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Nondiagnostic Computed Tomography–guided Percutaneous Lung Biopsies Are More Likely When Infection Is Suspected

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Purpose: The purpose of this study was to assess the incidence of nondiagnostic computed tomography–guided lung biopsy results, stratified by biopsy indication, and determine the final diagnosis in such cases.

Materials and Methods: Following institutional review board approval, pathology results from CT-guided lung biopsies over a 5-year period at 2 institutions were categorized as diagnostic or nondiagnostic. Each biopsy's indication was categorized as being for a lesion considered likely to be cancer, infection, or uncertain. For all nondiagnostic biopsies, the medical chart was reviewed to determine the final clinical diagnosis.

Results: A total of 660 biopsies were evaluated, 139 (21%) of which were nondiagnostic. Of these 139 patients, the final clinical diagnosis was infection in 37%, cancer in 30%, and a benign noninfectious diagnosis in 10%; 23% remained undiagnosed at last available follow-up. Among the patients in whom there was a high pretest suspicion for cancer, 13% were nondiagnostic, 45% of which were cancer and 27% were infection. Among biopsies of lesions with pretest probability for both cancer and infection, 51% were nondiagnostic; on clinical follow-up these were determined to be infection in 34% and cancer in 14%. When there was high pretest suspicion for infection, 73% were nondiagnostic, of which 13% were cancer on clinical follow-up, and 88% were infection. The rate of nondiagnostic biopsies was statistically significantly different ($P < 0.001$) among the 3 groups.

Conclusions: Nondiagnostic biopsies are common and occur most frequently when there is a moderate or high pretest suspicion for infection. Among all nondiagnostic biopsies, regardless of indication, cancer and infection were diagnosed on follow-up in similar proportions.

Key Words: percutaneous lung biopsies, chest biopsies, nondiagnostic, pneumonia, lung cancer

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Percutaneous computed tomography (CT)–guided lung biopsy (CTLB) is an important way to establish a diagnosis of cancer and, in some cases, infection.[1] It is well known that these types of biopsies, although generally safe, carry certain risks: most commonly, pneumothorax, and rarely death.[2–4] An additional "risk" is that the biopsy procedure may not yield diagnostic material, either due to a technical failure, insufficient material being obtained, sampling error, or inability of the pathologist to confidently identify the true abnormality.[2,5–7] Such an outcome is variably called "negative," "nondiagnostic," or "nonspecific" in the literature.

The rate of nondiagnostic CTLB reported in the literature ranges from 15% to 22%.[2,8] Variability in biopsy success has been attributed to technique, including number of passes,[8] the use of core versus fine-needle aspiration sampling,[9–11] needle trajectory,[12] and having a pathologist present to evaluate the sample.[13] Other groups have published that nodule characteristics affect the nondiagnostic rate of CTLB, with small size and presence of necrosis leading to lower rates of success.[2,5,8,14] To our knowledge, no studies have investigated the association between the pretest likelihood for cancer versus infection and the nondiagnostic rate. Overall, understanding the nondiagnostic rate on the basis of a set of predictive factors is important to accurately consent patients and to inform referring clinicians who must decide between various diagnostic options to obtain a diagnosis.

In this study, we had 2 primary aims. First, we sought to assess the rates of nondiagnostic results on the basis of the pretest suspicion for cancer, infection, or for lesions considered clinically uncertain. Second, we aimed to determine the ultimate clinical diagnosis in patients with nondiagnostic CTLBs, overall and stratified by the prebiopsy likelihood of the lesion being cancer versus infection.

We hypothesized that our overall nondiagnostic rate would be comparable to other institutions. We hypothesized that a high pretest likelihood of infection would be correlated with a higher nondiagnostic biopsy rate. We also hypothesized that nondiagnostic biopsies would most commonly represent infections, particularly in cases in which infection was initially suspected.

MATERIALS AND METHODS

The institutional review board approved this study and waived requirement of informed consent for this HIPAA-compliant study protocol.

