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Muzaffer Metintas, Guntulu Ak, Emine Dundar, Huseyin Yildirim, Ragip Ozkan, Emel Kurt, Sinan Erginel, Fusun Alatas and Selma Metintas

Chest 2010;137;1362-1368; Prepublished online February 12, 2010;
DOI 10.1378/chest.09-0884

ISSN:0012-3692

CHEST

Original Research

PLEURAL DISEASE

Medical Thoracoscopy vs CT Scan-Guided Abrams Pleural Needle Biopsy for Diagnosis of Patients With Pleural Effusions

A Randomized, Controlled Trial

Muzaffer Metintas, MD; Guntulu Ak, MD; Emine Dundar, MD; Huseyin Yildirim, MD; Ragip Ozkan, MD; Emel Kurt, MD; Sinan Erginel, MD; Fusun Alatas, MD; and Selma Metintas, MD, PhD

Background: **In cases of pleural effusion, tissue samples can be obtained through Abrams needle pleural biopsy (ANPB), thoracoscopy, or cutting-needle pleural biopsy under the guidance of CT scan (CT-CNPB) for histopathologic analysis. This study aimed to compare the diagnostic efficiency and reliability of ANPB under CT scan guidance (CT-ANPB) with that of medical thoracoscopy in patients with pleural effusion.**

Methods: **Between January 2006 and January 2008, 124 patients with exudative pleural effusion that could not be diagnosed by cytologic analysis were included in the study. All patients were randomized after the CT scan was performed. Patients either underwent CT-ANPB or thoracoscopy. The two groups were compared in terms of diagnostic sensitivity and complications associated with the methods used.**

Results: **Of the 124 patients, malignant mesothelioma was diagnosed in 33, metastatic pleural disease in 47, benign pleural disease in 42, and two were of indeterminate origin. In the CT-ANPB group, the diagnostic sensitivity was 87.5%, as compared with 94.1% in the thoracoscopy group; the difference was not statistically significant ($P = .252$). No difference was identified between the sensitivities of the two methods based on the cause, the CT scan findings, and the degree of pleural thickening. Complication rates were low and acceptable.**

Conclusion: **We recommend the use of CT-ANPB as the primary method of diagnosis in patients with pleural thickening or lesions observed by CT scan. In patients with only pleural fluid appearance on CT scan and in those who may have benign pleural pathologies other than TB, the primary method of diagnosis should be medical thoracoscopy.**

Trial registration: **clinicaltrials.gov; Identifier: NCT00720954.** ***CHEST 2010; 137(6):1362–1368***

Abbreviations: CT-ANPB = CT scan-guided Abrams needle pleural biopsy; CT-CNPB = CT scan-guided cutting-needle pleural biopsy; *df* = degrees of freedom

Pleural effusions are often the presenting feature of pleural disease. If clinical suspicion of malignancy is high in patients with such a finding, cytologic examination of pleural fluid samples is recommended.[1] When cytology is nondiagnostic, closed percutaneous needle biopsy has traditionally been performed blindly using a reverse-beveled needle, such as an Abrams or Ramel needle.[2-4] However, needle biopsy for pleural tissue was diagnostic in only 50% of patients presenting with malignant effusions.[5] For this reason, the role of closed pleural needle biopsy in diagnosing malignant effusions has been questioned.[5-7]

Medical thoracoscopy for cases of exudative pleural effusion not having any diagnosis by either clinical, radiologic, laboratory, or cytologic investigation[7,8] is the method that has been performed routinely in many clinics. In recent years, some authors suggest that real time CT scan-guided cutting-needle pleural biopsy (CT-CNPB), performed by a radiologist, is a promising technique for sampling the pleura, because it can improve diagnostic sensitivity to about 80% for pleural malignancy.[6,9-11]

