PROGNOSTIC ASSESSMENT OF 1310 PATIENTS WITH NON-SMALL-CELL LUNG CANCER WHO UNDERWENT COMPLETE RESECTION FROM 1980 TO 1993

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Objective: **The TNM staging system of lung cancer is widely used as a guide for estimating prognosis and selecting treatment modality. In 1997, the International Union Against Cancer and the American Joint Committee on Cancer have adopted a revised stage grouping for lung cancer. However, the validity of the new stage grouping has not been fully established. We investigated the prognoses of patients who had resection of non–small-cell lung cancer to confirm the validity of the revised classification.** ***Methods:*** **A total of 1310 patients with non–small-cell lung cancer underwent complete resection and pathologic staging of the disease in our hospitals from 1980 through 1993. A pulmonary resection was performed with a systematic nodal dissection. The survivals were calculated with the Kaplan-Meier method on the basis of overall deaths, and the survival curves were compared by log rank test.** ***Results:*** **There were significant differences in survival between patients with T1 N0 M0 and T2 N0 M0 disease and between those with T1 N1 M0 and T2 N1 M0 disease. However, there was no significant difference between patients with T2 N0 M0 disease and those with T1 N1 M0 disease. No significant difference in survival was observed among patients with T2 N1 M0, T3 N0 M0, and T3 N1 M0 cancer. Patients with different invaded organs of T3 subdivision (pleura, chest wall, pericardium, or diaphragm) had a different prognosis. There was no significant difference between patients with T3 N2 M0 disease and those with stage IIIB disease.** ***Conclusions:*** **We supported most of the revision, such as dividing stage I, dividing stage II, and putting T3 N0 M0 to stage IIB. Furthermore, we found some candidates for a subsequent revision, such as putting T3 N1 M0 to stage IIB, putting T2 N0 M0 and T1 N1 M0 together, regarding diaphragm invasion as T4, and putting T3 N2 M0 to stage IIIB. (J Thorac Cardiovasc Surg 1998;116:407-11)**

The TNM staging system of lung cancer is widely used as a guide for estimating prognosis and selecting treatment modality.[1-3] Recently some questions have arisen about whether the present TNM staging really reflects the exact prognosis.[4] In 1997, the International Union Against Cancer (UICC) and the American Joint Committee on Cancer have adopted a revised stage grouping.[5] However, the validity of the new stage grouping has not been fully established. In this report, we investigate the prognoses of 1310 patients with completely resected non–small-cell lung cancer on the basis of the pathologic TNM classification to confirm the validity of the revised classification and to analyze other prognostic factors.

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Patients and methods

A total of 1310 patients with non–small-cell lung cancer underwent complete resection and pathologic staging of the disease in our hospitals from 1980 through 1993. In this period, chest computed tomography, brain computed

Table I. *The characteristics of the 1310 patients in this study*

Characteristic	*No. of patients*	*Percentage*
Sex*		
Male	968	73.9
Female	342	26.1
Histologic type		
SQ	556	42.4
AD	645	49.3
LA	109	8.3
T factor		
T1	602	45.9
T2	564	43.1
T3	122	9.3
T4	22	1.7
N factor		
N0	803	61.3
N1	245	18.7
N2	260	19.8
N3	2	0.2
Stage		
Stage I	752	57.5
Stage II	197	15.0
Stage IIIA	337	25.7
Stage IIIB	24	1.8

SQ, Squamous cell carcinoma; *AD,* adenocarcinoma; *LA,* large cell carcinoma.

*Age: 28 to 85 years (mean, 64.5 years).

tomography, abdominal ultrasonography, and bone scintigraphy were routinely performed before operation to evaluate distant metastasis.[4] A randomized trial for postoperative adjuvant chemotherapy was conducted in this period, but the results revealed no survival advantage or disadvantage with our regimen (unpublished data). Induction therapy was not performed in this period especially for the patients who had been expecting a complete resection. A lobectomy or a pneumonectomy was performed with the dissection of hilar and mediastinal lymph nodes (systematic nodal dissection[6]). Lymph nodes were numbered according to lymph node mapping reported by Naruke and associates.[7] The patients were classified on the basis of the pathologic TNM classification of the UICC.[5] Histologic typing was determined according to the World Health Organization classification.[8] The survivals were calculated with the Kaplan-Meier method on the basis of overall death including operative deaths, and the survival curves were compared by log rank test.

