Cell Type Accuracy of Bronchoscopic Biopsy Specimens in Primary Lung Cancer

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Abstract:

Objective: To evaluate the diagnostic accuracy of bronchial biopsy specimens in establishing the specific cell type in primary lung cancer, and to study the influence of several factors on this accuracy.

Design: The patients with lung cancer diagnosed by bronchoscopic biopsy specimens, who subsequently underwent thoracotomy were studied. Pathology archive preparations of bronchial biopsy specimens and thoracotomy materials were reexamined by one pathologist. The following characteristics were evaluated in each patients: age, sex, bronchoscopic morphologic findings, location of bronchial lesion, presence of necrosis, tumor type, and degree of cell differentiation.

Patients: This study included 140 patients with primary lung cancer. Five patients were women and 135 were men with a mean age of 58.5 years (range 19 to 71).

Interventions: All of the pathology preparations were reexamined by one pathologist.

Results: Of the 140 patients, 124 (88.6%) had cell agreement. The overall concordance was 0.65. The best agreement was obtained for squamous cell carcinoma (Kappa, 0.68). Stage of the tumor and presence of necrosis had no effect on cell type agreement. Cell type accuracy was higher in central lesions than peripheral lesions ($p=0.06$). Mass lesions had higher histologic concordance than infiltrative lesions ($p<0.05$). Similar result was demonstrated by the degree of differentiation ($p<0.01$); the less the histologic differentiation, the greater the presence of diagnostic errors.

Conclusion: Many factors, such as tumor type, degree of cell differentiation, and the type of bronchial lesion can affect the cell agreement. We think that there will be difficulties in establishing the cell type by bronchoscopic biopsy especially in poorly differentiated tumors, large cell carcinoma and adenosquamous carcinoma.

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Key words: *bronchial biopsy, lung cancer, cell accuracy*

Introduction

Identification of the specific cell type in primary lung cancer is important because it is related to prognosis and response to therapy (1-3). Small cell lung cancer is more aggressive compared to the other histologic types and has a grater capacity of dissemination. The treatment of patients with small cell carcinoma is based mainly on the use of chemotherapy (4). Surgery is the therapy of choice for the remaining non-small cell lung cancers (5). Several reports have indicated differences among non-small cell carcinomas (5-7). For example, the ratio of extrathoracic metastases, especially brain metastases, is higher in patients with adenocarcinoma and large cell carcinoma compared to patients with squamous cell carcinoma. Many investigators suggest that preoperative systemic evaluation of extrathoracic

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extension in patients with adenocarcinoma and large cell carcinoma should be performed routinely (5,6). It has also been observed that prognosis seems better in the case of squamous carcinoma than adenocarcinoma (7).

Cancer-cell-type designation from preoperative diagnostic methods is not without errors. Transthoracic fine needle aspiration biopsy gives a true diagnosis in 60 to 90% (8-11), sputum cytologic examination in 82 to 90% (12,13), bronchial brushing in 58 to 82% (14), and bronchial biopsy in 62 to 97.5% of the cases (1,3,12,15,16). In our study, we aimed to evaluate the bronchoscopic biopsies, an important preoperative diagnostic method, with respect to cell concordance, and to investigate the effect of various factors on cell concordance.

Methods

The present study included 140 patients diagnosed as lung cancer and subsequently underwent thoracotomy between 1993 and 1996. The initial diagnosis was obtained by means of bronchial biopsy specimens in all patients. Five patients were women and 135 were men with a mean age of 58.5 years (range 19 to 71). The clinical files of the patients were analyzed. Pathology preparations of the bronchial biopsy specimens and thoracotomy materials were reexamined by one pathologist. The following characteristics were evaluated in each patient: age, sex, bronchoscopic morphologic findings, localization of bronchial lesion, presence or absence of necrosis, tumor type, and degree of cell differentiation. Morphologic findings detected during bronchoscopy were classified as mass, infiltration, and other findings (stenosis or nonspecific findings). According to bronchoscopic localization, tumors were classified as central (main or lobar bronchi) and peripheral (segmental or subsegmental bronchi). The World Health Organization classification was used for tumor classification (17). The differentiation degree of tumors was classified as well differentiated, moderately differentiated, poor differentiated, or undifferentiated.

