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Prognostic significance of visceral pleural invasion in the forthcoming (seventh) edition of TNM classification for lung cancer

Hyo Sup Shim[a,*], In Kyu Park[b], Chang Young Lee[b], Kyung Young Chung[b]

[a] Department of Pathology, Yonsei University College of Medicine, 134 Shinchon-dong, Seodaemun-gu, Seoul 120-752, Republic of Korea
[b] Department of Thoracic Surgery, Yonsei University College of Medicine, Seoul, Republic of Korea

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ABSTRACT

Background: The next revision to the TNM classification for lung cancer (the seventh edition) is scheduled to be released in 2009. However, the definition of visceral pleural invasion (VPI), which is a non-size-based T2 descriptor, still lacks in detail, and its validation is not included.
Methods: We analyzed 1046 cases of non-small cell lung cancer (NSCLC) with T1, T2, or T3 diseases from 1990 to 2005, and subclassified into p0–p3 according to the degrees of pleural invasion. Survival analyses were performed using Kaplan–Meier method. Then, all patients were subdivided into nine groups according to tumor size and pleural invasion, and we compared survival differences, primarily focusing on T2a and T2b diseases according to the seventh edition.
Results: There was no survival difference between patients with p1 and p2, thus we regarded p1 or p2 as VPI. There was survival difference between two groups, which are expected to be classified as T2b. The behavior of tumors larger than 5 cm but 7 cm or less with VPI was similar to T3 tumors.
Conclusions: VPI is a poor prognostic factor of NSCLC, and the penetration through the elastic layer of the visceral pleura regardless of its exposure on the pleural surface (pl and p2) should be defined as VPI. This study also indicates that VPI influences T stage dependent on tumor size, and it can be suggested that tumors of larger than 5 cm but 7 cm or less with VPI should be upgraded to T3 stage.

1. Introduction

Visceral pleural invasion (VPI) of lung cancer has been known as a poor prognostic factor [1–7]. VPI is also adapted as a non-size-based T2 descriptor in the TNM staging of the International Union Against Cancer (UICC) and the American Joint Committee on Cancer (AJCC) [8,9]. However, the sixth edition of TNM classification only states that a tumor of any size that invades the visceral pleura is classified as a T2 tumor [8,9]. There is no mention of what constitutes VPI.

The next revision to the TNM classification for lung cancer (the seventh edition) is scheduled to be released in 2009 [10,11]. Recommended changes in the seventh edition of T classification includes subdivision of T1 into T1a (≤2 cm) and T1b (>2 cm to ≤3 cm), and T2 into T2a (>3 cm to ≤5 cm or T2 by other factor and ≤5 cm) and T2b (>5 cm to ≤7 cm), and reclassification of T2 tumors >7 cm as T3 [10,11]. It is primarily based on a finer subdivision of tumor size. VPI remains as a non-sized-based T2 descriptor. For example, a tumor of size less than 5 cm that invades the visceral pleura is classified as T2a. However, the definition of VPI still lacks in detail and its validation is not included [10].

To evaluate the prognostic significance of VPI in the forthcoming (seventh) edition of TNM classification for lung cancer, we analyzed overall survival rates of patients with non-small cell lung cancer (NSCLC) according to the degrees of pleural invasion, and then compared survival differences among groups defined by tumor size and VPI, primarily focusing on T2a and T2b diseases.

2. Materials and methods

2.1. Patients

We analyzed archival slides and medical records from patients with NSCLC who underwent curative pulmonary resection from 1990 to 2005 at our institution. After excluding T4 or M1 disease, we selected 1046 cases. Clinical data (including age, sex, type of resection, tumor size, and survival time) were obtained from each patient's medical records, as shown in Table 1. All patients underwent pulmonary resection (segmentectomy or more) with systematic mediastinal lymph node dissection. The Institutional Review Board approved this retrospective study. The need for subsequent individual consent of patients whose records were

* Corresponding author. Tel.: +82 2 2228 2623; fax: +82 2 2227 7939.
E-mail addresses: shimhs@yuhs.ac, shimpool@freechal.com (H.S. Shim).

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Table 1
Clinicopathologic characteristics of patients.