Results

Patients' characteristics and TNM distribution are shown in Tables I and II. Five-year survivals of patients with T1 N0 M0, T2 N0 M0, T1 N1 M0, and T2 N1 M0 diseases were 80%, 65%, 57%, and 42%, respectively (Fig. 1). There were significant differences in survival between patients with T1 N0 M0 and T2 N0 M0 diseases ($P = .001$) and between patients with T1 N1 M0 and T2 N1 M0 diseases

Table II. *The distribution of patients in the TNM subsets*

Stage (old)	*TNM subset*	*No. of patients (%)*
Stage I	T1 N0 M0	480 (36.6)
	T2 N0 M0	271 (20.6)
Stage II	T1 N1 M0	57 (4.4)
	T2 N1 M0	141 (10.8)
Stage IIIA	T3 N0 M0	46 (3.5)
	T3 N1 M0	39 (3.0)
	T1 N2 M0	65 (5.0)
	T2 N2 M0	150 (11.4)
	T3 N2 M0	37 (2.8)
Stage IIIB	T4 N0 M0	6 (0.5)
	T4 N1 M0	8 (0.6)
	T4 N2 M0	8 (0.6)
	T2 N3 M0	2 (0.2)

($P = .02$). However, there was no significant difference between patients with T2 N0 M0 and T1 N1 M0 diseases.

Fig. 2 shows survival curves of T2 N1 M0, T3 N0 M0, and T3 N1 M0 diseases; there was no significant difference in survival among patients with T2 N1 M0 (5-year survival, 42%), T3 N0 M0 (5-year survival, 34%), and T3 N1 M0 (5-year survival, 38%) diseases.

To estimate the contribution of invaded organ to the prognosis, we compared survival curves of patients with T3 N0-1 M0 disease according to the invaded organ (Fig. 3). Patients with T3 N0 M0 disease and patients with T3 N1 M0 disease were united for the estimation because they had similar survival curves, whereas patients with T3 N2 M0 disease had significantly poorer prognoses. Patients with different invaded organs of T3 subdivision had different prognoses; pleura (5-year survival, 35%), chest wall (5-year survival, 26%), pericardium (5-year survival, 43%), and diaphragm (3-year survival, none).

Fig. 4 shows the survival curves of patients with T3 N2 M0 disease and patients with stage IIIB disease. The prognosis of patients with completely resected T3 N2 M0 disease (5-year survival, 11%) was poorer than that of patients with completely resected stage IIIB disease (5-year survival, 36%). There was no significant difference in survival between patients with T3 N2 M0 disease and those with stage IIIB disease.

Discussion

The TNM staging system of lung cancer was revised in 1997.[5, 6, 9] The staging system should be revised according to the prognosis of the patients

