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Research Article

Clinical Evaluation of TNM-7 and TNM-8 Stages in Patients with Non-Small Cell Lung Cancer

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Abstract

Objectives: The AJCC/UICC TNM (tumor, node, metastasis) classification is a system used to describe the anatomical extent and stage grouping of solid malignant tumors. This system provides a worldwide standardization and is updated periodically. In this study, we aimed to compare the staging of patients with operated Non-Small Cell Lung Cancer (NSCLC) according to TNM-7 and TNM-8.

Methods: In this study, we retrospectively analyzed data from 113 NSCLC patients resected without neoadjuvant therapy. Patients with another malignancy diagnosis were excluded from the study. Patients with multiple nodules were excluded because a clear TNM classification could not be made. We evaluated patients individually by restaging them using their post-operative pathology reports.

Results: The stage distribution according to TNM7 was as follows: IA: 30 (26.5%), IB: 14 (12,3%), IIA: 36 (31,8%), IIB: 16 (14.2%), IIIA: 13 (11,5%), IIIB: 2 (1,7%). Staging the cases according to TNM8, there is no case was down-staged, 60 (53%) were upstaged; most pronounced between stages IIA (TNM7) to IIB (TNM8), and IIB (TNM7) to IIIA (TNM8). Most of the upstages did not change the adjuvant treatment decision. Approximately 6% of patients experienced a change from IB to IIA.

Conclusion: In conclusion, a significant stage change was detected in patients whose stages were reevaluated using TNM7 and TNM8. Most of these upgrades do not change the treatment plan. This stage change may affect the adjuvant treatment decision in a small number of patients. With both classification systems, there was no statistical significance for disease-free survival (DFS) among subgroups, but the statistical significance for overall survival (OS).

Keywords: Lung cancer, staging, TNM classification

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Lung cancer is the leading cause of death worldwide from solitary organ cancer.[1] The tumor node metastasis (TNM) classification aims to standardize the definition of the anatomical extent of solid malignant tumors worldwide. It is important for clinicians as it enables them to prepare the treatment plan according to the patients' stages and to predict their prognosis. The TNM classification is constantly updated to improve results. The updated version of the TNM-7 version published in 2009 was accepted as TNM-8 in 2017.[2] The changes seen with TNM-8 are as follows; Tumors up to 3 centimeters (cm) were divided into 3 parts under the subgroup. While tumors between 3-7 cm were classified as T2 with the old classification, T2 tumors were changed to 3-5 cm in the new classification. Tumors 5-7 cm were accepted as T3 in the new classification. Tumors larger than 7 cm were accepted as T3 in the old and T4 in the new classifications. While the diaphragmatic invasion was accepted as T3 in the old classification, this

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situation was accepted as T4 with the new classification. Although it does not concern the target population of our study, the clinical staging, which was accepted as M1b in the old classification, was started to be evaluated as M1b and M1c according to the presence of single or multiple extrapulmonary metastases.

In this study, we aimed to classify patients with NSCLC who were resected without neoadjuvant treatment and staged according to TNM-7 according to TNM-8 and to re-evaluate the prognosis of patients according to stages. In this way, we aim to see whether the TNM-8 update contributes to our clinical practice.

Methods

The patient cohort consisted of patients with primary resected pNSCLC without neoadjuvant therapy. The study consisted of all consecutive patients resected and diagnosed between January 2010 and December 2016 at the Inonu University hospital. The study was performed according to the institutional ethical standards (Inonu University Medicine High School, Number: 2021/2088- 01-06-2021). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

The evaluation of the patients who were staged with TNM-7 during these periods was re-evaluated according to TNM-8. Patients were excluded from the study if they had another malignant disease. The patients were classified according to TNM-8 and evaluated separately in terms of overall survival (OS) and disease-free survival (DFS) among the stage groups. SPSS version 24 was used for data analysis. Kaplan-Meier-Log Rank analysis was used for survival analysis. Those with a P value of <0.05 were considered significant.

