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Research Article

Comparison of Seventh and Eighth Editions of TNM Staging Classification and Evaluation of Survivals in Operated Non-Small Cell Lung Carcinomas: Single Center Experience

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Abstract

Objectives: In this study, our purpose was to compare the survivals of the 7th and 8th editions of TNM staging system in non-small cell lung cancer (NSCLC).

Methods: We retrospectively compared pathological staging and survival of 209 patients who were operated with the diagnosis of NSCLC between 2006 and 2017. In this study, we did not include metastatic patients, patients receiving preoperative treatment, patients with low grade malignancy and patients with neuroendocrine carcinoma.

Results: Three of the 31 stage 1A changed to 1A1, 11 to 1A2, 17 to 1A3; 16 of the 40 stage 1B changed to 2A; 2 of the 38 stage 2B changed to 1B, 21 changed to 3A; 2 of the 41 stage 3A changed to 2B, 7 changed to 3B. When we grouped stages as I, II, III; there was a significant difference in prognostic effects between 7th edition stages (p=0.01) and 8th edition stages (p=0.02). Presence of surgical margin positivity, lymphatic, perineural and vascular invasion were poor prognostic factors (p<0.05).

Conclusion: In our study, we observed similar survival rates according to the 7th and 8th editions of TNM staging system which is used in the pathological staging of lung cancers.

Keywords: Non-small cell lung cancer, staging, survival

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Lung cancer is one of the most common malignant tumors and is the leading cause of cancer-related deaths worldwide.[1] Although there is considerable progress in screening and detection in earlier stages, new surgical tecniques and treatments like targeted therapy to treat advanced cancers, prognosis of lung cancer still remains poor.[2,3] Accurate staging of the tumor is important for prognostic evaluation and for determining stage-specific therapeutic strategy. TNM classification system is used for staging lung cancers where T refers to size and extent of primary tumor, N to location of

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involved lymph nodes and M to whether the cancer has metastasized.[4] The 7th edition of TNM staging system has been used in lung cancer since January 2010. The 8th edition of TNM lung cancer staging proposals was introduced in 2015 and has been implemented through January 2017 in countries besides United States of America.[5]

The T category was significantly updated in the 8th edition of TNM classification system. Since the increase of tumor diameter was found to be a poor prognostic factor, T category was changed. In the 7th edition, tumors smaller than 3 cm were classified as T1, tumors between 3 and 7 cm were classified as T2. In the 8th edition, tumor sizes up to 5 cm were divided into five categories as T1a, T1b, T1c, T2a, T2b, one step increase in every one centimeter increase. In the 7th edition, tumors between 3-5 cm and 5-7 cm were classified as T2a and T3, respectively. In the new staging system, tumors of 4-5 cm are classified as T2b, 5-7 cm as T3 and tumors larger than 7 cm as T4. In the 8th edition staging, the diaphragm invasion was classified as T4. Partial or total lung atelectasis, main bronchus invasion independent of the distance from carina was classified as T2. Extrathoracic metastasis was divided into M1b as single metastasis and M1c as multiple metastases. All of these revisions were made by the analyses of an international database built by data from 46 sites from 19 countries.[6–11]

In this study, our purpose was to compare the survivals of non-small cell lung cancer patients treated in our clinic according to 7th and 8th editions of TNM staging system in.

Methods

Patient Selection and Staging

This retrospective study included data from 209 patients operated and diagnosed as non-small cell lung cancer between 2006 and 2017 in a single center. In this study, we excluded patients with metastatic disease, non-operated patients, patients receiving preoperative treatment, patients with low grade malignancy (carcinoid tumor, adenoid cystic carcinoma) and patients with neuroendocrine carcinoma. We evaluated the effects of clinical and pathological features (age, gender, smoking history, type of surgery, surgical margin, histological subtype, lymphatic invasion (LI), perineural invasion (PNI), and vascular invasion (VI), visceral involvement, adjuvant therapy) and their effects on survival. We evaluated the differences in pathological stages and survival of patients based on the 7th and 8th editions of TNM staging system.

Statistical Analysis

We analyzed survival data using the Kaplan-Meier method. We defined OS and PFS as the interval between the first day of surgery and the date of death/last visit and type of progression, respectively. To evaluate the prognostic impact of the 7th and 8th editions of the TNM staging system, we estimated hazard ratios and their 95% confidence intervals using Cox proportional hazards model. We used log-rank test for comparison of survival differences between staging system editions.

