The IASLC Lung Cancer Staging Project

Proposals for the Revisions of the T Descriptors in the Forthcoming Eighth Edition of the TNM Classification for Lung Cancer

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Introduction: An international database was collected to inform the 8th edition of the anatomic classification of lung cancer. The present analyses concern its primary tumor (T) component.

Methods: From 1999 to 2010, 77,156 evaluable patients, 70,967 with non–small-cell lung cancer, were collected; and 33,115 had either a clinical or a pathological classification, known tumor size, sufficient T information, and no metastases. Survival was measured from date of diagnosis or surgery for clinically and pathologically staged tumors. Tumor-size cutpoints were evaluated by the running log-rank statistics. T descriptors were evaluated in a multivariate Cox regression analysis adjusted for age, gender, histological type, and geographic region.

Results: The 3-cm cutpoint significantly separates T1 from T2. From 1 to 5 cm, each centimeter separates tumors of significantly different prognosis. Prognosis of tumors greater than 5 cm but less than or equal to 7 cm is equivalent to T3, and that of those greater than 7 cm to T4. Bronchial involvement less than 2 cm from carina, but without involving it, and total atelectasis/pneumonitis have a T2 prognosis. Involvement of the diaphragm has a T4 prognosis. Invasion of the mediastinal pleura is a descriptor seldom used.

Conclusions: Recommended changes are as follows: to subclassify T1 into T1a (≤1 cm), T1b (>1 to ≤2 cm), and T1c (>2 to ≤3 cm); to subclassify T2 into T2a (>3 to ≤4 cm) and T2b (>4 to ≤5 cm); to reclassify tumors greater than 5 to less than or equal to 7 cm as T3; to reclassify tumors greater than 7 cm as T4; to group involvement of main bronchus as T2 regardless of distance from carina; to group partial and total atelectasis/pneumonitis as T2; to reclassify diaphragm invasion as T4; and to delete mediastinal pleura invasion as a T descriptor.

Key Words: Lung cancer, Lung cancer staging, T component, T descriptors, TNM classification, Tumor size.

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The 7th edition of the tumor, node, and metastasis (TNM) classification of lung cancer published in 2009 was based on the most thorough data-based revision ever done to date.[1–3] A retrospective international database including 81,495 evaluable patients collected from 1990 to 2000 by the International Association for the Study of Lung Cancer (IASLC) and analyzed by Cancer Research And Biostatistics (CRAB) was used for the revision.[4] The revision consisted of changes in the T descriptors that emphasized the prognostic impact of tumor size and redefined the classification of additional tumor nodules and malignant pleural effusion, the subclassification of M1, the validation of the classification for bronchopulmonary carcinoid tumors, and the rearrangement of stage grouping, whereas the N descriptors remained the same. Despite the magnitude of the database not all descriptors could be validated.[5] The limitations of the retrospective database prompted

the IASLC to launch a call for the collection of new data.[6] The call resulted in a new database of 77,156 evaluable patients diagnosed with lung cancer from 1999 to 2010.[7] This new database is being used now to inform the 8th edition of the TNM classification of lung cancer due to be published in 2016.

This article presents the results of the analyses of the new IASLC database performed by the members of the Primary Tumor (T) Subcommittee of the IASLC Staging and Prognostic Factors Committee and the statisticians of CRAB concerning the T component of the TNM classification and its descriptors. The analyses were conducted to achieve predefined objectives: to further assess the prognostic impact of tumor size; to assess the prognostic power of each descriptor defining the different T categories; and to study new conditions not included in the present T descriptors, such as differences between parietal pleura and rib invasion.[6]

PATIENTS AND METHODS

Population

The total number of patients diagnosed with lung cancer between 1999 and 2010 submitted to CRAB was 94,708. After exclusions, 77,156 (70,967 with non–small-cell lung cancer [NSCLC] and 6189 with small-cell lung cancer) remained for analysis.[7] In the NSCLC group, 33,115 patients met the T descriptors subcommittee's initial analytic requirements of M0 NSCLC, a complete set of either clinical (c) TNM or pathological (p) TNM, known tumor size, and sufficiently detailed T descriptors to support the assigned T category. There was sufficient clinical T descriptor information for 13,012 patients, including 12,449 who were eventually operated, distributed as follows: 10,084 (81.0%) cN0, 907 (7.3%) cN1, 1327 (10.7%) cN2, and 131 (1.1%) cN3. As for the analysis of the pathologic T, the population excluded those who had induction treatment and consisted of 30,018 patients with complete pTN and M0 tumors (9915 of these also provided complete cTN categories; Table 1). Their distribution according to the pN component is 22,257 (74.2%) pN0, 3465 (11.5%) pN1, 4157 (13.9%) pN2, and 139 (0.5%) pN3. Asia was the geographic region that contributed most to the IASLC database: 10,294 (79%) patients with clinically staged tumors and 23,838 (79%) with pathologically staged ones came from Japan, South Korea, and People's Republic of China (Supplementary Table 1, Supplemental Digital Content 1, http://links.lww.com/JTO/A834). Adenocarcinoma was the most common cell type, with 64% of tumors both clinically and pathologically staged. Squamous cell carcinoma followed with 25% of clinically staged tumors and 27% of pathologically staged tumors (Supplementary Table 2, Supplemental Digital Content 1, http://links.lww.com/JTO/A834). From the 30,018 patients with surgically resected and pathologically staged tumors, 28,150 (94%) were completely resected (Supplementary Table 3, Supplemental Digital Content 1, http://links.lww.com/JTO/A834). To assess the completeness of resection, the information given by the data providers was considered. When the specific residual tumor (R) status was unknown, the case was grouped in the "any R" category.

Statistical Analysis

Survival was measured from the date of diagnosis for clinically staged patients and date of surgery for pathologically staged patients. Overall survival was assessed using the Kaplan–Meier method. Prognostic groups were assessed using Cox proportional hazards regression analysis.[8] All survival and regression analyses were performed using SAS version 9.2.

Tumor-size cutpoints were evaluated using a running log-rank statistics produced by each hypothetical cutpoint in the pN0M0R0 data set graphed against tumor size.[9] This was performed both to confirm the 7th edition T category cutpoints defined by size (T1a, b; T2a, b; and T3) and to identify possible additional size increments that could be useful. For evaluating possible new size cutpoints, the tumor size that coincided with the highest log-rank statistics, rounded to the nearest 1 cm, was chosen as the optimal cutpoint. The chosen cutpoint was then tested in the context of the 7th edition

TABLE 1. Number of M0 Non–Small-Cell Lung Cancer Cases Passing Initial Screening[a]

	N0					Any N				
	Total	T1	T2	T3	T4	Total	T1	T2	T3	T4
Clinically staged										
Total	30,102	17,430	9498	2357	817	40,263	19,182	14,394	4380	2307
Analyzed	10,230	6436	2926	719	149	13,012	7100	4239	1305	368
Clinically staged, surgically managed										
Total	29,153	17,248	9200	2178	527	36,697	18,807	13,253	3664	973
Analyzed	10,084	6416	2873	682	113	12,449	7022	4049	1167	113
Clinically staged, nonsurgically managed										
Total	949	182	298	179	290	3566	375	1141	716	1334
Analyzed	146	20	53	37	36	563	78	190	138	157
Pathologically staged										
Total	26,722	12,857	10,510	2780	575	36,830	14,954	15,973	4756	1147
Analyzed	22,257	11,559	8411	2108	179	30,018	13,368	12,628	3620	402

[a]Criteria for T descriptor analysis: cases must have known tumor size, at least one T descriptor supporting the assigned T category, and no T descriptors suggesting a higher T category.