On the other hand, some authors have suggested that further detailed studies to determine the relationship

between the amount of pleural thickening and the diagnostic sensitivity of the Abrams needle biopsy are needed.[5,12] Abrams needle biopsy is easy to use, safe, inexpensive, and rapid, and can be performed as a bedside procedure in the department.[5] Actually, the only advantage of image-guided cutting needle biopsy is the CT scan guidance. Therefore, if we can use CT scan guidance for biopsies performed with an Abrams needle, we can increase the sensitivity of this traditional method. Additionally, it has been pointed out that prospective studies are needed to compare the sensitivity and the cost-effectiveness of closed pleural biopsy with Abrams needle with thoracoscopy in the setting of pleural malignancy and TB.[5,10,12] In this study, we compared the diagnostic sensitivity and safety of medical thoracoscopy with Abrams needle pleural biopsy under CT scan guidance (CT-ANPB) in patients with pleural effusion who require pleural tissue sampling.

Materials and Methods

This prospective, randomized, parallel study was conducted in the Chest Diseases Department of the Medical Faculty of Eskisehir Osmangazi University from January 2006 to January 2008. The study was approved by the Ethical Committee of Eskisehir Osmangazi University Medical Faculty (2006-06-07 and 2006/387).

Patients

Patients with the following criteria were admitted to participate in the study: evidence of exudative pleural effusion for which a specific diagnosis could not be determined by cytologic examination and willingness to participate in the study and undergo an invasive procedure. Exclusion criteria were as follows: patients <18 or >85 years old, pleural thickening or a pleural-based mass without pleural effusion in radiologic investigation, presence of parapneumonic effusion, any contraindication for pleural biopsy or medical thoracoscopy, or any other systemic disease that could affect CT scan. Patients were thoroughly informed before randomization into the study, and their written consent was requested.

Manuscript received April 10, 2009; revision accepted January 6, 2010.
Affiliations: From the Department of Chest Diseases (Drs M. Metintas, Ak, Yildirim, Kurt, Erginel, and Alatas), the Department of Pathology (Dr Dundar), the Department of Radiology (Dr Ozkan), and the Department of Public Health (Dr S. Metintas), Eskisehir Osmangazi University Medical Faculty, Eskisehir Osmangazi University, Eskisehir, Turkey.
Funding/Support: This study has been supported by the Research Fund of Eskisehir Osmangazi University (Project Number: 2007-11.008).
Correspondence to: Muzaffer Metintas, MD, Department of Chest Diseases, Eskisehir Osmangazi University Medical Faculty, Eskisehir, Turkey 26040; e-mail: muzaffermetintas@gmail.com

DOI: 10.1378/chest.09-0884

Patients were randomized after being hospitalized, and contrast enhancement CT scan of all patients was taken first with the Toshiba Aquilla 64 MDBT device (Tokyo, Japan). The thorax was scanned at a thickness of 5 mm from the apex of the lungs to the costophrenic recess. Before the analysis, 80 mL of nonionic contrast substance was administered through an arm vein, and the scan was initiated 30 s after the infusion of contrast medium. Findings were classified as in previous relevant publications.[13,14]

Randomization was carried out in compliance with the Consolidated Standards of Reporting Trials statement recommendations. A total of 31 envelopes were prepared at once for randomization. In each sequence four cards were prepared, two marked as A and two marked as B, which were then inserted into each envelope. Patients who picked the A card underwent CT-ANPB, and those who picked B underwent thoracoscopy. After completion of the preceding randomization sequence for four patients, a new envelope was initiated.

Patients in arm A who had a failed diagnosis by CT-ANPB underwent medical thoracoscopy. Patients for whom a precise diagnosis could not be determined after medical thoracoscopy underwent a second thoracoscopy or diagnostic thoracotomy on their consent. Patients who rejected these options and those with asbestos-related benign pleural disease, TB, or nontuberculous benign causes were followed with a minimum follow-up period of 12 months.

CT-ANPB and Medical Thoracoscopy

Abrams biopsy procedures were performed in arm A just after determination of the entry site with the aid of a CT scan, which was obtained before the procedure. The entry site was selected as the most suitable and accessible part of the lesion by looking at the hard copy of the CT scans while patients were in the bronchoscopy room.

