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ORIGINAL ARTICLE

Bronchoscopic biopsy for diagnosis of lung cancer in the absence of visible endobronchial abnormalities

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Abstract

Objective Bronchoscopy has been extensively used in the diagnosis of respiratory diseases, and particularly, malignant diseases. However, endoscopists do not normally perform bronchoscopic biopsy in case lesions are undetected via bronchoscopy. The aim of this study was to evaluate whether performing bronchoscopic biopsy could be established in the diagnosis of lung cancer in case of endobronchial abnormalities undetectable to the naked eye.

Methods We retrospectively analyzed 109 cases between January 2008 and December 2012. The inclusion criteria were confirmed lung cancer diagnosis, transbronchial biopsy performed in the absence of visible endobronchial manifestations, brushing, and bronchoalveolar lavage (BAL) according to the images obtained from high-resolution computed tomography (HRCT). Data regarding age, sex, pathology, tumor stage; the method of diagnosis; location of primary lesion (central, peripheral, or intermediate); tumor size, mediastinal lymph node metastasis, and the serum carcinoembryonic antigen (CEA) value were collected. The Pearson chi-square test or Fisher's exact and McNemar tests were used in the univariate analysis.

Results Among the 109 patients, the diagnosis of 37 (33.9%) patients was confirmed through bronchoscopy. Brushing and BAL had higher positive detection rates than biopsy ($P = 0.004$). There were no differences in the positive detection rates between the sex, pathology, lesion location, tumor size, lymph node metastasis, and the serum CEA value ($P > 0.05$ for all groups).

Conclusion Despite the normal appearance of the endobronchial manifestations, lesions undetectable by bronchoscopy could be indicated. Therefore, we suggest performing bronchoscopic biopsy and that brushing and BAL might increase the positive detection rate of bronchoscopic examination.

Key words: bronchoscope; lung cancer; biopsy

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Since the application of bronchoscopy [1], the diagnosis of lung disease has become facilitated, which has greatly improved the understanding of respiratory diseases. Bronchoscopy is a critical and indispensable tool, particularly for the diagnosis of pulmonary neoplasms. Because of its safety, convenience, and cost-effectiveness, bronchoscopy has been extensively used in the respiratory department. However, in case of abnormalities undetectable by bronchoscopy, endoscopists do not normally perform bronchoscopic biopsy. This phenomenon might possibly decrease the rate of detection. Furthermore, the lack of a specimen would hinder the identification of genetic mutations that could guide clinical treatment. The aim of this study was to evaluate the role of bronchoscopic biopsy in detecting lung cancer in the presence of lesions undetectable by bronchoscopy.

Materials and methods

Patients

We conducted a retrospective study that included consecutive cases with confirmed diagnoses of lung cancer without visible endobronchial abnormalities, for which a transbronchial lung biopsy (TBLB) was performed depending on the images obtained from high-resolution computed tomography (HRCT) between January 2008

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Table 1 Characteristics of the cases

Features	*n*	%
Sex		
Male	64	58.7
Female	45	41.3
Pathology		
Adenocarcinoma	93	85.3
Squamous carcinoma	11	10.1
SCLC	3	2.8
other	2	1.8
Location		
Central	11	10.1
Intermediate	18	16.5
Peripheral	80	73.4

SCLC, small cell lung cancer

Table 2 Positive detection rates of brushing and BAL and biopsy by bronchoscopy

Features	Positive		*P*
	n	%	
Brushing and BAL	34	31.2	0.004
Biopsy	21	19.3	
combined above examinations	37	33.9	

and December 2012. In total, 109 patients were enrolled. The variables included age, sex, pathology, tumor stage; the method of diagnosis; location of primary lesion (central, peripheral, or intermediate); tumor size, mediastinal lymph node metastasis, and the serum carcinoembryonic antigen (CEA) value. The CEA was detected in 96 serum samples using enzyme-linked immunosorbent assays.

Methods

Various Olympus electronic bronchoscopes (Japan) were used for performing the procedures, and the bronchoscopies were performed in accordance with the standard protocols. Briefly, the bronchoscopies were performed orally, and 2% lidocaine was administered as the anesthetic. In all cases, a full inspection of the tracheobronchial tree was performed. After the inspection, the lesion was localized using HRCT, and forceps were inserted to conduct TBLB at the nearest bronchial mucosa to the lesion (2–3 samples). Subsequently, bronchial brushing and bronchoalveolar lavage (BAL) were performed. The results of the transbronchial needle aspiration were not included in the analyses.

All patients signed informed consent forms before endoscopy. The ethics committee of our institution approved the study.

Statistical analysis

All data were analyzed using the SPSS software version 22 (SPSS Inc., USA). The Pearson chi-square test or Fisher's exact and McNemar tests were used in the univariate and multivariate analyses. A P value < 0.05 was considered statistically significant.

Table 3 Comparisons between the positive detection rates of different groups by bronchoscopy

Features	Total	Positive		χ^2	*P*
		n	%		
Sex					
Male	64	25	39.1	1.81	0.178
Female	45	12	26.7		
Pathology					
Adenocarcinoma	93	29	31.2	2.149	0.143
Squamous carcinoma	11	5	45.5		
SCLC	3	2	66.7		
Other	2	1	50.0		
Location					
Central	11	7	38.9	1.105	0.575
Intermediate	18	5	45.5		
Peripheral	80	25	31.3		
T stage					
T1–2	75	25	33.3	0.040	0.841
T3–4	34	12	35.3		
N stage					
N0–1	52	15	28.8	1.153	0.283
N2–3	57	22	38.6		
CEA value					
Positive	34	10	29.4	0.364	0.546
Negative	62	22	35.5		
Missing	13				

SCLC, small cell lung cancer

Results

In total, 109 patients were enrolled between January 2008 and December 2012, including 64 (58.7%) men and 45 (41.3%) women with a mean age of 58.4 years (range, 18–82 years). Herein, 93 out of 109 patients had adenocarcinoma (85.3%), 11 had squamous carcinoma (10.1%), and only 3 had small cell lung cancer (2.8%). The locations of the lesions were central in 11 (10.1%) cases, peripheral in 80 (73.4%), and intermediate in 18 (16.5%) cases (Table 1).