Variables	p0 (n = 680)	p1 (n = 86)	p2 (n = 141)	p3 (n = 139)	Total (n = 1046)
Age (years)					
Mean ± S.D.	61 ± 9	61 ± 8	62 ± 10	61 ± 9	61 ± 9
Range	28–81	38–79	35–80	35–76	28–81
Sex					
Male	539 (79.3)	56 (65.1)	105 (74.5)	118 (84.9)	818 (78.2)
Female	141 (20.7)	30 (34.9)	36 (25.5)	21 (15.1)	228 (21.8)
Type of resection					
Pneumonectomy	221 (32.5)	28 (32.6)	64 (45.4)	69 (49.6)	382 (36.5)
Bilobectomy	90 (13.2)	13 (15.1)	12 (8.5)	13 (9.4)	128 (12.2)
Lobectomy	367 (54.0)	45 (52.3)	65 (46.1)	57 (41.0)	534 (51.1)
Segmentectomy	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)
Histologic types					
Squamous cell carcinoma	368 (54.1)	37 (43.0)	55 (39.0)	87 (62.6)	547 (52.3)
Adenocarcinoma	251 (36.9)	44 (51.2)	76 (53.9)	38 (27.3)	409 (39.1)
Large cell carcinoma	41 (6.0)	4 (4.7)	3 (2.1)	8 (5.8)	56 (5.4)
Adenosquamous carcinoma	20 (2.9)	1 (1.2)	7 (5.0)	6 (4.3)	34 (3.3)
Size					
≤3 cm	279 (41.0)	30 (34.9)	34 (24.1)	24 (17.3)	367 (35.1)
>3 cm to ≤5 cm	270 (39.7)	35 (40.7)	64 (45.4)	57 (41.0)	426 (40.7)
>5 cm to ≤7 cm	91 (13.4)	11 (12.8)	28 (19.9)	41 (29.5)	171 (16.3)
>7 cm	40 (5.9)	10 (11.6)	15 (10.6)	17 (12.2)	82 (7.8)
Pathologic N stage					
N0	372 (54.7)	42 (48.8)	71 (50.4)	57 (41.0)	542 (51.8)
N1	129 (19.0)	11 (12.8)	19 (13.5)	35 (25.2)	194 (18.5)
N2	170 (25.0)	29 (33.7)	49 (34.8)	44 (31.7)	292 (27.9)
N3	9 (1.3)	4 (4.7)	2 (1.4)	3 (2.2)	18 (1.7)

Data are given as number (%).

evaluated was waived because individuals were not identified in this study.

2.2. Pathologic evaluation and grouping

Histopathologic typing was done according to the World Health Organization criteria [12]. The degree of pleural invasion was reviewed in detail. When tumor abutted the visceral pleura or the pleura was puckered, the elastic-van-Gieson stain was performed. Pleural invasion was classified according to the previously described criteria [13,14]: p0, tumor with no pleural involvement beyond its elastic layer (Fig. 1A); p1, tumor that extends beyond the elastic layer of the visceral pleura but is not exposed on the pleural surface (Fig. 1B); p2, tumor that is exposed on the pleural surface but does not involve adjacent anatomic structures (Fig. 1C); and p3, tumor that involves adjacent anatomic structures (Fig. 1D).

All patients were divided into nine groups, A–I, according to the tumor size and pleural invasion (p0–p3), as shown in Table 2. Primarily focusing on the T2a and T2b stages, we compared survival rates of groups B–D (being classified as T2a), and those of groups E–I (being classified as T2b or T3). Overall survival rates were also examined in the patients with N0 disease.

2.3. Statistical analysis

Overall survival rate was evaluated by using the Kaplan–Meier method, and statistical differences in survival were determined by means of log-rank test. The Cox-proportional hazards model was applied to the multivariate survival analysis. The statistical difference was considered to be significant if the p-value was less than 0.05. All statistical data were analyzed using SPSS for Windows ver. 15.0.

3. Results

3.1. Clinicopathologic characteristics

Patients' characteristics are shown in Table 1. There were 818 men and 228 women aged 28–81 years (mean 61 years). The degrees of pleural invasion were p0 state in 680 patients (65.0%),

Table 2
Nine groups according to tumor size and pleural invasion.

Group	Tumor size	Pleural invasion[a]	All patients, number (%)	Patients with N0, number (%)	Expected T stage[b]
A	≤3 cm	p0	279 (27)	176 (33)	T1
B	≤3 cm	p1 and p2	64 (6)	36 (7)	T2a
C	>3 cm to ≤5 cm	p0	270 (26)	131 (24)	T2a
D	>3 cm to ≤5 cm	p1 and p2	99 (9)	48 (9)	T2a
E	>5 cm to ≤7 cm	p0	91 (9)	46 (9)	T2b
F	>5 cm to ≤7 cm	p1 and p2	39 (4)	17 (3)	T2b
G	>7 cm	p0	40 (4)	19 (4)	T3
H	>7 cm	p1 and p2	25 (2)	12 (2)	T3
I	Any size	p3	139 (13)	57 (11)	T3

[a] According to the previously described criteria (see text).
[b] According to the forthcoming (seventh) edition of TNM classification for lung cancer.