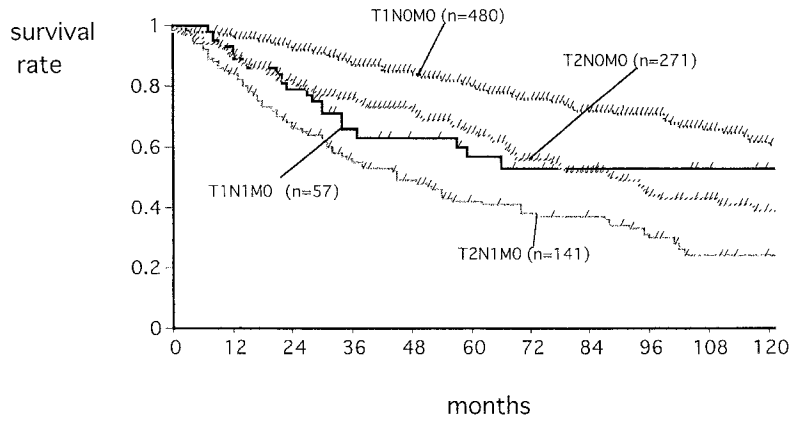

Fig. 1. The postoperative survival curves of patients with T1 N0 M0, T2 N0 M0, T1 N1 M0, and T2 N1 M0 diseases show that there are significant differences between the prognoses of patients with T1 N0 M0 and T2 N0 M0 diseases ($P = .001$) and between those of patients with T1 N1 M0 and T2 N1 M0 diseases ($P = .02$).

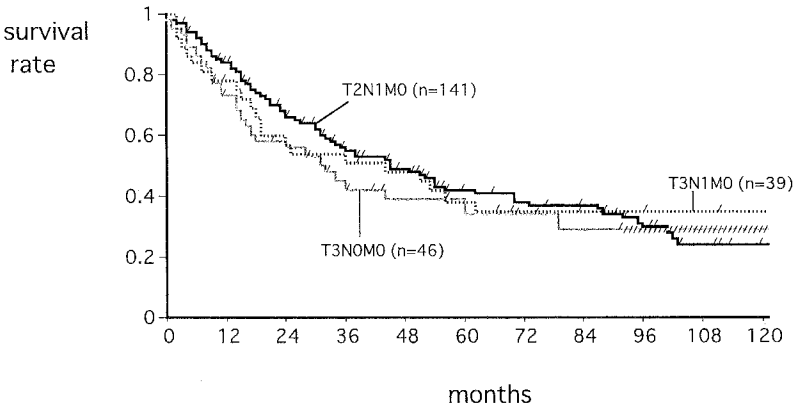

Fig. 2. The postoperative survival curves show that there are no significant differences in the survivals among of patients with T2 N1 M0, T3 N0 M0, and T3 N1 M0 diseases.

who have relatively homogeneous backgrounds. In this present study, with which we attempted to assess the validity of the revision, we limited the cases to 1980 through 1993 because preoperative examinations in our institute were similar in this period.[4]

In the revised TNM staging, stage I is divided into stage IA and stage IB. Stage II is also divided into stage IIA and stage IIB. Our results supported these divisions, because there were statistically significant differences between the prognoses of patients with T1 N0 M0 and T2 N0 M0 diseases and between those of patients with T1 N1 M0 and T2 N1 M0 diseases. However, there was no difference between patients with T2 N0 M0 and T1 N1 M0 diseases. Mountain[9] also reported that the survivals of patients with T2 N0 M0 and T1 N1 M0 diseases were 57% and 55%. T2 N0 M0 subgroup and T1 N1 M0 subgroup may be included in the same group (it does not mean T1 N1 M0 should be included in stage I).

T3 N0 M0 subgroup is included in stage IIB in the revised TNM staging. Because there was no difference between the prognosis of patients with T2 N1 M0 and T3 N0 M0 diseases, our results supported the revision. On the other hand, T3 N1 M0 is still controversial. Some investigators reported that patients with T3 N1 M0 diseases and patients with T3 N2 M0 diseases had a similar prognosis.[10] However, others including us[2, 11, 12] reported that patients with T3 N1 M0 diseases had a more preferable prognosis than patients with T3 N2 M0 diseases. Mediastinal nodal involvement is