Results

Of the 113 patients in our study, 100 (88.5%) were male and 13 (11.5%) were female. The median age at diagnosis in the entire patient population was 61 (41-81). When the patients were evaluated according to the pathological subtypes, 52 (46%) of the patients were adenocarcinoma and 58 (54%) were squamous cell carcinoma. 74 (65.5%) of the patients in our study received adjuvant chemotherapy. The median follow-up period of the patients was 43 months (41-81). During this follow-up period, the number of patients who developed recurrence was 41 (36.3%), and the number of patients who died was 48 (42.5%). We summarized patients' clinical and pathological characteristics in Table 1. When the patients were staged according to the TNM-7 classification, the number of patients; Stage IA was 30 (26.5%), Stage IB 14 (12.3%), IIA 36 (31.8%), IIB 13 (11.5%), IIIB 2 (1.7%). When the same patients are evaluated according to TNM-8 staging; IA 30 (26.5%), IB 7 (6.2%), IIA 8 (7.1%), IIB 37 (32.7%), IIIA 27 (24%), and IIIB 4 (3.5%) was detected. We summarized the stages of the patients with both classification systems in Table 2. Patients were evaluated as OS and DFS between groups according to both classifications. While there was no statistically significant difference in DFS between the groups according to the TNM-7 classification (p>0.05), it was very close to the statistical significance limit in terms of DFS according to the TNM-8 classification (p=0.089). Similarly, when the patient groups are evaluated in terms of OS; there was statistical significance with both classifications (p<0.05). OS and DFS plots of patients are shown in figure 1 and figure 2.

Table 1. Clinicopathological and Demographic Data

	Min-Max	Median	n (%)
Gender			
Male	-	-	100 (88.5)
Female			13 (11.5)
Age	41-81	61	
Smoking			
No	-	-	12 (10.6)
Yes			101 (89.4)
Fallow-up	3-86	43	
Histological Type			
Squamous	61	-	61 (54)
Adenocancer	52		52 (46)
Adjuvant Treatment			
No	-	-	39 (34.5)
Yes			74 (65.5)
Recurrence			
No	-	-	72 (63.7)
Yes			41 (36.3)
Exitus			
No	-	-	65 (57.6)
Yes			48 (42.4)

Table 2. Distribution of patients according to 7th and 8th editions of TNM staging

	TNM-7 n (%)	TNM-8 n (%)
IA	30 (26.5)	30 (26.5)
IB	14 (12.3)	7 (6.2)
IIA	36 (31.8)	8 (7.1)
IIB	16 (14.2)	37 (32.7)
IIIA	13 (11.5)	27 (24)
IIIB	2 (1.7)	4 (3.5)
Total	113	113

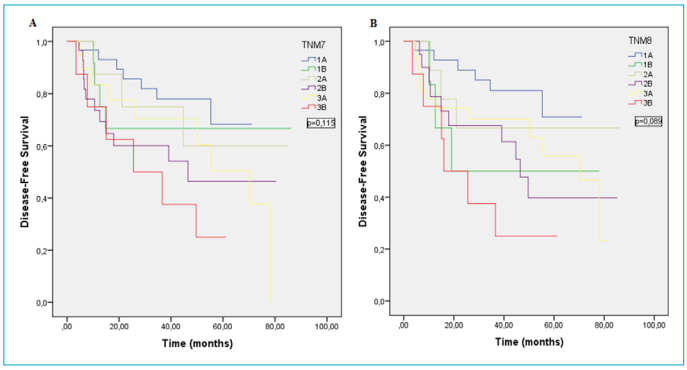

Figure 1. Disease-Free Survival According to TNM-7 and TNM-8.

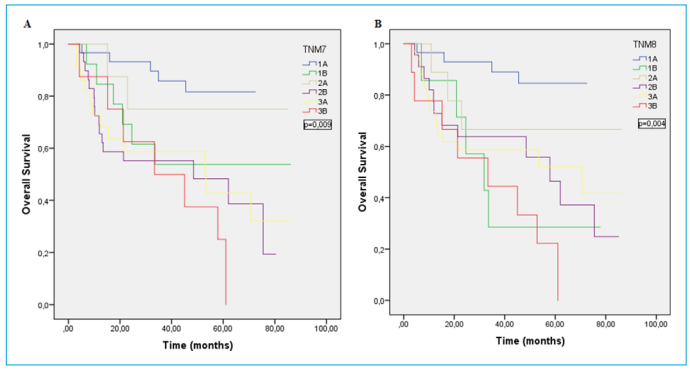

Figure 2. Overall Survival According to TNM-7 and TNM-8.

