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Diagnostic value of ultrasound guided transthoracic tru-cut biopsy in thorax malignancies

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Abstract:

AIM: To investigate the diagnostic value of ultrasound (US) guided transthoracic fine needle aspiration biopsy (TTFNA) and US guided transthoracic tru-cut biopsy (TTTCB) in malignant thorax lesions.

MATERIALS AND METHODS: Patients who underwent US guided transthoracic biopsies between April 2014 and May 2017 were retrospectively evaluated. Patients who were diagnosed as thoracic malignancy and both TTTCB and TTFNA performed for the same lesion were included in the study. The diagnostic accuracy of TTTCB, TTFNA and their combination were analyzed. The diagnostic accurracy of methods were statistically compared by McNemar Test.

RESULTS: Thirty two patients were included in the study. Ultrasound guided TTFNA and/or TTTCB were diagnostic in 30 (93.8%) of them. TTFNA was diagnostic in 23 (%71.8), TTTCB were diagnostic in 26 (%81.2) of these pateints. Seven (77.7%) of 9 patients in which TTFNA was not diagnostic, TTTCB was diagnostic. The diagnostic accuracy was 71.8% and 81.2% for TTFNA and TTTCB, respectively. When TTTCB and TTFNA were performed consecutively in the same procedure, the overall diagnostic accuracy was 93.7%. There was no difference between the diagnostic accuracy of US-guided TTFNA and TTTCB (P=0.508). The diagnostic accuracy of combination of TTFNA and TTTCB was significantly higher than that of TTFNA alone (P=0.016). During the procedures, pneumothorax which did not require chest tube insertion was detected as complication in 1 case (3.1%).

CONCLUSION: Diagnostic accuracy of US-guided TTFNA and TTTCB is high and has no superiority to each other. Combining both procedures under the quidence of US increases the diagnostic accuracy statistically significantly.

Keywords:

Fine-needle aspiration biopsy, thoracic ultrasonography, transthoracic lung biopsy

Introduction

What makes ultrasonography (USG) so popular in the diagnosis of pulmonary conditions in recent years is that the ability to perform diagnostic procedures in real time and not expose the patient or the physician to radiation. Its safety and efficacy has been established in many diagnostic procedures including identifying the thoracentesis site, insertion of chest tubes, transthoracic fine-needle aspiration biopsy (TTFNAB), diagnosis of pneumothorax, and, notably, detecting pleural fluid.[1]

Lesions that are located in the periphery of the lungs with no air trapped between the chest wall and the lesion can easily be identified using USG. There are many different methods that can be used to diagnose such peripheral lesions. These include fluoroscopy, computed tomography (CT),

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ultrasound-guided biopsy, fiberoptic bronchoscopy, electromagnetic navigation bronchoscopy, virtual bronchoscopic navigation, and surgical biopsy. These methods are inferior to USG because some are expensive, some require advanced expertise and experience, some are more invasive, and some involve radiation exposure.[2-5] Ultrasound-guided TTFNAB is readily accessible and cheap with a high diagnostic accuracy, does not involve radiation exposure, is less invasive, does not require general anesthesia or sedation, supports procedures in real time, and is associated with low morbidity, mortality, and complication rates.[6-11]

Many studies have provided evidence on the safety and efficacy of TTFNAB for peripheral tumors of the lung and chest wall lesions. On the other hand, in mediastinal lesions adjacent to the chest wall, hematological malignancies such as lymphoma and sarcomas, and certain necrotic-cavitary parenchymal mass lesions, TTFNAB may not always be helpful in establishing the diagnosis and tissue biopsy for histopathological diagnosis may be required.[12] In this case, ultrasound-guided transthoracic tru-cut biopsy (TTTCB) procedure may be used. Tru-cut (TC) biopsy is superior to TTFNAB because it better preserves the tissue architecture for histopathological examination.[13,14]

Due to the limited number of studies conducted on this topic by pulmonologists and to foster the interest of pulmonologists in this area, this study was designed to evaluate the diagnostic value of ultrasound-guided TTTCB.