The distance between the entry site and the target point was measured two-dimensionally by thoracic CT scans. For instance, Figure 1*A* shows that the entry site was 13 cm away from the bottom edge of the scapula and 7 cm away from the spinal process of the vertebrae. In another example, the entry site was 0.5 cm above the carina horizontally and 9 cm away from the midsternal line laterally (Fig 1*B*). Measurements were made according to the scale located on CT scans. After taking the measurements described above, the entry site for Abrams needle was marked on the skin of the patient as the corresponding point for the lesion on the CT scan. Four to six biopsy specimens were taken from the parietal pleura using Abrams needle through the same entry point by an experienced pulmonologist (G. A.) in a bronchoscopy/thoracoscopy room.[15]

Medical thoracoscopy was done with a rigid thoracoscope (Karl Storz; Tuttlingen, Germany) under mild sedation and local anesthesia by a team that consisted of M. M. plus G. A. or M. M. plus H. Y. At least six biopsy specimens were taken from abnormal sites of parietal pleura at thoracoscopy. After each procedure, the biopsy specimens were immediately fixed in formalin and sent to the pathology department for histopathology analysis. If suspicion of tuberculous pleurisy was high, then one further biopsy specimen was sent to the laboratory in an isotonic saline solution for bacteriologic investigation, including a search for *Mycobacterium tuberculosis*.

Biopsy samples were evaluated by the same pathologist in the Eskisehir Osmangazi University Medical Faculty Pathology Department. The cases were categorized primarily as benign and malignant, and those that were malignant were also categorized according to the cell properties. Immunohistochemical stains were used to differentiate tumors of mesothelial origin from those of epithelial origin. Among these, there were antibodies, such as carcinoembryonic antigen, Ber Ep4, B 72.3, and CD 15 (Leu M1), as well as mesothelial cell determinants, such

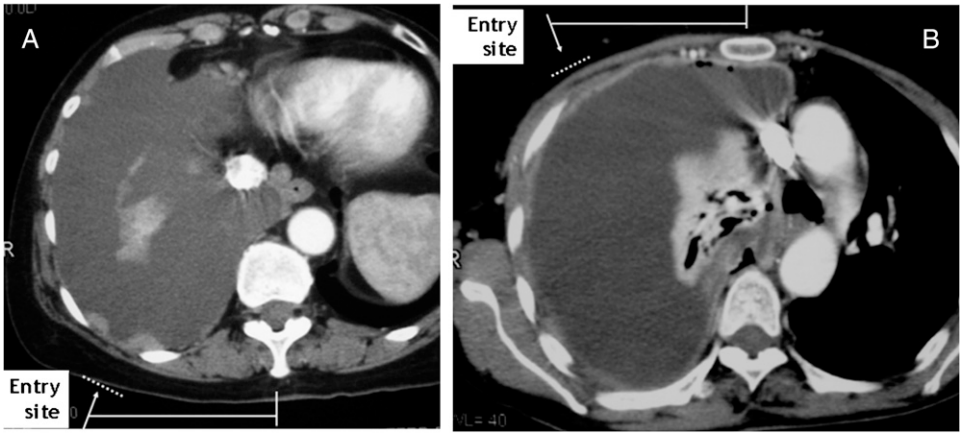

FIGURE 1. Choosing the entry site for CT scan-guided Abrams needle pleural biopsy. Examples of an entry site away from the bottom edge of the scapula and from the spinal process of the vertebrae (*A*) and above the carina horizontally and away from the midsternal line laterally (*B*).

as calretinin, Wilms tumor 1, thrombomodulin, and cytokeratin 5/6. Additionally, epithelial membrane antigen, vimentin, p53, and wide-spectrum keratin were used when required. The pathologist also stained the specimens with Ziehl-Neelsen to investigate for acid-resistant bacilli (*M tuberculosis*).

Statistical Analysis

Considering that the diagnostic sensitivity was 90% for thoracoscopy[16] and 80% for CT-ANPB,[17] sample size needed for this study was estimated at a minimum of 48 patients in each arm, with a power of 80% and a significance of 5%. However, we extended the number of patients up to 62 for both arms in case some patients were excluded in the course of the study.