Results

The total number of patients in this trial was 209, and the median follow-up period was 30 months (range 2-138 months). Most of the patients were male (176 patients [84%]), and 22 (11%) had never smoked. Fiftytwo percent had adenocarcinomas. We summarized patients' clinical and pathological characteristics in table 1.

Table 1. Clinicopathological and Demographic Data

	Min-Max	Median	n (%)	P
Age	39-82			
≤65		62	134 (64.1)	0.361
>65			75 (35.9)	
Follow-up Duration (Months)	2-138	30		
Status				
Died			71 (34)	
Alive			138 (66)	
Relapse-free Survival	2-138	23		
Recurrence				
No			106 (50.7)	
Yes			103 (49.3)	
Gender				
Male			176 (84.2)	0.258
Female			33 (15.8)	
Histological Type				
Squamous			91 (43.5)	0.215
Adenocancer			108 (51.7)	
NSCLC			10 (4.8)	
Adjuvant Treatment				
No			75 (35.9)	0.360
KT/RT			134 (64.1)	
Type of Resection				
Wedge Resection			15 (7.2)	0.779
Lobectomy			166 (79.4)	
Pneumonectomy			78 (13.4)	
Surgical Margin				
positive			15 (7.2)	0.015
negative			194 (92.8)	
Smoking				
No			22 (10.5)	0.290
Yes			187 (89.5)	
LI				
No			123 (61.8)	0.028
Yes			76 (38.2)	
PNI				
No			160 (82.1)	0.004
Yes			35 (17.9)	
Pleural Invasion				
No			129 (63.9)	0.118
Yes			73 (36.1)	
VI				
No			132 (66.7)	0.004
Yes			66 (33.3)	

Surgical margin positivity, lymphatic, perineural and vascular invasion were poor prognostic factors (p<0.05). Multivariate analysis showed that PNI (p=0.02) and VI (p=0.04) were independent prognostic factors. Sixty-six % of patients were alive during the analysis. Median relapse-free survival time was 23 months; median overall survival time was 81 months. Two-year OS rate and five-year OS rate were 82% and 57%, respectively. We summarized 2-year and 5-year survival data based on the 7th and 8th editions of TNM staging system in table 2. We illustrated survival graph according to stages in figure 1. We summarized stage migrations according to 7th and 8th edition of TNM stages in tables 3 and 4. When we grouped stages as I, II, III; there was a significant difference in survival between 7th edition stages (p=0.01) and 8th edition stages (p=0.02) There was no statistically significant difference between stages 1 and 2 with respect to the staging classification, whereas there was a statistically significant difference between the stages 1-3 and 2-3.

Discussion

The newly revised 8th edition of TNM staging system introduced changes to T and M categories but there were no changes in the N category. In this study, we compared the pathologic stage and prognosis in stage 1-3 non-small cell lung cancer patients who were operated according to the 7th and 8th editions of TNM staging. Due to revisions in the staging classifition definitions in the 8th edition, our patients' 7th edition stages also changed. Three of the 31 stage 1A changed to 1A1, 11 to 1A2, 7 to 1A3; 16 of the 40 stage 1B changed to 2A; 2 of the 38 stage 2B changed to 1B, 21 changed to 3A; 2 of the 41 stage 3A changed to 2B, 7 changed to 3B. When the stages were grouped (I-II-III), there was a difference in survival according to stages TNM 7th stage (p=0.01) and in TNM 8th stage (p=0.02). The effect of staging on survival was similar in both classifications.

Table 2. Survival results according to 7th and 8th editions of TNM staging

7th TNM	died/n	2 years OS	5 years OS
1A	8/31	83	60
1B	10/40	92	66
2A	17/57	85	49
2B	13/38	89	70
3A	22/41	65	42
3B	1/2	50	50
8th TNM	**died/n**	**2 years OS**	**5 years OS**
1A1	0/4	100	100
1A2	3/13	92	52
1A3	6/17	75	58
1B	6/23	95	66
2A	4/19	88	68
2B	20/69	85	52
3A	26/55	79	57
3B	6/9	44	29