All patients presenting for CTLB over a 5-year period between October 1, 2009 and September 30, 2014 at 2 clinical sites were identified for review. The 2 clinical sites included an academic tertiary care hospital and an affiliated Veterans Affairs medical center. All biopsy requests were

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reviewed in advance by an attending thoracic radiologist, with additional workup before biopsy obtained as needed. All biopsies were performed by an attending thoracic radiologist or a closely supervised cardiothoracic radiology fellow (each fellow performs >50 biopsies per year). Biopsies were performed on 64-slice CT scanners using conventional (nonfluoroscopic) biopsy mode with fine-needle aspiration samples obtained by a 19 G coaxial system using either 22 or 23 G fine-needle aspiration samples alone or in combination with 20 G core samples. Core specimens were occasionally, but not routinely, obtained at the discretion of the performing radiologist in consultation with an onsite pathologist; typically core samples were obtained when the onsite pathologist, after review of fine-needle aspirates, believed that the aspirates would be insufficient to render a diagnosis. An attending or fellow pathologist was always present in the procedure room to evaluate sample adequacy.

Exclusion criteria for our study included: biopsies for lesions outside of the lungs or pleura (eg, chest wall); a previous CTLB from the same patient already included in the data set; aborted biopsies in which no samples were obtained (eg, patient intolerance of the procedure); and biopsies obtained for clinical trials in patients who had already been diagnosed. Patients scheduled for biopsy in which the procedure was cancelled before any needle touched the chest were not part of the data set.

All CTLBs were coded on the basis of the (1) clinical indication for biopsy, (2) the pathology results from the biopsy, and (3) final clinical diagnosis determined in cases of a nondiagnostic biopsy. The coding for each is described below.

The categories for "clinical indications for biopsy" are as follows:

(1) Suspect cancer: pretest probability of approximately 80% or greater likelihood of malignancy, with the objective of the biopsy being to establish a cell type.
(2) Clinically uncertain: both cancer and infection were considered possible, and the patient did not fall into category 1 or 3. The objective of such biopsies was to determine proper management in cases in which imaging follow-up alone was considered inappropriate.
(3) Suspect infection: pretest probability of approximately 80% or greater likelihood of infection, with the objective of the biopsy being to guide antibiotic selection.

These categories were determined by a detailed analysis of the biopsy requisition, all available clinical notes, and all available imaging results preceding the biopsies. Explicit statements in the medical record indicating estimates (numeric or otherwise) for the pretest likelihood were heavily weighted. Pathology results and clinical outcomes were not considered in determining pretest probability. Coding was performed by a cardiopulmonary radiology fellow (author B.M.H.) in consultation with an attending cardiothoracic radiologist (author D.M.N.). Examples of how sample cases were determined are presented in Table 1.

Pathologic biopsy outcomes were determined by reviewing all pathology and microbiology reports generated from biopsy specimens. Biopsies were considered nondiagnostic if the pathology and microbiology studies performed on a biopsy specimen failed to confirm a diagnosis of cancer, a *specific* benign entity, or a causative organism (or family of organisms) to the degree that a targeted antibiotic therapy could be selected. In particular, biopsy results that yielded blood, necrosis, fibrous tissue, benign bronchial cells, macrophages, atypical cells, or nonspecific inflammation were considered nondiagnostic.

The "final clinical diagnosis" in cases of nondiagnostic biopsies was determined by comprehensive review of the electronic medical record, including clinical notes, laboratory data, behavior on subsequent imaging, and surgical specimens. A final diagnosis was considered to be "cancer" if a subsequent biopsy (whether surgical or by means of CT or bronchoscopic guidance) or procedure (such as surgical resection or mediastinoscopy) was diagnostic of such. Infection was considered the ultimate diagnosis if a subsequent CT biopsy or other tissue specimen identified a specific organism or family of organisms, or if the lung abnormalities behaved in a manner consistent with infection and inconsistent with cancer (eg, completely resolved on subsequent imaging). The final clinical diagnosis was coded as a "specific benign entity" if a subsequent biopsy yielded a specific result. Some cases lacked sufficient subsequent records to provide a definite final diagnosis.

During the chart review, patient age, sex, lesion size, biopsy method (fine-needle aspiration +/−core), and any prebiopsy antibiotic administration were recorded for each patient.