The primary end point of this study was the determination of sensitivity and complication rate of both invasive methods in the diagnosis of pleural diseases. SPSS version 12.0 software (SPSS Inc.; Chicago, IL) was used for statistical analysis. Sensitivities were compared using the χ^2 test.

RESULTS

The total number of patients included in the study was 124, with 72 men and 52 women; the mean age was 60.9 ± 13.5 years. The distribution of diagnoses for patients included in the study is shown in Table 1.

The randomization diagram-trial profile of patients in the study is shown in Figure 2. Thoracoscopy was performed on 62 patients, 33 (53%) men and 29 (47%) women. The mean age was 61.1 ± 14.3 years (*r*, 27-85). CT-ANPB was performed on 62 patients, 39 (63%) men and 23 (37%) women. The mean age was 60.8 ± 14.8 years (*r*, 22-84). There were no differences in terms of sex ($\chi^2 = 1.19$; degrees of freedom [*df*] = 1; $P = .27$), age ($t = 0.126$; $df = 122$; $P = .90$), the distribution of diagnoses between the two groups ($\chi^2 = 0.492$; $df = 2$; $P = .921$), or the distribution of malignant cases inside the groups ($\chi^2 = 0.330$; $df = 2$; $P = .848$). Two cases were of indeterminate origin. Because these two patients died after, but unrelated to, thoracoscopy, a final diagnosis could not be reached.

As seen in Figure 2, 48 of 62 patients who underwent CT-ANPB were evaluated after diagnosis. Diagnostic sensitivity of CT-ANPB for 48 patients with malignant or tuberculous pleural effusion was 87.5% (42/48). For the thoracoscopy group, 51 patients of the 62 patients who underwent thoracoscopy were evaluated after diagnosis. Diagnostic sensitivity of thoracoscopy for 51 patients with malignant or tuberculous pleural effusion was 94.1% (48/51). There was no significant difference between the two methods regarding diagnostic sensitivity ($\chi^2 = 1.310$; $df = 1$; $P = .252$).

Diagnosis was achieved with the use of thoracoscopy in four of six patients in whom a specific diagnosis was not reached with CT-ANPB. The final diagnoses for these four patients were as follows: mesothelioma in two, lung cancer metastasis in one, and other organ metastasis in one. We could not achieve a diagnosis in two patients with thoracoscopy. Tuberculous pleurisy was diagnosed in one of these patients clinically because of an elevated adenosine deaminase level (68 units/dL); this patient improved with anti-TB treatment. In the other patient, after

Table 1—*Distribution of Diagnoses of 124 Patients Included in the Study*

Diagnosis	No.	%
Malignant mesothelioma	33	26.6
Malignant pleural effusion due to lung cancer	29	23.4
Malignant pleural effusion due to other organ carcinomas	18	14.5
Tuberculous pleurisy	19	15.3
Benign asbestos pleurisy	13	10.5
Rheumatoid pleurisy	1	0.8
Uremic pleural effusion	1	0.8
Chronic cardiac failure	4	3.2
Radiotherapy-related pleural effusion	1	0.8
Viral pleural effusion	1	0.8
Paramalignant pleural effusion	2	1.6
Indeterminate cases	2	1.6