The Kappa analyzis was used to evaluate the overall concordance. The concordance for each cell type was also analyzed using this statistical test. It was considered lowest when the Kappa value was less than 0.20, poor if it was between 0.21 and 0.40, moderate between 0.41 and 0.60, good between 0.61 and 0.80, and excellent if it was more than 0.80. To compare proportions, we used the Fischer exact test. The logistic regression was performed for variables that reached statistical significance. The Mantel-Haenszel test was used to compare these variables. The Odds ratio (OR) and the corresponding 95% confidence interval (95% CI, OR) was also calculated for these parameters.

Table 1. Comparison between BB specimen and thoracotomy diagnosis

	THORACOTOMY (T)				
BRONCHOSCOPY (B)	S	A	LC	AS	TOTAL (B)
Squamous (S)	**109**	7	3	2	121
Adeno (A)	2	**14**	–	–	16
Large cell (LC)	–	–	**1**	1	2
Adeno squamous (AS)	–	1	–	–	1
Total (T)	111	22	4	3	140

Results

Table 1 demonstrates the bronchoscopic biopsy and thoracotomy cell type diagnosis of the 140 patients. Histologic diagnosis obtained by bronchoscopic biopsy specimens and thoracotomy was same in 124 of 140 patients (88.6%).

Table 2 indicates the Kappa values corresponding to each of the histologic types studied, as well as the percentage of bronchial biopsy accuracy compared with thoracotomy. The overall concordance between the histologic diagnosis obtained by bronchial biopsy specimens and the one derived from the thoracotomy specimens was 0.65. The best agreement was obtained for squamous cell carcinoma (Kappa, 0.68). One hundred nine of the 121 patients (90.1%) whose squamous cell carcinoma was diagnosed by bronchial biopsy specimens had this cell type on the thoracotomy, while 109 of the 111 patients (98.2%) who finally had this histologic variety have previously had their conditions diagnosed as such by bronchial biopsy specimens. Large cell carcinoma and adenosquamous carcinoma presented lower histologic agreement than squamous cell carcinoma and adenocarcinoma.

Table 2. Histologic concordance between bronchoscopic material and surgical specimen of the different lung cancer cell types

Tumor type	Concordance (%)	Kappa
Squamous cell carcinoma	90.1	0.68
Adenocarcinoma	87.5	0.66
Large cell carcinoma	50	0.48
Adeno squamous carcinoma	0	0.27
Total (T)	88	0.65

Table 3 shows the effect of various factors on cell agreement between bronchial biopsy and thoracotomy. Stage of the tumor and presence of necrosis had no effect on cell type agreement. Cell agreement was higher in central lesions compared to peripheral lesions (p=0.06).

Table 3. Several factors related to the presence or absence of histologic concordance

	CONCORDANCE		
	Presence	Absence	p value
STAGE (%)			NS
Stage I	17 (85)	3 (15)	
Stage II	38 (92.7)	3 (7.3)	
Stage IIIA	56 (88.9)	7 (11.1)	
Stage IIIB	13 (81.3)	3 (18.7)	
BRONCHIAL LESION (%)			†p<0.05
Mass†	82 (94.2)	5 (5.8)	
Infiltrative†	32 (80)	8 (20)	
Other findings	10 (76.9)	3 (23.1)	
BRONCHOSCOPIC LOCALIZATION (%)			p=0.06
Central (Main or Lobar bronchi)	78 (92.8)	6 (7.2)	
Peripheral (Segmental or subsegmental bronchi)	46 (82.1)	10 (17.9)	
NECROSIS (%)			NS
Presence	14 (87.5)	2 (12.5)	
Absence	110 (88.7)	14 (11.3)	
DIFFERENTIATION (%)			§p< 0.01
Well§*	30 (96.7)	1 (3.3)	*p< 0.05
Moderately	70 (93.3)	5 (6.7)	
Poor§	21 (72.4)	8 (27.6)	
Undifferentiated*	3 (60)	2 (40)	

NS: Not significant

Mass lesions had higher histologic concordance than infiltrative lesions and other morphologic findings (p<0.05). A similar result was demonstrated by the degree of differentiation (p<0.01); the less the histologic differentiation, the greater the presence of diagnostic errors.