The proportions of nondiagnostic biopsies were calculated for the study group overall and stratified by the clinical indication. Confidence intervals (CIs) of 95% were also calculated. A χ^2 test was performed to assess for statistically significance differences in the nondiagnostic biopsy rates between the 3 pretest probability groups. Fisher exact test were used to assess for statistically significant associations between multiple risk factors and nondiagnostic results including lesion size in the case of cancers and lesion size and any prebiopsy administration of antibiotics in the case of infections. Statistical significance was defined as a P-value ≤ 0.05. Estimates of the biopsy technique's sensitivity for cancer and infection were calculated for the study population overall and stratified by the biopsy indication. CIs of 95% were also calculated for sensitivity and specificity. Statistical analysis was performed using QuickCalcs (GraphPad, La Jolla, CA).

RESULTS

During the 5-year study period, 839 CTLBs were performed. After exclusions, 660 biopsies on 660 patients were included for analysis, 440 (67%) from the academic tertiary care hospital and 220 (33%) from the Veterans Affairs Medical Center. Excluded biopsies were as follows: biopsies of chest wall or mediastinal lesions (79), biopsies of known cancers to obtain tissue for clinical trials (76), and biopsy aborted before samples were obtained (24). Fine-needle aspirates were obtained in all patients. Core biopsy samples were obtained in 92 (14%) patients.

The mean patient age was 67 years (range, 23 to 91 y), and 33% of the patients were female. The average lesion size was 3.1 cm (interquartile range, 1.7 to 4.0 cm). Patients with nondiagnostic biopsies averaged 62 years of age, and 35% were female, with an average lesion size of 2.8 cm (interquartile range, 1.5 to 3.4 cm).

The indication for biopsy was "suspect cancer" in 540 cases (82%), "clinically uncertain" in 98 cases (15%), and "suspect infection" in 22 cases (3%).

Pathology results were nondiagnostic in 139 cases (21%; 95% CI, 18%-24%) overall. This included 73

TABLE 1. Illustrative Examples for Determination of Pretest Probability

Pretest Probability	Clinical Examples
Suspect cancer	(1) 65-y-old woman, smoker, with 2.3 cm spiculated nodule discovered on lung cancer screening CT. (2) 39-y-old woman, never-smoker, with 2.8 cm part solid nodule that has persisted for 3 mo, and was incidentally discovered on pulmonary embolism protocol CT. (3) 61-y-old man with newly diagnosed rectosigmoid mass and multiple lung nodules on chest CT. Order states: "confirm presence of metastatic disease."
Clinically uncertain	(1) 78-y-old man, never-smoker, with upper lobe 4.4 cm mass-like consolidation, no prior imaging, with constitutional symptoms and clinical note stating: "This could represent fungal infection or malignancy; cocci titers negative." (2) 61-y-old man with a history of laryngeal carcinoma and a 3.9×1.5 cm area of consolidation. The radiology reports reads: "Consider infection or malignancy." (3) 59-y-old man with a history of HIV and a cavitary lung mass. Radiology report states: "Malignancy is most likely. Infection also possible."
Suspect infection	(1) 45-y-old woman with relapsed acute myelogenous leukemia, neutropenic fever, and rapidly enlarging right upper lobe consolidation. Order for biopsy states: "Antibiotics not working. Evaluate for organism." (2) 51-y-old man with myelodysplastic syndrome and lung nodules that are interpreted in radiology report as "suggestive of invasive fungal infection." Limited response to antibiotics. (3) 68-y-old man with hemophagocytic lymphohistiocytosis, multiple lung nodules, and culture negative discitis-osteomyelitis. Clinical note states: "need to tailor antibiotics." (4) 65-y-old woman status post liver transplant with a history of cutaneous nocardia infection and multiple enlarging lung nodules. Biopsy order states: "evaluate for pulmonary nocardia."

patients (14%; 95% CI, 11%-17%) of the suspect cancer group, 50 (51%; 95% CI, 41%-61%) of the clinically uncertain group, and 16 (73%; 95% CI, 52%-87%) of the suspect infection group ($P < 0.001$ for comparison of the nondiagnostic biopsy rates among the 3 groups). A detailed depiction of the biopsy results is presented in Table 2.