Materials and Methods

Patient population

We retrospectively reviewed the clinical records of patients with peripherally located lung lesions, mediastinal lesions, or a lung lesion with a metastatic mass lesion located at the chest wall, who were found eligible for biopsy using USG and who had a diagnostic biopsy procedure performed between April 2014 and May 2017 at the ultrasound unit of our pulmonology department. The files of patients with a confirmed diagnosis of thoracic malignancy were set aside. In order to increase the diagnostic accuracy and avoid time loss when establishing diagnosis, TTTCB and TTFNAB may be performed in the same session from the same site if the patient is likely to have a hematological malignancy, the lesion has widespread necrotic areas radiographically, and there is adequate distance between the tumor and the healthy lung tissue to qualify for TTTCB (at least 2 cm), and if the lesion sits on the chest wall without moving with breathing, at the USG unit of our department. Patients who had diagnostic TTTCB and TTFNAB performed on the same lesion in the same session were included in this study. The clinical, radiographic, and demographic data; anatomic location of the lesion; dimensions of the biopsied lesion; number of biopsies per lesion; procedure-related complications; diagnosis established by ultrasound-guided biopsy (TTTCB-TTFNAB); the definite diagnosis if this method did not provide the diagnosis; and definitive diagnostic method used on all patients were recorded. The study was designed based on the requirements of the international Helsinki declaration. This study was approved by the local Ethics Board.

Procedures

Thoracic ultrasound for thoracic lesions

One experienced pulmonologist (CD) performed the thoracic ultrasound examination using a General Electric Logic 7 machine and 3.5 MHz convex probe, in the abdominal mode. The scan starts in the region where the lesion was originally identified in sitting position. If needed, the scan was continued in supine, oblique, and lateral decubitus positions by moving the probe transversally and longitudinally along the intercostal spaces, including the parasternal line; middle- and lateral clavicular lines; anterior, middle, and posterior axillary lines; lateral and medical scapular lines; and along the paravertebral line to cover the entire thoracic region including normal areas.

Thoracic ultrasound-guided transthoracic tru-cut and fine-needle aspiration biopsy procedures

Before the biopsy procedure, patient's consent is documented; pulmonary function tests are completed; and complete blood count, blood chemistry, and coagulation parameters are reviewed. Patients with a platelet count lower than 50,000/μL or international normalized ratio greater than 1.3 and patients who do not consent to the ultrasound-guided biopsy procedure are excluded. During the procedure, free-hand technique or indirect technique may be used. No premedication or sedation is administered before the procedure. The procedure site and the ultrasound probe are cleaned with iodine solution-alcohol. The FNAB procedure is performed using a 22G spinal needle attached to a 20 mL syringe (Set Medical San, Istanbul, Turkey) from an access site that is scanned with power Doppler to make sure it is safe with no vascular structures in the vicinity. After accessing the target lesion, the needle is moved like a folding fan and specimen is aspirated from different parts of the target tissue. Aspiration was discontinued when sufficient visible material or hemorrhagic material was sucked into the syringe [Figure 1]. The TC biopsy procedure is performed through the same access site using a 16G × 16 cm (GALLINI, Mantova, Italy) automatic TC biopsy set. Before the procedure, when

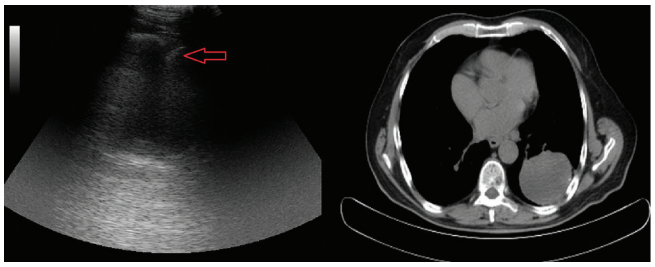

Figure 1: Thoracic USG-guided TTFNAB procedure in a patient with peripherally located tumor in the left lung in a thoracic CT. (Sonographically a 6x6 cm hypoechoic lesion, the biopsy needle is marked with a red arrow)

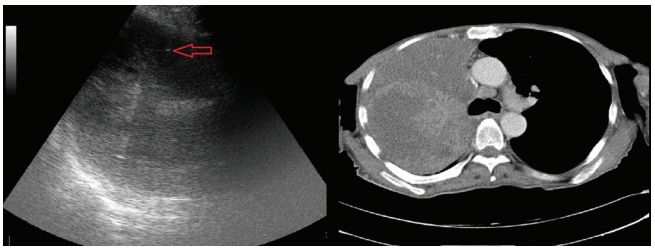

Figure 2: Thoracic USG-guided TTTCB procedure in a patient with peripherally located tumor in the right lung in a thoracic CT. (Sonographically a 10x9 cm hypoechoic lesion, the tru-cut biopsy needle is marked with a red arrow)

making the incision with the TC biopsy set, the site to be biopsied inside the tumor should be at least 2 cm distant to healthy pulmonary parenchymal tissue to avoid injury to the lung parenchyma [Figure 2].