The changes in the stages of the patients were examined with the new classification system. Stage change was observed in 60 (53%) of 113 patients examined in our study. No patient with change in stage IA was detected. The number of patients who passed from IB to IIA stage was 7, the number of patients who passed from IIA to IIB was 35, the number of patients who passed from IIB to IIIA was 16, and the number of patients who passed from IIIA to IIIB was 2. Approximately 80% of the patients whose stages changed were horizontally upgraded, while 20% of the patients were upgraded between vertical groups. In the vast majority of patients whose stage was changed, the decision for adjuvant chemotherapy was not affected by stage change. However, a total of 7 patients had upgraded from Stage IB to Stage IIA. When the data of these 7 patients were re-examined, 3 patients received adjuvant chemotherapy and 4 patients did not. Adjuvant treatment was not considered appropriate for 1 of 4 patients who did not receive chemotherapy by the physician. The other 3 patients did not accept adjuvant treatment.

Discussion

In this study, we evaluated the classification of operated NSCLC patients according to TNM-7 and TNM-8 staging systems and the variation between groups. According to the new staging system, the majority of the patients showed upstage. However, a significant part of these upstages was among the groups that were already offered adjuvant therapy. In both staging systems, differences between stage groups in terms of DFS and OS were as expected. It is known from previously published studies that adjuvant therapy is most effective in patients with positive lymph nodes.[3] When the stage groups of the patients were examined, there was no patient change in the Stage IA group. In the stage IB group, the number of patients decreased by half. The area that we can call the 'grey zone' for the adjuvant treatment of lung cancer is Stage IB patients. There are different opinions on the guidelines on this issue. ESMO recommends adjuvant systemic therapy for patients with a tumor diameter of 4 or 5 cm although its contribution to survival in stage IB patients is controversial.[4] On the other hand, NCCN recommends adjuvant treatment at this stage in cases where there are some high risk factors, including tumor diameter greater than 4 cm, vascular invasion, and a history of inadequately performed oncological surgery.[5] However, the situation of giving treatment to Stage IB patients around the world still raises debates. The decrease in the number of IB patients in our study and the inclusion of these patients in the IIA group is also important in this respect. As a result of the evaluation of our study, there has been less 'grey zone' discussion with the TNM-8 classification. We retrospectively reviewed the data of 7 patients who were upgraded to stage IIA and checked whether they received adjuvant therapy. 3 of these patients received adjuvant treatment and 4 patients did not receive adjuvant treatment. In these patients who did not receive treatment, the patients were informed about the survival benefit of adjuvant chemotherapy and the side effects of the treatment, and the profit and loss situation were explained to the patients. Patients did not receive treatment because they did not accept adjuvant chemotherapy. The other 3 patients received chemotherapy. The median follow-up period of 3 patients who received chemotherapy was 22 months, and there was no recurrence in these patients. 3 of the patients who did not receive chemotherapy did not come to their follow-ups, and the other 1 patient is followed up without recurrence. The greatest number of patient changes were seen from IIA to IIB group, but there was no change in the treatment plan because there was no change in the adjuvant treatment recommendation at these stages. As a result, in our study, approximately 6% of patients experienced a stage change that could affect the treatment decision. This means more adjuvant treatment with TNM-8, more treatment-related side effects and more cost.

In a recently published study, it was determined that the TNM-8 classification did not differ about OS and prognosis after longer follow-up periods.[6]

The limitations of our study are that it was single-centered, the number of patients was small, and the median follow-up period was limited. With the participation of larger centers increasing the number of patients and increasing the median follow-up time to over 60 months, we can more clearly evaluate the clinical reflection of the TNM-8 classification.

Disclosures

Ethics Committee Approval: The study was performed according to the institutional ethical standards (Inonu University Medicine High School, Number: 2021/2088-01-06-2021).

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Conflict of Interest: Authors declare that there is no conflict of interest.

Authorship Contributions: Concept – A.G.; Design – A.G.; Supervision – A.G.; Materials – A.G.; Data collection &/or processing – A.G.; Analysis and/or interpretation – N.A.; Literature search – A.G.; Writing – A.G.; Critical review – N.A.

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