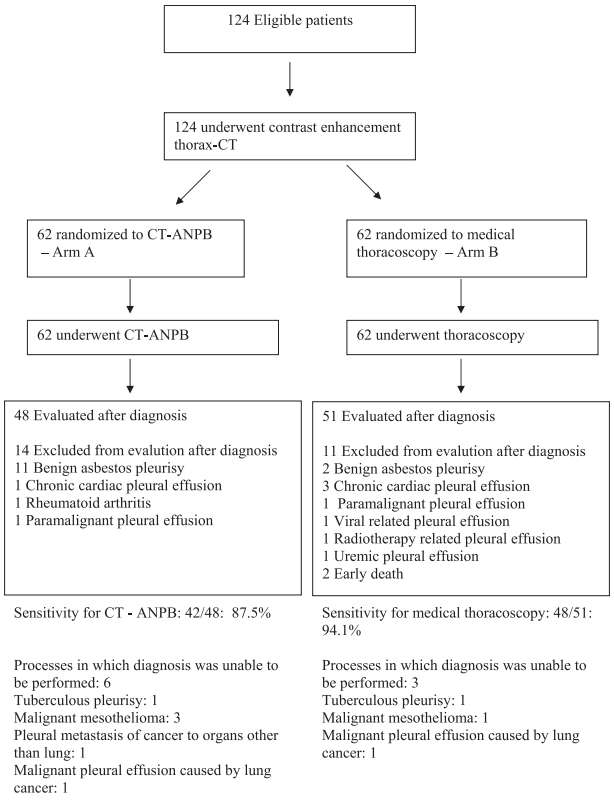

FIGURE 2. Randomization trial profile of the patients. CT-ANPB = CT scan-guided Abrams needle pleural biopsy.

6 months of follow-up the pleural fluid and clinical signs of a malignant disease became abundant again, and with second thoracoscopy mesothelioma has been diagnosed in the patient.

Rates of sensitivities for both methods regarding the diagnosis are shown in Table 2. Diagnostic sensitivity of CT-CNPB for 38 malignant cases was 86.8% (33/38; 95% CI, 76.1%-97.5%); the same rate for thoracoscopy was 95.2% (40/42; 95% CI, 88.7%-100%). There was no statistical difference between the two methods for all malignant cases ($\chi^2 = 1.761$; $df = 1$; $P = .184$). Table 3 shows the sensitivity of the two methods regarding radiologic characteristics for CT scan of the thorax. Three of 11 patients with smooth pleural thickening showed no positive result with CT-ANPB. Of these three patients, two had malignant mesothelioma and one had tuberculous pleurisy. One of two cases of malignant mesothelioma was able to be diagnosed using thoracoscopy, whereas disease in the other two patients was not able to be diagnosed using thoracoscopy.

On examination of Table 3, we can see that only four of 99 (4%) patients had pleural effusion without thickened pleura. Any kind of pleural change could be observed in other patients. We evaluated whether pleural thickness affects diagnostic sensitivity of both methods. The findings are shown in Table 4.

Of the 27 cases, 22 (82%) with pleural thickening < 1 cm were diagnosed with CT-ANPB and 25 of 27 (93%) by thoracoscopy; no statistical difference was seen. For both methods there was also no statistical difference in cases with pleural thickening > 1 cm.

The type and frequency of complications for both methods is shown in Table 5. In one patient from the Abrams needle group who had pleural fluid on CT scan but no pleural thickening, hemorrhage occurred after the procedure, which required tube thoracostomy and blood transfusion. No further treatment was required for this case. Pneumothorax occurred in one case in the Abrams group. Tube thoracostomy for 3 days was required to treat the pneumothorax. Percutaneous emphysema around the entry site, which occurred frequently in the thoracoscopy group, was not observed in any case in the Abrams group.

Discussion

Although CT-CNPB and medical thoracoscopy have a higher diagnostic yield than closed pleural biopsy in malignant disease, both are more expensive and time consuming.[16,18-20] Image-guided pleural biopsy, on the other hand, can be performed in outpatient conditions[9,10,19] and can be used in patients without pleural effusion. It requires an experienced radiologist, a disposable cutting biopsy needle, and extra use of CT scanning, and it must be performed in the radiology department. As an alternative, CNPB can be performed under ultrasound guidance.[6-11,19,21]

Table 2—*Sensitivity Rates of CT Scan-Guided Abrams Needle Pleural Biopsy and Thoracoscopy*

	CT-ANPB		Thoracoscopy		
Diagnosis	No. Performed	Sensitivity (%)	No. Performed	Sensitivity (%)	*P* Value[a]
Malignant mesothelioma	15	12 (80)	18	17 (94)	.308
Malignant pleural effusion caused by lung cancer	15	14 (93)	14	14 (100)	1.000
Pleural metastasis due to other organ carcinomas	8	7 (88)	10	9 (90)	1.000
Tuberculous pleurisy	10	9 (90)	9	8 (89)	1.000

CT-ANPB = CT scan-guided Abrams needle pleural biopsy.
[a]Two-sided Fisher exact test.