Pathologic examination

The procedure was performed in real time. There was no onsite pathologist available during the procedure. Cytologic specimens were prepared using both alcohol fixation and air-dry techniques. The remaining specimens were fixated in 95% alcohol to be used to prepare the cell block. The TC biopsy specimens were fixated in 95% alcohol and sent to the pathology laboratory. At the pathology laboratory, Papanicolaou stain or May–Grunwald Giemsa was used to stain the slides fixated with 95% alcohol and air-dried slides, respectively. Hematoxylin-eosin stain was used on the 3-micron slides cut from the TTTCB and TTFNAB cell blocks embedded in wax. If required, immunohistochemistry was used to examine the cell block sections.

Statistical analysis

The data were analyzed using the SPSS 17.0 for Windows (IBM Inc., Released 2008, Chicago, IL, USA) computer software. In the descriptive statistics, continuous variables were expressed as mean ± standard deviation and categorical variables were expressed as percentages. Group data were analyzed using Chi-square test. McNemar's test was used to compare the diagnostic accuracies of ultrasound-guided TTTCB and TTFNAB procedures. $P < 0.05$ was considered statistically significant.

Results

A total of 150 patients had ultrasound-guided biopsy procedure (TTFNAB + TTTCB) performed during the study period. A total of 32 patients who had ultrasound-guided TTFNAB and TTTCB performed in the same sessions were included in this study. The mean age of the patients was 60.2 ± 14.1 years (range: 23–86 years), and 8 were (25%) women and 24 (75%) were men. The most common complaint was weight loss (34.3%), the most common chest X-ray finding was a mass, and the most common CT scan finding was peripherally located mass. The demographic and radiographic findings of the patients are summarized in Table 1.

A review of the biopsied lesion sites revealed that twenty (62.5%) were a peripheral mass lesion in the lungs, seven (21.8%) were a metastatic mass lesion that originated from a mass in the lungs, and five (15.6%) were a mediastinal mass adjacent to the chest wall. With regard to the dimensions of the lesions, the mean long-axis diameter was 8.4 ± 2.7 (5–14) cm, 8.8 ± 3 (5–13) cm, and 4.6 ± 2 (2–8) cm for the lung lesions, mediastinal lesions, and chest wall lesions, respectively. The mean number of TTTCBs per lesion was 1.03 ± 0.1 and the mean number of TTFNABs was 1.09 ± 0.2.

Thirty (93.8%) out of the 32 patients who had thoracic ultrasound-guided TTFNAB and TTTCB could be diagnosed. Diagnosis was established using TTFNAB in 23 (71.8%) and using TTTCB in 26 (81.2%) patients. Diagnosis using ultrasound-guided TTFNAB could be established in 23 patients and 9 patients could not be diagnosed. In seven (77.7%) out of nine patients who could not be diagnosed using TTFNAB, TTTCB proved to be diagnostic. Four (44.4%) patients who were not diagnosed with this method had hematological malignancies. Diagnosis using ultrasound-guided TTTCB could be established in 26 patients and 6 patients could not be diagnosed. In four (66.6%) out of six patients who could not be diagnosed using TTTCB, TTFNAB proved to be diagnostic. One (16.6%) patient who was not diagnosed with this method had a hematological malignancy. The diagnostic distribution of patients who had ultrasound-guided TTTCB and TTFNAB is shown in Table 2.

The diagnosis in one of the two (6.2%) patients who could not be diagnosed using thoracic ultrasound-guided TTFNAB and TTTCB was established using CT-guided TTFNAB. These patients were ultimately diagnosed with lymphoma and non-small cell carcinoma, respectively. Only one patients (3.1%) developed pneumothorax

that did not require chest tube placement during the procedure.