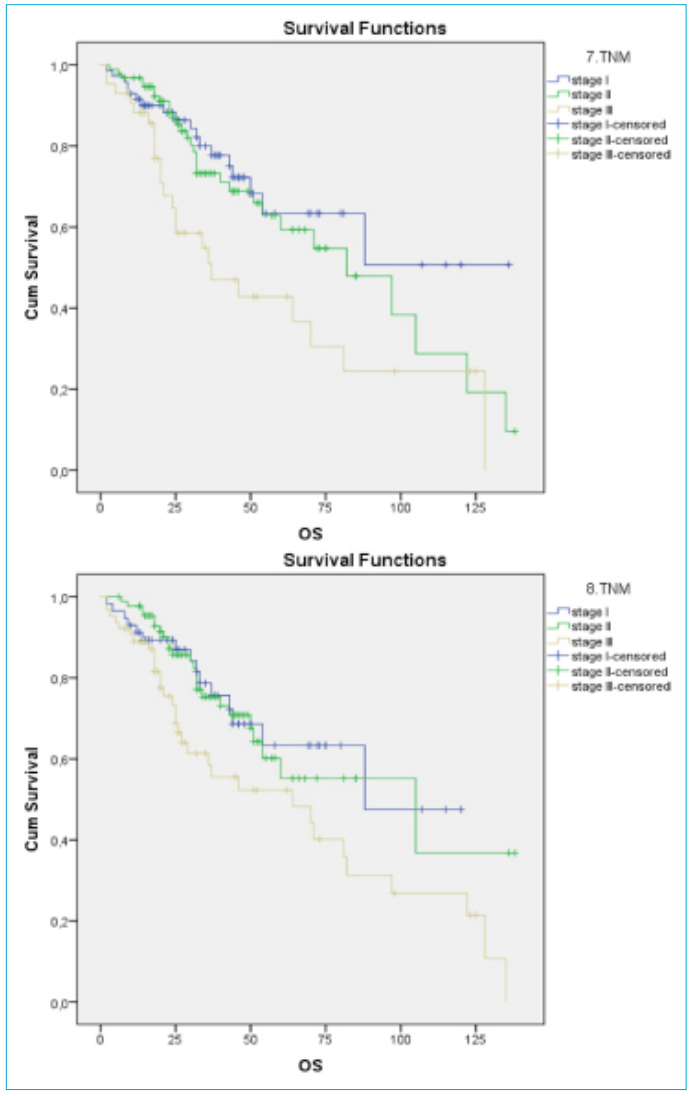


Figure 1. Survival according to 7th (above) and 8th (below) editions of TNM staging.

Table 3. Variation of stages according to 7th and 8th editions of TNM staging

		8th TNM								
		IA1	IA2	IA3	IB	IIA	IIB	IIIA	IIIB	Total
7th TNM	IA	3	11	17						31
	IB	1	2	21		16				40
	IIA					3	54			57
	IIB				2		13	23		38
	IIIA						2	32	7	41
	IIIB								2	2
	Total	4	13	17	23	19	69	55	9	

Table 4. Distribution of patients according to 7th and 8th editions of TNM staging

		N0	N1	N2	N3
7th TNM	T1a	IA (12)	IIA (3)	IIIA (3)	IIIB
	T1b	IA (19)	IIA (7)	IIIA (4)	IIIB
	T2a	IB (41)	IIA (32)	IIIA (8)	IIIB
	T2b	IIA (14)	IIB (8)	IIIA (4)	IIIB
	T3	IIB (30)	IIIA (11)	IIIA (4)	IIIB
	T4	IIIA (4)	IIIA (3)	IIIB (2)	IIIB
8th TNM	T1a	IA1 (5)	IIB	IIIA (1)	IIIB
	T1b	IA2 (12)	IIB (2)	IIIA (2)	IIIB
	T1c	1A3 (17)	IIB (9)	IIIA (4)	IIIB
	T2a	IB (21)	IIB (20)	IIIA (4)	IIIB
	T2b	IIA (19)	IIB (12)	IIIA (4)	IIIB
	T3	IIB (25)	IIIA (11)	IIIB (3)	IIIC
	T4	IIIA (19)	IIIA (10)	IIIB (3)	IIIC

The updated T, M, and overall TNM stage of the 8th staging system show improvement compared to the 7th edition in discriminatory ability between adjacent subgroups and are independent predictors for prognosis.[12] In a study conducted on patients receiving chemoradiotherapy at stage 3 in 2018, both OS and PFS were found to be similar according to T and N categories in both 7th and 8th editions.[13] The prognosis in lung cancer does not only depend on the extent of the tumor and anatomical staging, but molecular characteristics of the tumor, comorbidities, histological subtypes and geographic location also play role in survival. [14] In our study, we have found that the 8th edition of TNM pathological staging system in non-small cell lung cancer was similar to the 7th edition for predicting prognosis. Our study had several limitations. Our study is a retrospective study with a limited number of operable patients in a single center. It does not cover the clinical and radialogical staging of patients, which can be addressed in future studies.

Disclosures

Ethics Committee Approval: The Ethics Committee of School of Medicine, Marmara University provided the ethics committee approval for this study (09/2019/1100).

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Conflict of Interest: None declared.

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