of the pleura, there were 69 cases of thickened pleura (≥ 3 mm) and 36 of nonthickened pleura (<3 mm) in the correctly diagnosed group. The incorrectly diagnosed group contained 12 cases of thickened pleura (≥ 3 mm) and 23 cases of nonthickened pleura (<3 mm). Accuracy fell significantly ($P=0.001$) for patients with pleurae <3 mm in thickness (61.0%) compared to ≥ 3 mm in thickness (85.2%). And then, in the size of needle, in the correctly diagnosed group, 40 cases were performed by 16 G biopsy needle and 65 cases were performed by 18 G needle biopsy. In the incorrectly diagnosed group, six cases were performed by 16 G biopsy needle and 29 cases were performed by 18 G needle biopsy. The accuracy afforded by 18 G needles was significantly less than that afforded by 16 G needles (69.1% vs. 87.0%, $P=0.022$). The last, in the pleural morphology, the correctly diagnosed group consisted of 20 cases of

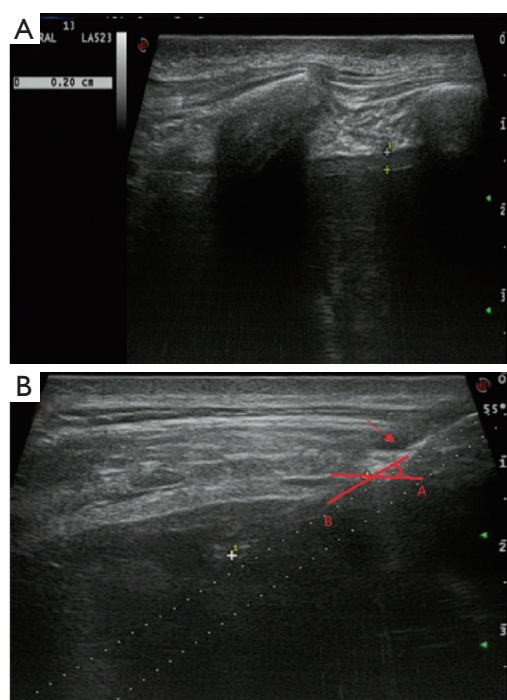


Figure 2 Images of a 76-year-old man was diagnosed with tuberculous hydrothorax. (A) Thoracic Ultrasound evaluation before biopsy showed parietal pleural thickness that was measured to be 2.0 mm; (B) line A is the tangent at the point of pleural entry of the needle (arrow). Line B is drawn perpendicular to line A. The angle is defined as acute angle that between the line A and line B.

pleural nodules and 85 cases without pleural nodules. But, there were 1 cases of pleural nodules and 34 cases without pleural nodules in the incorrectly diagnosed group. Compared to non-nodular pleurae, the diagnostic accuracies afforded by pleurae with nodules/masses was significantly higher (95.2% vs. 71.4%, $P=0.026$). Ultimately, multivariate logistic regression showed that pleural thickness [odds ratio (OR): 0.278, $P=0.003$] and needle size (OR: 0.291, $P=0.018$) independently predicted diagnostic accuracy (Table 3).

We included 140 cases, all of whom underwent diagnostic thoracentesis and PCNB, and 79 of whom also later underwent Abrams biopsy. No severe intrathoracic hemorrhage was recorded; the principal complication was pneumothorax (four cases after thoracentesis + PCNB and 15 cases after thoracentesis + PCNB + Abrams).

Discussion

Our study shows that US-guided pleural cutting needle

Table 1 The diagnostic classifications of initial US-guided PCNBs and final diagnosis

Types of diagnosis	US-guided PCNBs	Final diagnosis
Malignant disease	26	43
Malignant mesothelioma	3	5
Metastatic carcinoma	23	38
Carcinoma of the lungs	23	34
Lymphoma	0	2
Oviduct serous carcinoma	0	1
Esophageal carcinoma	0	1
Specifically benign	31	45
Benign mesothelioma	3	5
Tuberculosis	27	39
Eosinophilic abscess	1	1
Nonspecifically benign	79	49
Inconclusive	4	3
Total	140	140

PCNB, percutaneous needle biopsy

biopsy is effective with overall diagnostic accuracy in 75.0%, sensitivity and specificity of malignant diagnosis in 58.1% and 99.0%, respectively. In 1989 Macleod *et al.* were the first to introduce cutting needle biopsy using blind needles to explore large PEs (20). Soon afterward, ultrasound-guided Tru-cut PB was first reported by Chang *et al.* (15). Subsequent reports of US-guided PCNB proved the effectiveness of the technique; the overall diagnostic rate was 63% to 94%, and the sensitivity in terms of malignancy detection was 61% to 80% (12-15,21). In the present study, the diagnostic accuracy was 75.0%, within the range of prior publications. In terms of malignancy, our diagnostic sensitivity was 58.1%, slightly lower than the lowest reported sensitivity (14). We have an analysis of the following reasons. Firstly, we encountered 43 malignant cases, which is more than most previous studies. Chang *et al.* reported a 70% sensitivity, slightly higher than our value (15). But, Chang *et al.* included only 10 malignant cases (15). However, in another study, Metintas *et al.* (14) biopsied 49 patients with malignant pleural disease, the largest amount of malignant cases in previous studies, reported a diagnostic sensitivity of 61.2%, close to our 58.1%. Therefore, although the diagnostic sensitivity of