Table 4 indicates variables that influenced the cell type accuracy of the bronchial biopsy specimens the most, as well as their corresponding OR and the 95%CI, OR. The likelihood of a correct diagnosis using the bronchial biopsy specimen was 1, 1.3, and 1.6 times higher for well-differentiated tumors than for the moderately differentiated, poorly differentiated, or undifferentiated carcinomas, respectively. It was 1.1 and 1.2 times higher for mass lesions than for infiltrative lesions and other findings, respectively.

Table 4. Variables that influenced the histologic accuracy of the bronchial biopsy specimen the most

	R*	p value	OR	95%CI, OR
Degree of cell differentiation	- 0.24	0.0004		
Well differentiated			1.00	–
Moderately differentiated			0.95	0.88-1.05
Poorly differentiated			0.75	0.59-0.95
Undifferentiated			0.62	0.30-1.27
Bronchial lesion	- 0.08	0.009		
Mass			1.00	–
Infiltrative			0.85	0.72-0.99
Other findings			0.82	0.60-1.10

*R= regression coefficient

Discussion

The overall agreement found in our series is good (Kappa, 0.65) and similar to many previous studies. The Kappa value obtained in those series varied between 0.50 and 0.76 (2,3,12,15). The distribution of tumor type in those series probably has affected the overall agreement. Adenosquamous carcinoma was excluded in most of the series (2,12). Our study included the patients with adenosquamous cell carcinoma. We could acquire a higher agreement value if those patients were excluded from the study.

Several factors affect the cell agreement between bronchoscopic biopsy specimen and thoracotomy specimen (1-3). The most important factors are specific cell type and the differentiation degree of tumor (2,15). The cell agreement for large cell carcinoma is lower than the other tumor types (1,2,15). According to Matsuda et al. (15), there is lack of cell differentiation in this tumor type and small biopsy specimens can be insufficient to make correct cell typing. Most investigators reported good agreement for squamous cell carcinoma and adenocarcinoma. (2,12). The Kappa value for small cell carcinoma is 0.60 to 0.80 in many series (2,12,15,18). The best agreement (Kappa 0.68) was found for the squamous cell carcinoma in our series. We found that the worst agreement was for the adenosquamous cell carcinoma (Kappa 0.27) and large cell carcinoma (Kappa 0.48). Our series had no small cell carcinoma.

The degree of differentiation is closely related to cell type agreement (2,19). Cataluna et al (2) reported that the probability of accuracy was 25 times higher when the patient had a well-differentiated cancer rather than an undifferentiated cancer. Feinstein et al (19) obtained similar results. It was recommended that poorly differentiated tumors should be simply classified as non-small cell or small cell carcinoma (3). We found that the cell agreement was lower in both poorly differentiated and undifferentiated tumors compared to well-differentiated tumors. But this difference was not as significant as in comparision to a previous study (2).

The presence or absence of necrosis in bronchial biopsy specimen can affect cell type agreement. It was found that the presence of necrosis in bronchial biopsy speci-

mens was related to a decreased cell type agreement (2). In contrast, our results indicated that the absence or presence of necrosis in bronchial specimens had no effect on cell agreement in primary lung cancer. We determined that the stage and bronchoscopic localization of the tumor had no significant effect on cell type accuracy, which is similar to the results of Cataluna et al. (2). There were significant associations between the type of bronchial lesion and bronchoscopic biopsy accuracy in our series. Mass lesions had higher concordance than infiltrative lesions in the present series.

In conclusion, the value of bronchoscopic biopsy in the establishment of the cell type is related to various factors. These factors include the degree of differentiation, tumor type, and the type of bronchial lesion. We think that there will be difficulties in establishing the cell type by bronchoscopic biopsy especially in poorly differentiated tumors, large cell carcinoma and adenosquamous carcinoma.

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