The diagnostic success rate in malignant conditions of the lungs was 71.8%, 81.2%, and 93.7% for ultrasound-guided TTFNAB alone, for TTTCB alone, and TTFNAB and TTTCB in combination, respectively.

Although more patients were diagnosed using thoracic ultrasound-guided TTTCB, the difference in diagnostic success rate with TTFNAB was not statistically significant (P = 0.508). Although more patients could be diagnosed when two procedures were used in combination, the difference to TTTCB alone was not statistically significant (P = 0.125). Thus, the combined use of the two procedures was significantly superior to TTFNAB alone (P = 0.016) [Table 3].

Discussion

In this study where, we evaluated the diagnostic value of thoracic ultrasound-guided TTTCB, we came to the conclusion that there is no statistically significant difference in terms of diagnosis rate between ultrasound-guided TTFNAB and TTTCB (P = 0.508), and combined use of TTFNAB and TTTCB in the same session improves the diagnostic success rate (P = 0.016). Thirty-two patients were included in this study. The diagnostic success of ultrasound-guided TTFNAB alone was 71.8% versus 81.2% for ultrasound-guided TTTCB alone. Combined use of both procedures in the same session improves the diagnostic success rate to 93.7%. Only one (3.1%) patient developed pneumothorax that did not require chest tube placement during the procedures.

Different studies report the diagnostic success of thoracic ultrasound-guided TTFNAB between 64.5% and 96.8%.[15-18] A great majority of these studies emphasize the importance of being able to perform the ultrasound-guided TTFNAB in real time, which is considered a major advantage. Being able to track the needle movements inside the lesion to be biopsied in real time thanks to the thoracic ultrasound offers a major benefit for the clinician who performs the procedure and helps to avoid injury to the lung's parenchyma. Another advantage provided by the real-time procedure is to be able to direct the biopsy needle to avoid areas of the lesion that exhibit a different sonographic pattern, i.e., necrotic regions, and to access the lesion from the cavity wall.[19] For these reasons, ultrasound-guided TTFNAB is considered a safe and effective diagnostic procedure. In our series, the diagnostic success rate was 71.8%. Out of nine patients who could not be diagnosed with thoracic ultrasound-guided TTFNAB, four (44.4%) had hematological malignancies (three lymphomas and one acute myeloid leukemia). The diagnostic value of FNAB is low for benign lesions, lymphomas, and hematological malignancies.[20] Excisional biopsy is the preferred method to histopathologically diagnose lymphomas. In addition to FNAB şeklinde kısaltılabilir, TC tissue-dissecting biopsies may not always be helpful in the diagnosis of lymphomas either. This is because it is not possible to perform the immunophenotypic, cytogenetic, and immunoassay studies that are needed for the diagnostic procedure on small-sized biopsies.[21] We believe that the relatively lower diagnostic success of thoracic ultrasound-guided TTFNAB in this study may be explained by hematological malignancies.

Table 1: Demographics-radiographic findings

Demographics and radiographic findings	*n* (%)
Age (years/SD)	60.2±14.1
Gender (male/female)	24/8 (75/25)
Smoking history (package years/SD)	34.9±20.4
Thoracic CT	
Peripheral lesion	20 (62.5)
Mediastinal-hilar LAP	23 (71.8)
Mediastinal mass	5 (15.6)
Atelectasis	4 (12.5)
Pleural fluid	4 (12.5)
Consolidation	1 (3.1)

CT: Computerized tomography, LAP: Lymphadenopathy, SD: Standard deviation

Table 2: Definite diagnosis of subjects who could and could not be diagnosed using thoracic ultrasound-guided transthoracic fine-needle aspiration biopsy and transthoracic tru-cut biopsy

Diagnosis	TTFNAB		TTTCB	
	Diagnostic, *n* (%)	Not diagnostic, *n* (%)	Diagnostic, *n* (%)	Not diagnostic, *n* (%)
Non-small cell carcinoma	7 (30.4)	2 (22.2)	7 (26.9)	2 (33.3)
Squamous cell carcinoma	7 (30.4)	1 (11.1)	6 (23.1)	2 (33.3)
Adenocarcinoma	4 (17.5)	1 (11.1)	5 (19.2)	-
Sarcomatoid carcinoma	2 (8.8)	-	2 (7.8)	-
Lymphoma	1 (4.3)	3 (33.4)	3 (11.5)	1 (16.6)
Small cell carcinoma	1 (4.3)	-	1 (3.8)	-
Other (AML-Thymoma, etc.)	1 (4.3)	2 (22.2)	2 (7.8)	1 (16.6)
Total	23 (100)	9 (100)	26 (100)	6 (100)

