PROXIMAL BRONCHIAL INVASION OF LUNG CANCER: A CLINICOPATHOLOGICAL STUDY

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ABSTRACT

Objective: To investigate the characteristics of proximal bronchial invasion of lung cancer for different types. Methods: Proximal bronchus of 151 operatively resected specimens of hilar type lung cancer were selected for cross-sectional pathological study. Forty-one specimens were obtained from total pulmonectomy, and 110 from pulmonary lobectomy. Results: Evidence showed that the direct invasion of tumor cells through the submucosal layer or multiple layers was the major form of lung cancer spread; 96.6% of the cancerous invasion occurred at the proximal bronchial wall less than 1.5 cm apart from the margin of the cancer. The extension of invasion was correlated with the histopathologic type of cancer, mode of invasion and TNM classification (pT, pN). Besides, the invasion in the bronchial wall by metastatic lymph nodes was also an important way for the cancer to spread. Conclusion: In order to achieve the radical removal of a tumor, it is imperative to keep a distance of 1.5 cm or more between the excision margin of the bronchus and the tumor, and to completely resect the hilar and mediastinal lymph nodes.

Key words: Lung cancer, Pneumonectomy, Clinicpathology, Neoplasm invasion

From January 1994 to December 1996, 151 operatively resected specimens from hilar lung cancer cases or patients were subject to histopathological study in Henan Cancer Hospital. The purpose was to explore pathologically the characteristics of proximal bronchial invasion of lung cancer with various histopathologic types, and then to provide the rational basis for the determination of safe resection size of bronchus and the selection of a proper operation mode.

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MATERIALS AND METHODS

Clinical Data

The 151 specimens were all newly resected during pneumonectomy from patients with lung cancer who had never received chemotherapy or radiotherapy. Among them, 41 specimens were obtained from total pneumonectomy (including 2 specimens from total pneumonectomy plus prominence), 110 specimens from pulmonary lobectomy (including 10 specimens from sleeve lobectomy and 8 specimens from wedge bronchoplasty). Pathologically, 102 specimens were squamous cell carcinoma, 23 adeno-carcinoma, 12 small cell carcinoma, 7 large cell carcinoma and 7 adeno-squamous cell carcinoma.

Methods

The bronchus wall was cut open along its longitudinal axis to view by the naked eye the location, size, and the morphology of the cancer, as well as the extension and the levels of the tumor metastasis. The data were recorded. The minimal distance from the base of tumor to the excision margin of the bronchus was measured. Cross-sectional specimen of bronchus wall was made, each 0.5 cm apart from the margin of cancer. Lymph nodes were removed and classified according to Naruke[1] method of lymph node mapping for lung cancer and labeled respectively and made as specimens. The specimens were fixed in 10% formalin solution for 24–48 hours and then parafine-embeded, and sectioned successively for microscopic

examination.

RESULTS

Correlation between the Cut Length of the Bronchus and the Cancerous Residual at the Cut End

The cut length of the bronchus (distance from excision margin of bronchus to the base of tumor) in our groups was 0.4—5.0 cm with an average of 1.72 cm. Cancerous residuals were found at the cut end in 6 cases microscopically (Table 1). Of them, three ones were of squamous cell carcinoma, two adeno-carcinoma and one small-cell carcinoma. Their distances from the cut end to the cancer base were 0.4, 0.5, 0.8, 1.0, 1.0 and 1.3 cm respectively.

The Invasion Extension of Lung Cancer along the Bronchial Wall

In 145 specimens without the cut end cancerous residual, 96.6% (140/145) of bronchus wall cancerous invasion occurred at a distance less than 1.5 cm apart from the cancerous margin (Table 2). The most part occurred at a distance of 0.6–1.0 cm, rating 59.3%; next those of 1.1—1.5 cm, 20.0%. Among the various types of lung cancer, the small cell carcinoma spreads with the longest distance. The invasion distance upper than 1.5 cm account for27.3% total cases with small cell carcinoma. Of them, the longest distance was 1.9 cm. Then for the large cell carcinoma, 57.1% of invasion distance were more than 1.0 cm.

Table 1. Correlation of the bronchus cut length with the cancerous residual at the cut end

Cut length (cm)	Cases	Cut end cancerous residual	*P*
<1.0	21	3	>0.05
1.0-1.5	57	3	<0.05
>1.5	73	0	

Table 2. Invasion distance to the proximal bronchus of lung cancer

Invasion distance (cm)	Histopathologic types					Total
	Squamous	adeno-	small	large	adeno-squamous	
≤0.5	18	2	0	2	3	25
0.6–1.0	61	16	6	1	2	86
1.1—1.5	19	3	2	3	2	29
>1.5	1	0	3	1	0	5

Modes of Invasion of Lung Cancer to the Bronchus Wall

Direct invasion of cancerous cells through mucous, submucous or multiple layers was the most frequent mode (Table 3). The distances were 0.5, 1.3 and 1.9 cm respectively. The invasion through lymph nodes to the bronchus wall occurred most frequently in the cases of adenocarcinoma, rating 21.4%. The invasion distance might be more than 3.1 cm apart from the cancerous margin.