Table 3—*Sensitivity of the Two Methods According to the Distribution of Pleural Pathologies Observed in CT Scans*

CT Scan Findings	CT-ANPB		Thoracoscopy		*P* Value[a]
	No. Performed	Sensitivity (%)	No. Performed	Sensitivity (%)	
Only pleural effusion	1	1	3	2	1.000
Circumferential nodular pleural involvement	3	3	2	2	
Separate nodular involvement	9	8 (89)	12	11 (92)	1.000
Irregular pleural thickening	24	22 (92)	22	21 (95)	1.000
Smooth pleural thickening	11	8 (73)	11	11 (100)	.214
Pleural based mass with effusion	…	…	1	1	

See Table 2 for expansion of abbreviation.
[a]Two-sided Fisher exact test.

Some authors suggest that the technique of Abrams needle pleural biopsy still has a place in the diagnosis of exudative pleural effusions and should not be abandoned because of its lower cost and its relatively high safety, simplicity, and diagnostic sensitivity for metastatic pleural diseases and tuberculous pleurisy.[5,12,22]

The limitation of Abrams biopsy is the blindness of the procedure. In the thoracoscopic procedure, a sample is taken on visual observation, which overcomes this problem, and the diagnostic sensitivity is notably increased. Use of cutting needle biopsy under CT scan guidance overcomes this problem.[6] When the thick or seemingly problematic pleural zone is located using CT scan, diagnostic sensitivity is increased to $>80\%$.[11,19] Could this not be performed in a bronchoscopy suite as for Abrams needle? If it could, it would bring about two advantages: First, a simple and inexpensive method such as Abrams pleural biopsy could be applied; second, CT scan guidance would be ensured in the bronchoscopy room. The idea for the present study arose in light of the above discussion.

We performed Abrams needle biopsy using standard procedures. The only difference was to mark the most probable lesion area on the patient's skin, as determined by CT scan of the thorax before the biopsy procedure (Fig 1). Because CT scan was already obtained for these patients, our application did not bear any additional cost to the standard application of Abrams needle. In conclusion, we did not find any significant difference between the sensitivity of the procedures (87.5% vs 94.1%; $P = .252$). Regarding the diagnosis of malignant pleural diseases or tuberculous pleurisy, there was no statistical difference between the sensitivities of the two methods (86.8%-95.2%, $P = .184$ for malignant diseases and 89%-90%, $P = .737$ for tuberculous pleurisy).

The sensitivity of both methods was similar in patients with malignant pleural effusion due to either lung or other cancer and tuberculous pleurisy. There was a small but nonsignificant difference between the two methods (80% vs 94%) in malignant mesothelioma. We previously reported that the success rate of CT-ANPB was 83% in mesothelioma, a finding which is similar to the present study.[17]

In our study, no difference was found between the two methods in terms of the CT scan appearance of pleural pathology (Table 3). When an analysis was made regarding the pleural thickness, no difference could be found between the two methods in our series. In the study by Maskell and colleagues,[6] for patients with a pleural thickness <5 mm the sensitivity of CT scan-guided needle biopsy was 75%. Therefore, if a CT scan-guided biopsy is performed in cases with minor pleural thickness, there may be a lower probability that a sufficient amount of tissue will be obtained. However, Abrams needle is capable of obtaining larger samples; thus, the difficult sampling problem associated with that group of patients may not be encountered with Abrams needle.

CT-CNPB can be performed in patients with pleural thickness without pleural fluid, which is not convenient when using Abrams needle. However, the rate of patients without fluid is $<10\%$, and most of them are benign asbestos pleurisy or fibrothorax.[13,14]

Table 4—*Sensitivity of the Two Methods Regarding the Presence of Pleural Thickness in CT Scan of the Thorax*

Pleural Thickening	CT-ANPB		Thoracoscopy		*P* Value[a]
	No. Performed	Sensitivity (%)	No. Performed	Sensitivity (%)	
≥ 1 cm	21	20 (95)	24	23 (96)	1.000
<1 cm	27	22 (82)	27	25 (93)	.420
P value[a]	.211		1.000		

See Table 2 for expansion of abbreviation.
[a]Two-sided Fisher exact test.