The clinically determined outcomes of lesions that had nondiagnostic biopsies were cancer in 42 cases (30%; 95% CI, 23%-38%), infection in 51 (37%; 95% CI, 29%-45%), and a benign noninfectious diagnosis in 14 (10%; 95% CI, 6%-16%). There were 32 (23%) patients who had insufficient records to render a definite final diagnosis. Among the subgroup of patients for whom cancer was most suspected, nondiagnostic biopsies cases were subsequently determined to be cancer in 33 cases (45%; 95% CI, 34%-57%), infection in 20 (27%; 95% CI, 18%-39%), a benign noninfectious diagnosis in 7 (10%; 95% CI, 4%-19%), and unknown (insufficient information) in 13 (18%). Among the subgroup of patients with a "clinically uncertain" lesion, nondiagnostic biopsy cases were subsequently determined to be cancer in 7 cases (14%; 95% CI, 7%-27%), infection in 17 (34%; 95% CI, 22%-48%), a benign noninfectious diagnosis in 7 (14%; 95% CI, 22%-48%), and unknown (insufficient information) in 19 (38%; 95% CI, 26%-52%). Among the subgroup of patients for whom infection was most suspected, nondiagnostic biopsy cases were subsequently determined to be cancer in 2 cases (13%; 95% CI, 2%-47%) and infection in 14 (87%; 95% CI, 63%-98%). These results are summarized in Table 3.

The sensitivity of a single percutaneous biopsy procedure was 91.8% (471/513) for cancer (95% CI, 89%-94%), 53% (16/30) for benign noninfectious etiologies (95% CI, 36%-70%), and 40% (34/85) for infection (95% CI, 30%-51%). The sensitivity for detecting cancer was higher with lesions > 2 cm compared with lesions ≤ 2 cm (92% vs. 82%, $P = 0.02$). The sensitivity for detecting infection was not statistically significantly associated with size or prior antibiotic administration; however, power for this calculation is lacking. There was a trend toward a higher sensitivity with larger lesions (45% for > 2 cm vs. 30% for ≤ 2 cm, $P = 0.22$) and lesions not previously treated with empiric antibiotics (43% vs. 31%, $P = 0.35$).

The specificity of a single percutaneous biopsy procedure was 99% (108/109) for detection of cancer (95% CI, 94%-99%) and was 100% (541/541) for detection of infection (95% CI, 99%-100%).

DISCUSSION

In our study of 660 CTLBs, 21% were nondiagnostic. The rates of nondiagnostic CTLBs were highest in the "suspect infection" group (73%) and the "clinically uncertain" group (51%). The nondiagnostic rate was low (14%) in the "suspect cancer" group.

For patients with nondiagnostic biopsies in the suspect cancer group, cancer was ultimately confirmed in 45%, whereas in the suspect infection group, infection was eventually confirmed in 87%.

TABLE 2. Pathology Results by Indication for the Biopsy (n [%; 95% CI])

Clinical Outcome	All Patients (n = 656)	Suspect Cancer (n = 540)	Clinically Uncertain (n = 98)	Suspect Infection (n = 18)
Cancer	471 (72; 68%-75%)	442 (82; 78%-85%)	29 (30; 21%-39%)	0 (0; 0%-21%)
Infection	34 (5; 4%-7%)	14 (3; 2%-4%)	14 (14%; 9%-23%)	6 (33; 16%-56%)
Benign, not infection	16 (2; 1%-4%)	11 (2; 1%-4%)	5 (5; 2%-12%)	0 (0; 0%-21%)
Nondiagnostic	135 (21; 18%-24%)	73 (14; 11%-17%)	50 (51; 41%-61%)	12 (67; 44%-84%)

"Suspect Cancer" = strong pretest suspicion for cancer.
"Clinically Uncertain" = pretest suspicion for both cancer and infection.
"Suspect Infection" = strong pretest suspicion for infection with the objective of the biopsy being to identify a causative organism and target antibiotic therapy.

TABLE 3. Final Clinical Diagnosis in Cases for Which the Initial Biopsy Was Nondiagnostic (n [%])

Clinical Outcome	All Patients (n = 139)	Suspect Cancer (n = 73)	Clinically Uncertain (n = 50)	Suspect Infection (n = 16)
Cancer	42 (30)	33 (45)	7 (14)	2 (13)
Infection	51 (37)	20 (27)	17 (34)	14 (87)
Benign, not infection	14 (10)	7 (10)	7 (14)	0
Uncertain at last available follow-up	32 (23)	13 (18)	19 (38)	0

We report a sensitivity for diagnosis of infection of 91.8%. However, 23% of patients with nondiagnostic biopsies in our study had insufficient records to render a definitive clinical outcome. If some of these patients were in fact false negative for detection of infection, then the sensitivity would be decreased (the minimum sensitivity that would result if all of these patients were false negatives is 86.4%.