Of the 109 patients, 37 (33.9%) were diagnosed bronchoscopically, 34 (31.2%) by brushing and BAL, and 21 (19.3%) by biopsy. Brushing and BAL were identified to have higher positive detection rates than biopsy on the McNemar test (P = 0.004; Table 2). There were no statistically significant differences in the positive detection rates between the sex, pathology, lesion location, tumor size, lymph node metastasis, and the serum CEA value (P > 0.05 for all groups; Table 3)

Patients without a bronchoscopically confirmed diagnosis were diagnosed with another method. Twenty-nine cases (26.6%) were confirmed by transthoracic biopsy,

Table 4 The method used in the confirmation of diagnosis

Methods	Positive	
	n	%
Bronchoscope	37	33.9
Transthoracic biopsy	29	26.6
Pleural fluid	16	14.7
Surgery	26	23.9
Sputum	1	0.9

16 cases (14.7%) through analysis of the pleural fluid, 26 cases (23.9%) by surgery, and one case (0.9%) through sputum analysis (Table 4).

Of the 109 patients, none experienced uncontrollable bleeding after undergoing the standard procedures of brushing, BAL, and biopsy. Only 7 patients experienced slight bleeding, which was effectively managed using topical adrenaline.

Discussion

Lung cancer is the most common cause of cancer-related deaths worldwide, and most patients are diagnosed at an advanced stage [2]. Along with the extensive application of low-dose helical CT for screening lung cancer [3–5], the detection rates of solitary pulmonary nodules (SPNs) increased. The most common methods used in the diagnosis of SPNs are bronchoscopy, transthoracic needle aspiration, and surgical biopsy [6]. The diagnostic rate of malignant lesions by traditional TBLB ranged 14–63%, depending on the size and location of the lesions, and the skill and experience of the bronchoscopist [7]. There have been several developments in bronchoscopic technologies in order to improve diagnostic yields, including radial probe endobronchial ultrasonography, and in navigation systems, including electromagnetic navigation bronchoscopy and virtual bronchoscopy [8]. Despite the availability of several bronchoscopic approaches, TBLB, and brushing and BAL through bronchoscopy are still the most widely used techniques for diagnosis. Common bronchoscopy is used even more extensively because of its safety, convenience, and cost-effectiveness. However, studies seldom show the percentages when lesions are not detected by bronchoscopy [9–10]. Nowadays, biopsy specimens have become increasingly important for clinicians. It was reported that 87% of adenocarcinoma patients harbor driver gene mutations [11]. Biopsy specimens are required for the detection of these mutations, particularly for adenocarcinoma.

In this study, out of the 109 cases of undetectable endobronchial lesions, most involved adenocarcinoma (85.3%) and/or were peripheral lesions (73.4%). Consistent with previous studies, the total positive detection rate was 33.9% (37/109) [9–10]. Among the adenocarcinoma cases, 29 (31.2) showed positive results through TBLB, brushing, or BAL. Although the positive detection rate was not as high as that for other pathologies (45.5–66.7%), no statistically significant differences between them were observed. It is necessary to perform brushing and biopsy, because the incidence of adenocarcinoma was high in the whole lung cancer group and in patients who had lesions undetectable by bronchoscopy.

Brushing and BAL had significantly higher diagnostic positive detection rates than biopsy (31.2% vs. 19.3%, $P = 0.004$; Table 2). This might be because brushing and BAL could be performed within a much larger range, whereas only a small specimen could be obtained by biopsy with a rather limited range. The combination of biopsy with brushing and BAL could slightly increase the diagnostic positive detection rate of bronchoscopic examination.

There were no differences in the diagnostic positive detection rates according to sex, pathology, lesion location, tumor size, lymph node metastasis, and the serum CEA value. It appears that the positive detection rate does not relate to clinical factors. For example, the location of the lesions did not influence the positive detection rates. Furthermore, we investigated whether mediastinal lymph node metastasis affected the positive detection rates and found that mediastinal lymph node metastasis and hilar lymph node metastasis did not differ in their positive detection rates. We suggest this could primarily be because of the insufficient number of cases for obtaining positive results, and secondly, because the clinical factors evenly and dispersedly influenced the positive detection rates, which indicated any element could not have a statistically significant influence on the positive detection rates. In fact, as long as cancer cells invaded the bronchial mucosa, positive results could be obtained by biopsy or brushing, although no lesions were visible to the naked eye.

Of the 109 patients, none experienced uncontrollable bleeding after undergoing the standard procedure of brushing, particularly for biopsy. Therefore, biopsy is a sufficiently safe option for patients with lesions undetectable by bronchoscopy.

In conclusion, normal endobronchial manifestations could indicate lesions undetectable by bronchoscopy. Therefore, we suggest that endoscopists perform biopsy, brushing, and BAL. In addition to their safety, brushing and BAL might increase the positive detection rates by bronchoscopic examination.

Conflicts of interest

The authors indicated no potential conflicts of interest.

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