Table 5—*Complications of Diagnostic Methods*

Complications	CT-ANPB (n = 62)	Thoracoscopy (n = 62)
Minor bleeding	2	2
Major bleeding[a]	1	0
Hypotension	4	3
Syncope	1	0
Pain[b]	3	4
Fever	0	2
Percutaneous emphysema	0	10
Extended air leakage[c]	0	2
Pneumothorax	1	0
Percutaneous edema	2	0
Wound infection[d]	0	1
Nausea	0	1

See Table 2 for expansion of abbreviation.
[a]Bleeding at a level requiring a tube thoracostomy and blood transfusion.
[b]Pain requiring additional analgesic.
[c]Air leakage > 3 d.
[d]Infection limited to the wounded area, which recovers fully with antibiotics.

In both cases, biopsy would not be sufficient for the final diagnosis, which requires further clinical and radiologic investigations as well as follow-up.

In this study, the results of the patients in whom benign asbestos pleurisy, rheumatoid pleurisy, paramalignant pleural effusion, viral infection-related pleural effusion, or radiotherapy-related pleural effusion was diagnosed were not considered for evaluation, because direct observation of pleura and a considerable time period of follow-up of patients were required for the exact diagnosis. The advantage of medical thoracoscopy is certainly that the biopsies can be taken from several areas of the thoracic cavity, including the diaphragm and visceral pleura of the lung, under direct observation.

When the two methods were compared in terms of complications, both were observed to be safe. In one patient, with presence of fluid only, to whom Abrams needle was applied, a hemorrhage developed that required tube thoracostomy and blood transfusion.

In conclusion, we suggest that the present method of CT-ANPB be used as a first diagnostic evaluation after cytologic investigation of the fluid in those cases with pleural thickness or pleural lesion observed in the thorax CT scan. This group comprises a significant majority of the patients with pleural pathology.[13,14] However, in patients with only fluid appearance on CT scan, thoracoscopy should be the first method used in order to improve the chances for a final diagnosis. Also, if benign asbestos pleurisy or any other benign disease other than TB is suspected, the first method for diagnosis should preferentially be thoracoscopy for the exclusion of malignancy. For example, in cases in which there is no pleural thickening, procedures other than thoracoscopy, which are performed without seeing the pleural space, may increase the risk of vascular injury, especially in patients with high hydrostatic vascular pressure in parietal pleura. CT-CNPB should be used preferentially in cases in which there is only pleural thickening but no pleural fluid. Furthermore, in very rare occasions in which small single lesions are located in spots that may be difficult to reach with an Abrams needle, such as posterior to the scapula or adjacent to the vertebral column or the sternum, CT-CNPB or thoracoscopy is preferred. On the other hand, for some cases an additional advantage of thoracoscopy is that diagnostic and therapeutic aims, such as drainage and pleurodesis, can be achieved in a single session.

Acknowledgments

Author contributions: *Dr M. Metintas:* contributed to the idea for and design of the study, performing thoracoscopy, and drafting and editing of the manuscript.
Dr Ak: contributed to the idea for and design of the study and performing thoracoscopy.
Dr Dundar: contributed to performing histopathologic studies on biopsy samples of the patients.
Dr Yildirim: contributed to performing thoracoscopy.
Dr Ozkan: contributed to investigating CT scans of the patients.
Dr Kurt: contributed to managing the patients in the clinic and editing the manuscript.
Dr Erginel: contributed to managing the patients in the clinic.
Dr Alatas: contributed to managing the patients in the clinic.
Dr S. Metintas: contributed to the idea for and design of the study and drafting the manuscript.
Financial/nonfinancial disclosures: The authors have reported to *CHEST* that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

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