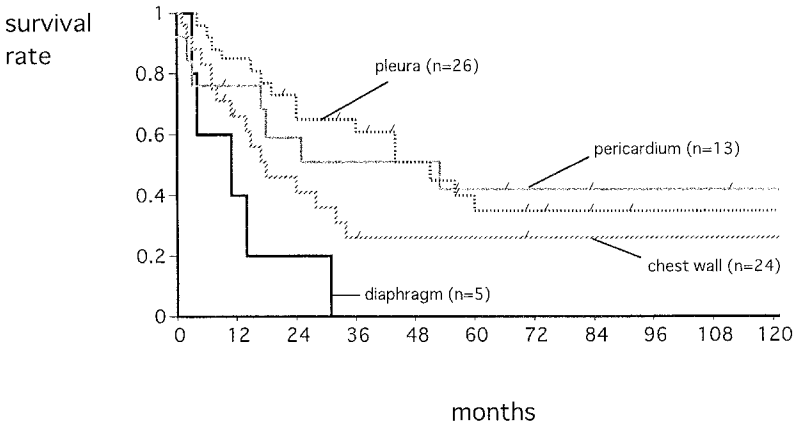

Fig. 3. The postoperative survival curves of patients with T3 N0-1 M0 diseases show that, according to the invaded organ, patients with resected T3 tumors invading the diaphragm have a poor prognosis.

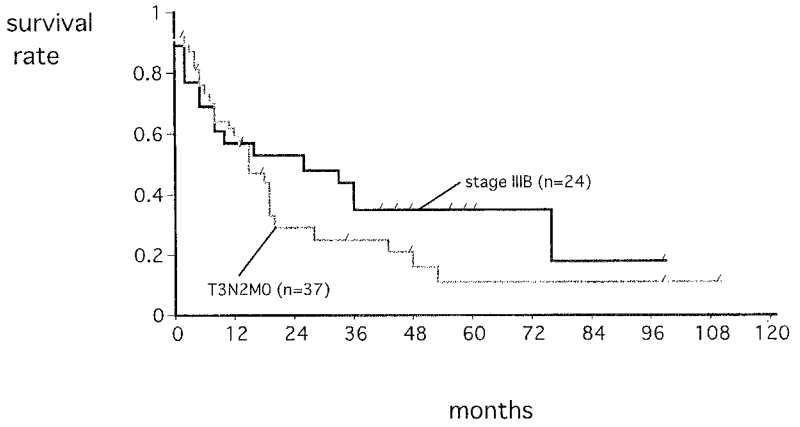

Fig. 4. The postoperative survival curves of patients with T3 N2 M0 and stage IIIB diseases show that there is no significant difference between the prognoses.

one of the most important prognostic factors and strongly influences survival in patients with lung cancer. Although T3 N1 M0 may be another candidate of subgroup in stage IIB, further studies are required to find correct grouping.

Some investigators[11] pointed out that T3 factors were heterogeneous. For the comparison of the prognosis according to the invaded organ, patients with N2 diseases were excluded to eliminate the influence of N factor.[13] In our patients with lung cancer invading diaphragm, there were no 3-year survivors. There has been only one report concerning the prognosis after the resection of the tumors invading the diaphragm.[11, 14] Weksler and associates[14] reported 8 cases with resected T3 tumors invading the diaphragm in which there were no 4-year survivors, although 3 of the patients died of other causes. Some cancer cells in the lymph on the diaphragm flow to the abdominal lymph system, which is impossible to dissect. Tumors invading the diaphragm may be a candidate of T4 subgroup; however, the examination of a large number of cases, such as a multicenter study, is required.

Patients with T3 N2 M0 diseases who have undergone complete resection had poor prognoses.[15] There was no difference between the survival of patients with T3 N2 M0 diseases and that of patients with stage IIIB disease. One of the reasons for the similarity is that most of our patients with stage IIIB disease were selected cases (ie, only 2 patients had N3 disease and 64% of patients in the T4 classification had N0-1 diseases). However, it still suggests

that T3 N2 M0 diseases are extensively advanced and that the T3 N2 M0 subgroup may be included in stage IIIB.

Most of our results supported the revision of the staging system proposed by the UICC and the AJCC in 1997. However, on the basis of our results, we present here some candidates for a subsequent revision. We ask for the assessment of our proposal by other investigators. After thorough discussions based on various results from different institutions, the next revision of the TNM staging would reflect the prognosis more precisely.[3, 6]

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