In our study, the diagnostic performance of transthoracic fine-needle aspiration biopsy is consistent with previously reported studies in the literature. A recently published examination by Fontaine-Delaruelle et al[8] of 980 CTLBs in a multicenter study from France had "negative results" in 15% of biopsies and a 90% sensitivity for the detection of neoplasm, which compares to our 21% nondiagnostic rate and 92% sensitivity. "Negative results" were defined similarly as our nondiagnostic category in this study. A meta-analysis by Rivera et al[15] that pooled both core and fine-needle aspiration biopsies reported a nondiagnostic rate of 22% for the detection of neoplasm.

There is a paucity of data about performance of CTLBs for the detection of infection. Two small studies in patients with hematologic malignancies[16] and in patients following solid organ transplant[17] evaluated the ability of CT biopsies to diagnose infection in these very specific patient populations. The study on patients with hematologic malignancies included 17 cases of confirmed or presumed fungal infections, of which 12 were positive on biopsy (sensitivity 71%) and 4 had nondiagnostic biopsies (nondiagnostic rate of 24%). The study of biopsies in patients with prior solid organ transplantation evaluated all indications for biopsy and not just for the diagnosis of infection. This study reported a nondiagnostic biopsy rate of 21 of 45 patients (47%); the reported sensitivity for detection of invasive fungal infection was 60%. Both of these studies reported sensitivities for detection of infection significantly higher than our study's reported 39%. The differences could be due to biopsy technique, patient selection/population, variations in antibiotic regimens, and/or differences in coding of false-negative and true-negative biopsies.

Our study has a number of possible implications for patient care. First, the likelihood of a nondiagnostic CTLB dramatically increases if there is a high pretest probability of infection. Per our data, obtaining a sufficient sample to find a causative organism is relatively hard with our standard biopsy techniques, which does include sending samples for microbiology. When referring physicians request such procedures, the nondiagnostic rate should be discussed and weighed against the procedure risks.

While we hypothesized that a nondiagnostic CTLB would overwhelmingly turn out to be infection on follow-up, this was not the case. Infection and cancer were eventually diagnosed in a significant number of patients regardless of indication, and, therefore, both entities must remain on the differential diagnosis after a nondiagnostic CTLB; however, the relative proportions of patients with underlying pathology of cancer or infection may be different from what was measured if clinical outcomes were known for all patients. Our results are in keeping with prior results from Quint et al[18] that evaluated final clinical diagnoses in 60 patients with benign nonspecific and nondiagnostic biopsies (we collectively refer to these 2 categories as nondiagnostic in this paper), where they found malignancy in 37% of patients on clinical follow-up. Quint and colleagues had a similar proportion of patients with unknown final clinical diagnoses (28% for Quint vs. 21% in our sample). It is important for radiologists, referring clinicians, and patients to understand that nondiagnostic CTLB results do not equal benign results, and further follow-up and/or diagnostic interventions may be warranted.

Our identification of an association between lesion size and sensitivity for detection of lung cancer by biopsy is consistent with prior literature. It has been well-documented that small nodules, variably defined as < 1.5 cm or 1.0 cm in size, are associated with increased rates of nondiagnostic CTLBs.[5,7,14,19] Here we defined small nodules as ≤ 2.0 cm in size. In cases of infection, the lack of an association of biopsy failure with small size and prebiopsy antibiotics is likely the result of low power; infections were less common than cancer in our study, and the number of patients in these subgroups was small.

Our study has several limitations. The first is the retrospective design, which is particularly important given that the pretest indication for biopsy was a variable in our analysis. Second, our 2 clinical sites, including a large academic institution and a Veterans Affairs medical center, may limit generalizability to other practice settings; in particular, the prevalence of endemic fungal infections is known to vary geographically. In addition, our technique may not mirror that in all practice settings: fine-needle aspiration favored biopsies obtained using a minimum number of passes with an on-site pathologist available to determine sample adequacy.

In summary, our study found that nondiagnostic pathology results are common for CTLBs, particularly when there is high pretest suspicion for infection. Nondiagnostic results are not necessarily indicative of benignity, and both cancer and infection should be considered regardless of pretest suspicion for either. It is important to recognize the limitations of available diagnostic procedures, particularly when advising referring clinicians and when counseling/consenting patients.