Table 2 Univariate analysis of the factors influencing diagnostic yield

Variables	Correct diagnoses (n=105)	Incorrect diagnoses (n=35)	P
Patient			
Age (year) (mean ± SD)	55.3±15.4	55.3±14.4	0.982
Sex			0.573
Male	80	25	
Female	25	10	
Pleura			
Thickness (mm)			0.001
<3	36	23	
≥3	69	12	
Morphology			0.026
Non-nodular pleura	85	34	
Nodular pleura	20	1	
Biopsy			
Needle size (gauge)			0.022
18	65	29	
16	40	6	
Angle (mean ± SD)	38.5±13.6	37.0±15.0	0.602
Number of punctures			0.404
1–2	10	1	
3–4	84	31	
≥5	11	3	
Contrast enhancement			0.287
No	71	27	
Yes	34	8	
Region of insertion			0.558
Non-diaphragm	51	15	
Diaphragm	54	20	
Location			0.659
Left thorax	49	15	
Right thorax	56	20	

The correct diagnoses were composed of true positive and true negative cases. The incorrect diagnoses were composed of false-positive, false-negative, and inconclusive cases.

Table 3 Multivariate analysis to determine the factors influencing diagnostic yield

Variables	P	Odds ratio	95% confidence interval
Thickness	0.003	0.278	0.119–0.652
Needle size	0.018	0.291	0.105–0.806
Morphology	0.120	0.189	0.023–1.541

this study is slightly lower than previous reports, we believe that the sensitivity of malignancy of this study is still highly representative because of the large number of malignant cases. Secondly, there are two sizes of biopsy needle (18 and 16 G) were used in this study. And smaller size biopsy needle (18 G) was used in 94 times, accounting for 67%. As has been said before, Metintas *et al.* (14) reported the number of cases and diagnostic sensitivity of malignancy similar to ours, but the diagnostic sensitivity in terms of malignancy is still slightly higher than our study. But what is different from us is that, in the Metintas *et al.* (14) study, all cases had used larger size biopsy needle (16 G) for biopsy. We think this one of the possible reasons why the diagnostic sensitivity of malignancy in our study is low compared to more recent studies. Finally, in this study, 19 of 43 malignant cases had no thickening of the pleura, which accounted for 44.2% of the malignant cases. The smaller size biopsy needle and thinner pleura may all affected the amount of material in biopsy and ultimately affected the diagnostic sensitivity of malignancy.

Although US-guided PCNB is valuable for diagnosing pleural disease, the failure rate ranges from 8% to 37% (12–15,21). Few previous reports have explored factors affecting diagnostic failures in large samples. To the best of our knowledge, ours is the first such study. We included 140 cases; divided them into those with correct and incorrect diagnoses; and explored relevant patient, pleural, and biopsy-related factors (Table 2). Univariate analyses showed that pleural thickness, pleural morphology, and needle size differed significantly between the two groups ($P<0.05$); ultimately, multivariate analyses confirmed that pleural thickness and needle size independently predicted diagnostic accuracy (Table 3).

Chang *et al.* and Metintas *et al.* reported diagnostic sensitivities in terms of malignancy of 70% and 61.2%, respectively, using 16 G cutting needles (14,15). However, using a larger diameter (14 G) needle, Koegelenberg *et al.* reported an overall diagnostic rate of 62.9% and a

sensitivity of 66.7% in terms of malignancy detection (12). Heilo *et al.* found that the use of a larger cutting needle (14 vs. 18 G) afforded no additional diagnostic benefit (22). However, Adams *et al.* found that cutting needle biopsy was more sensitive than fine needle aspiration for diagnosing malignancies, including mesothelioma (23,24). John *et al.* found that increasing the needle caliber enhanced the diagnostic yield of percutaneous biopsy (25). Our findings, similar to those of Adams *et al.* And John *et al.*, also showed that needle size significantly influences diagnostic accuracy. We found that the diagnostic accuracy of biopsy using a 16 G needle could reach 87.0%, significantly higher than the 69.1% associated with use of an 18 G needle ($P=0.022$). Adams *et al.* and Heilo *et al.* focused principally on malignancy or malignant pleural mesothelioma (22-24). We were concerned with all relevant diseases, including those for which diagnoses failed or were unclear. Our case distribution was malignancy in 30.7%, specifically benign in 32.1%. We are of the view that diagnostic accuracy is greatly aided by the use of a 16 G needle.