Table 3. Invasion modes of lung cancer

Invasion modes	Histopathologic types					Total
	Squamous	adeno-	samll	large	adeno-squamous	
Direct invasion						
mucous	10	2	0	0	2	14
submucous	18	7	1	2	2	30
multilayers	71	12	10	5	3	101
Node invasion*	1(54)	3(14)	1(7)	0(5)	0(4)	5(84)

Notes: * excluding those fused with the primary tumor; The numbers in the () mean the numbers of node metastasis

Clinical Staging Factors and Invasion Distance

In the cases classified as T_1, T_2, T_3 or N_0, N_1, N_2 according to the TNM classification, most of the cancer invasion distances were 0.6–1.0 cm, without significant difference ($P>0.05$) among various groups. However, in the cases with an invasion distance of more than 1.0 cm, the number of patients classified as T_3 was greater than T_1 ($P<0.05$), the same was also seen in the cases of N_2 as compared with N_0 ($P<0.01$, Table 4).

Table 4. TNM staging and invasion extension

TNM staging	Invasion extension(cm) <0.5	0.6-1.0	1.1-1.5	>1.5	Total
Tumor staging (T)					
T_1	5	16	3	0	24
T_2	15	50	14	3	82
T_3	5	20	12	2	39
Node staging (N)					
N_0	15	38	8	0	61
N_1	7	22	5	0	34
N_2	3	26	16	5	50

DISCUSSION

In the surgical treatment of lung cancer, due to the specific tree anatomic structure and the restricted extensibility of the bronchus, the resectable bronchus size is always limited. The incidence of post-operative cut end cancerous residual ranged from 2.2–14.7%,[2] greater than in other organs. In the recent years, with the increased indications for surgical treatment of lung cancer and the increased number of patients with bronchoplasty, the problem of cut end cancerous residual and the cancer recurrence has become more and more prominent, the incidence attaining as high as to 28.4%.[3]

How many cm is the safe resection size from bronchus cut end to cancer margin for the surgical resection of lung cancer? This is a problem attracting the attention of many surgeons both at home and abroad and with controversy. According to Shields,[4] the safe cut length needs only >0.5 cm; Tomita M, et al.[5] stressed that it must be >2 cm; surgeons at home pointed out that the cut margin must be more than 1.2 cm distant from the cancerous base.[6] The present study, a microscopic observation of 145 operatively resected proximal bronchus of lung cancer at different cross-sections, showed that the rates of cancer invasion extension more than 0.5 cm, 1.0 and 1.5 cm are 82.8%, 23.4% and 3. 4% respectively. 96.6% of cancer invasion occurred at the bronchus wall at a distance under 1.5 cm from the cancer margin. Even in the cases with different T lesions (T_1, T_2, T_3) or different N lesions (N_0, N_1, N_2), most part of cancer invasion extension attained to 0.6–1.0 cm without significant difference among different groups (P>0.05). Based on these data, we considered that the safe resection extension of bronchus must be more than 1.5 cm. In our study, the bronchus resection size was ≤1.5 cm in 78 cases, >1.5 cm in 73 patients with an average of 1.72 cm. The cut end cancerous residuals occurred in 6 patients for the former group (7.7%) and none for the latter group. The difference is significant (P<0.05).

There were data indicating that the invasion of cancerous cells through mucous layer is uncommon. This fact only occurred for our group in few patients with squamous cell carcinoma or with cancer in early stages (none one of multi-origin) with an invasion extension less than 0.5 cm. More frequent is the invasion through submucous or multi-layers with an invasion extension as high as of 1.9 cm. This may be the cause that some specimens present "normal" under the naked eye view but show the presence of cancerous invasion under a microscope. In addition, the invasion extension is correlated with the histopathologic type and the TNM staging factors of the cancer. Among various types of lung cancer, the invasive capability of small cell carcinoma is the strongest, with a longest invasion distance, next the large cell carcinoma; the invasive distance of squamous cell carcinoma is similar with adenocarcinoma. An analysis of 34 cases with invasion extension >1.0 cm showed that the number of T_3 was remarkably greater than T_1 (P<0.05), the number of N_2 was also greater than N_0. It is evident that the resection line defined only by naked eye view during operation is not reliable. It must be defined according to the histopathologic type of the cancer and combined with pathologic staging data. For patients with poorly differentiated carcinoma, serious invasion or accompanied with mediastinal lymph node metastasis, the distance from excision margin to cancer margin must be as long as possible. The intra-operative frozen section examination must be carried out in these cases if necessary.

Metastasis by lymph nodes to the proximal bronchus is an another form of cancer spread. In our group, there were 84 patients with node metastasis (57.9%). It is more active in the cases of adenocarcinoma, small cell carcinoma and large cell carcinoma than the squamous cell carcinoma. The invasion rate of node metastasis of adenocarcinoma is the greatest (21.4%), 60% of the total. This type of metastasis is different from the intra-wall node invasion. It mainly invades the external tunica of bronchus wall, may be distant from the tumor and easy to be neglected. Therefore, it is important to pay attention to the relation of lymph nodes around the bronchus and under the tracheal prominence with the bronchus wall when removing radically the regional lymph nodes.

The results of our study suggested that to select a rational operation mode is the key point for the safe resection of invaded bronchus. We consider that for cancer invading the orifice of lobar bronchus or near the main bronchus, the sleeve lobectomy can augment the length of the bronchus cut end, better than wedge bronchoplasty. In the case of cancer invading main bronchus, bronchus of neighboring lobe or main

branch of pulmonary artery, the choice of high level radical treatment is more important rather than to choose sleeve lobectomy of bronchus or pulmonary artery branch. Provided the cardio- pulmonary functions are supportable, it would be better to choose radical total pneumonectomy than to choose palliative bronchoplasty. For prominence reconstruction, due to the high tension at the anastomotic site, it is difficult to keep the distance from cut end to cancer margin greater than 1.5 cm. In these cases the resection line must be defined according to the results of frozen section examination. Further study may be needed for the impact of pre-operative general treatment to the cancer invasion along the bronchus wall.

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