REFERENCES

1. Harter L, Moss A, Goldberg H, et al. CT-guided fine-needle aspirations for diagnosis of benign and malignant disease. *Am J Roentgenol*. 1983;140:363–367.
2. Li H, Boiselle PM, Shepard JO, et al. Diagnostic accuracy and safety of CT-guided percutaneous needle aspiration biopsy of

the lung: comparison of small and large pulmonary nodules. *Am J Roentgenol*. 1996;167:105–109.
3. Ohno Y, Hatabu H, Takenaka D, et al. CT-guided transthoracic needle aspiration biopsy of small (≤20 mm) solitary pulmonary nodules. *Am J Roentgenol*. 2003;180:1665–1669.
4. Geraghty PR, Kee ST, McFarlane G, et al. CT-guided transthoracic needle aspiration biopsy of pulmonary nodules: needle size and pneumothorax rate. *Radiology*. 2003;229: 475–481.
5. Tsukada H, Satou T, Iwashima A, et al. Diagnostic accuracy of CT-guided automated needle biopsy of lung nodules. *Am J Roentgenol*. 2000;175:239–243.
6. Hur J, Lee H-J, Nam JE, et al. Diagnostic sccuracy of CT fluoroscopy–guided needle aspiration biopsy of ground-glass opacity pulmonary lesions. *Am J Roentgenol*. 2009;192: 629–634.
7. Yeow K-M, Tsay P-K, Cheung Y-C, et al. Factors affecting diagnostic accuracy of CT guided coaxial cutting needle lung biopsy: retrospective analysis of 631 procedures. *J Vasc Interv Radiol*. 2003;14:581–588.
8. Fontaine-Delaruelle C, Souquet P-J, Gamondes D, et al. Negative predictive value of transthoracic core-needle biopsy: a multicenter study. *Chest*. 2015;148:472–480.
9. Arakawa H, Nakajima Y, Kurihara Y, et al. CT-guided transthoracic needle biopsy: a comparison between automated biopsy gun and fine needle aspiration. *Clin Radiol*. 1996;51: 503–506.
10. Laurent F, Latrabe V, Vergier B, et al. Percutaneous CT-guided biopsy of the lung: comparison between aspiration and automated cutting needles using a coaxial technique. *Cardiovasc Intervent Radiol*. 2000;23:266–272.
11. Boiselle PM, Shepard JA, Mark EJ, et al. Routine addition of an automated biopsy device to fine-needle aspiration of the lung: a prospective assessment. *Am J Roentgenol*. 1997;169: 661–666.
12. Gupta S, Krishnamurthy S, Broemeling LD, et al. Small (≤2-cm) subpleural pulmonary lesions: short- versus long-needle-path CT-guided biopsy—comparison of diagnostic yields and complications. *Radiology*. 2005;234:631–637.
13. Austin JH, Cohen MB. Value of having a cytopathologist present during percutaneous fine-needle aspiration biopsy of lung: report of 55 cancer patients and metaanalysis of the literature. *Am J Roentgenol*. 1993;160:175–177.
14. Montaudon M, Latrabe V, Pariente A, et al. Factors influencing accuracy of CT-guided percutaneous biopsies of pulmonary lesions. *Eur Radiol*. 2004;14:1234–1240.
15. Rivera MP, Mehta AC, Wahidi MM. Establishing the diagnosis of lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2013;143(suppl): e142S–e1465.
16. Nosari A, Anghilieri M, Carrafiello G, et al. Utility of percutaneous lung biopsy for diagnosing filamentous fungal infections in hematologic malignancies. *Haematologica*. 2003; 88:1405–1409.
17. Hsu JL, Kuschner WG, Paik J, et al. The diagnostic yield of CT-guided percutaneous lung biopsy in solid organ transplant recipients. *Clin Transplant*. 2012;26:615–621.
18. Quint LE, Kretschmer M, Chang A, et al. CT-guided thoracic core biopsies: value of a negative result. *Cancer Imaging*. 2006; 6:163–167.
19. Hiraki T, Mimura H, Gobara H, et al. Incidence of and risk factors for pneumothorax and chest tube placement after CT fluoroscopy–guided percutaneous lung biopsy: retrospective analysis of the procedures conducted over a 9-year period. *Am J Roentgenol*. 2010;194:809–814.