Thickening of the pleura or pleural nodules/masses evident on US or CT is an important sign of malignancy and an important indicator of PB (26-28). We routinely chose the thickest part of the pleura for biopsy. We found that the diagnostic accuracy of biopsy correlated significantly with pleural thickness. Diagnostic accuracy for cases with nonthickened pleurae (<3 mm) was lower than that for cases with thickened pleurae (≥ 3 mm) (61.0 vs. 85.2%, $P<0.05$). Niu *et al.* found no significant correlation between diagnostic accuracy when a pleural thickness of 15 mm was used to divide patients into two groups prior to CT-guided core needle biopsy of pleural lesions (16). However, in US-assisted PCNB, Metintas *et al.* found that the diagnostic sensitivity for cases of pleural thickness <1 cm was significantly lower than that for thickness ≥ 1 cm (42.9% vs. 80%) (14). It is interesting that Niu *et al.* included cases with pleural lesions/pleural thickening >5 mm maximum; PEs were not present in all cases (16). However, Adams *et al.* reported that PCNB of pleurae 0.2 to 0.5 cm in thickness afforded reliable histological diagnosis (23). In fact, 3 mm is often used for the standard to determine pleural thickening (29). In our clinic, we encounter many patients with unexplained PEs who require biopsy to allow us to plan treatment; such patients often have nonthickened pleurae (<3 mm). Thus, we compared cases with pleural thickness <3 and ≥ 3 mm and found that the diagnostic accuracy was 85.2% for the latter patients. In the work of Niu *et al.*, all cases had a pleural

thickness >5 mm, and the diagnostic accuracy of CT-guided PCNB of pleural lesions was 89.2%, close to our figure for those with pleural thickness ≥ 3 mm (16). This means that when the pleural thickness was ≥ 3 mm, US-guided PCNB afforded a high diagnostic rate. However, when the pleural thickness was <3 mm, the diagnostic accuracy was only 61.0%. In such cases, the lower diagnostic rate may be associated with smaller fragmented specimens. Thus, if patients with thin pleurae and unexplained PEs are not diagnosed via US-guided PCNB diagnosis, and other indicators or clinical symptoms suggest pleural positivity, follow-up biopsy or the use of other diagnostic methods is considerable (30,31).

Qureshi *et al.* found that US was effective at diagnosing malignant PEs; the suggestive signs were pleural thickness >10 mm, pleural nodularity, and diaphragm thickness >7 mm (27). Our diagnostic accuracy for cases with focal thickening or pleural nodules/masses was 95.2%. A total of 21 cases with focal pleural thickening or pleural nodules/masses were found in the present study, of which 17 (81%) were positive, including 10 malignancies, five tuberculosis cases, and two mesotheliomas; there were four negative cases (19%). Therefore, the presence of focal pleural thickening or nodules/masses is an important predictor of positivity even before biopsy. We found, in univariate analyses, that pleural nodules/masses were associated with a higher biopsy-indicated diagnostic rate than biopsy of non-nodular pleurae (95.2% vs. 71.4%, $P=0.026$). However, in multivariate analyses, the pleural morphology was not statistically significant. It is important to note that areas with pleural nodules/masses or focal thickening are usually the thickest regions. We encountered 21 cases of pleural nodules/masses and focal thickening. Of these, a pleural thickness ≥ 3 mm was evident in 17 cases; only four cases had a pleural thickness <3 mm, and one of these was a false negative. It should be noted that pleural morphology and thickness may be closely related; thus, in multivariate analyses, each may reduce the diagnostic accuracy afforded by the other. The diagnostic yield of cases with a pleural thickness ≥ 3 mm was significantly higher than that of cases with a pleural thickness <3 mm, so the choice of a thicker biopsy site improved the diagnostic rate. We selected pleural nodules/masses and regions of focal thickening for biopsy, which increased diagnostic accuracy. We believe that thorough scanning prior to biopsy is essential to locate regions of focal thickening or pleural nodules/masses and to biopsy those sites. The many causes of diagnostic failure include the biopsy of an unaffected

area, inadequate tissue, or differences in pathological stages. Successful PB is reflected in not only specimen quantity but also quality. We suggest that thickened pleurae and pleural nodules/masses are so often positive because disease development is rather advanced or local disease is more obvious. Thus, the selection of such pleural regions for biopsy may improve diagnostic accuracy.

Our study has certain limitations: (I) the retrospective design creates a risk for selection bias. Because of the retrospective characteristics, the variables selected in our study were not comprehensive. For example, we could not get the accurate PE volume of all cases. The use of contrast agents, the selection of biopsy needles and the selection of puncture angles were not random, but subjective. Most patients were punctured three to five times to enhance diagnostic accuracy. The number of other punctures was less in this study; (II) not all biopsies were performed by the same operators, and we did not determine whether the operator affected diagnostic accuracy.

In conclusion, US-assisted PCNB is safe and affords a high diagnostic yield. Pleural thickness (<3 *vs.* ≥3 mm) and the size of the biopsy needle (18 *vs.* 16 G) were significantly correlated with the diagnostic yield.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: This study was approved by the Scientific Research Ethics Review Committee of the First Affiliated Hospital of Guangzhou Medical University.

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