AML: Acute myeloid leukemia, TTFNAB: Transthoracic fine-needle aspiration biopsy, TTTCB: Transthoracic tru-cut biopsy

Table 3: Comparison of diagnostic success rates of ultrasound-guided transthoracic fine-needle aspiration biopsy and transthoracic tru-cut biopsy

	Number of diagnosed subjects (*n*)	Diagnostic success (%)	*P*
TTFNAB only	23/32	71.8	0.508
TTTCB only	26/32	81.2	0.125
TTFNAB + TTTCB	30/32	93.8	0.016

TTFNAB: Transthoracic fine-needle aspiration biopsy, TTTCB: Transthoracic tru-cut biopsy

Thoracic ultrasound-guided TTTCB procedure, similar to TTFNAB, is a safe and reliable procedure that is performed under USG guidance and in real time. For a thoracic lesion to be identified sonographically and biopsied under USG guidance, it must be located with no air trapped between the lesion and the chest wall, or in other words, there must not be lung parenchyma containing air in between. Even a very small amount of air-containing lung parenchyma between the lesion and the chest wall will make the lesion undetectable sonographically.[22] Although it is suggested that the use of thicker and sharper needles in thoracic ultrasound-guided TTTCB procedure may be associated with a higher complication rate, reports in the literature indicate comparable rates for TTFNAB and TTTCB.[23] While some studies that compare FNAB and TC biopsy procedures report no difference in complication rate and diagnostic accuracy, some demonstrated a higher diagnostic accuracy for the TC biopsy procedure.[23-25] Advocates of TTFNAB emphasize the fact that the procedure is less traumatic with a lower complication rate, while advocates of the TTTCB point out that it is possible to establish the diagnosis with a larger tissue size without the need for a cytologist. Although the diagnostic success rate of ultrasound-guided TTTCB was higher than TTFNAB in our study, the difference was not statistically significant (81.2% vs. 71.8%, $P = 0.508$). The reason for the nonsignificant difference may be because it was possible to use immunohistochemistry staining methods on cell blocks prepared from specimens collected with TTFNAB.

The most important conclusion of this study is the significant improvement in diagnostic success if TTFNAB and TTTCB are used in combination on the lesion. Diacon *et al*.,[26] in their 155-subject series, reported a diagnostic success of 82% for thoracic ultrasound-guided TTFNAB versus 76% for TTTCB and demonstrated a significant improvement (89%) in diagnostic success if the two procedures were combined. The authors concluded that combining TTFNAB and TTTCB offers a high diagnostic accuracy with a low complication rate and pointed out that TTTCB and TTFNAB are complementary methods. The results of this study support our observations. Combining the two procedures improved our diagnostic success to 93.7%. The reason the diagnostic success rate of TTFNAB is higher than TTTCB in this study is due to the relatively higher incidence of hematological malignancies in our series. The incidence of patients with a definitive diagnosis of hematological malignancies was 18.7% in this study versus 3.2% in the study by Diacon *et al*.[26] Studies have shown that TC biopsies have a higher diagnostic accuracy, especially in nonepithelial malignancies. This is due to the tendency of nonepithelial malignant cells to exhibit a high intercellular adherence (Türkçe'sinde 'hücre içi' denilmiş!) and a high homogenicity, which makes aspiration more difficult.[26,27]

One limitation of this study is that it involves a single center and a limited number of patients. Thus, the results of this study should be interpreted only in the present context and not as final conclusions. Another limitation is the retrospective and nonrandomized study design. The first patients included in the study are from our learning period with limited experience, and we may have been selective with regard to tumor size. We may have preferred TTFNAB as the only diagnostic method for smaller tumors.

Conclusion

We believe that TTTCB added to the ultrasound-guided TTFNAB improves diagnostic success with very low complication rates, and a combined use of TTFNAB and TTTCB is advisable, especially for larger lesions that fully sit on the chest wall and do not move with breathing, and which have been identified as potential hematological malignancies clinically and radiographically.

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Conflicts of interest
There are no conflicts of interest.

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