Getting familiar with the forthcoming eighth edition of TNM classification of lung cancer: from the T to N and M descriptors

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Lung cancer is one of the most common cancers worldwide, and is the leading cause of death from cancer in the United States (1). With the recent advances in screening, diagnosis, and treatment of this disease, guidelines are constantly being reviewed to provide the best in detection and therapy. Currently, the new TNM classification for lung cancer is being proposed by the International Association for the Study of Lung Cancer (IASLC), and the 8th edition of TNM staging system is expected to be released in 2016. The changes that are expected to occur to the T descriptors in lung cancer staging were presented in the July issue of the *Journal of Thoracic Oncology* by Ramón Rami-Porta *et al*. (2) in "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". The proposed revisions of the N and M descriptors have also been accepted to publish this year in the *Journal of Thoracic Oncology* (3,4).

The 7th edition of TNM classification, which is of current use, was released in January 2010. It grouped tumor sizes into 4 categories T1 (a and b), T2, and T3, compared to only 2 groups in the previous one. This classification was praised for the large databases that were available for review, and for the changes it brought to the T and M staging system. Despite the advances this classification offered, it had several limitations, including diversity and origins of the database, as it did not have adequate worldwide representation, and was collected in the 90s, during an era when more advanced imaging such as PET scan was not available. In addition, despite the scale of the database not all descriptors could be validated (5).

Prompted by those limitations, in the article of Rami-Porta *et al*. mentioned above (2), a new database collected from 1999 to 2010 was used for the T descriptors of the new edition. This database included 77,156 evaluable patients: 70,967 with non-small cell lung cancer and 33,115 had either a clinical or a pathological classification as well as sufficient T information. A careful analysis of survival and prognosis based on the T descriptors demonstrated a clear downward shift in survival with each centimeter increase in tumor size, suggesting a new T staging system with more subsets that differ in size by 1 cm is needed. The authors thus proposed the following revision: the cutoff between T1 and T2 remains at 3 cm, but T1 will include subclasses T1a (≤1 cm), T1b (>1 to ≤2 cm), and T1c (>2 to ≤3 cm). T2 will include T2a (>3 to ≤4 cm) and T2b (>4 to ≤5 cm). T3 will go from 5 to 7 cm, as there was no difference found in survival at the 6 cm cutoff. Finally T4 will have tumors >7 cm. This data-driven revision shows that, as previously thought, the larger the tumor is, the worse the prognosis. In addition to these size classifications, other important changes have been suggested based on the association between the prognosis and specific descriptors. For example, tumors involving the main bronchus have shown similar prognosis to the T2 subset, and will be classified as such, regardless of the distance to the carina. Previously, tumors closer than 2 cm from the carina were labeled T3. Conversely tumors invading the diaphragm will be labeled T4, rather than the current T3 as this was found to be a poor prognostic indicator. Either partial or total atelectasis, or pneumonitis caused by the tumor will go under T2, in comparison

to total atelectasis being under T3 currently. Finally, mediastinal pleural invasion, which is an entity difficult to determine clinically, will no longer be a T subset.

Using the same approach but different databases, proposals for N and M revision were also accepted to publish in the *Journal of Thoracic Oncology* (3,4). Briefly, although current N descriptors adequately predict the prognosis, a more precise sub-classification of N1 into N1a (single station) and N1b (multiple stations); and N2 into N2a1 (single N2 station without N1 involvement), N2a2 (single N2 station with N1 involvement) and N2b (multiple N2 stations) were proposed (3). Regarding M descriptor, the current M1b was recommended to sub-classified into M1b (single distant metastatic lesion) and M1c (multiple distant metastatic lesions) due to better survival observed in patients with M1b than with M1c (4). All these proposed revisions including those of T descriptors will be incorporated into the 8th edition of TNM staging system.

These changes are important to better prognosticate patients, and will help in better determining patients that are eligible for surgery. However, despite these advances, the authors do note limitations. Specifically for the T descriptors in Rami-Porta *et al.*'s article, the database that was used did not always have all descriptor needed for analysis, e.g., the tumor size was always available, but not all characteristics of said sample was recorded. Further, the T3 and T4 subsets did have a smaller size, so some comparisons could not be made for these subsets, and as such were not reported. In addition, the database is largely taken from Asia, and as such is also not ideal worldwide representative of the disease and selection bias might exist. Finally, in the era of targeted therapy, since sensitizing mutations such as of EGFR and ALK significantly impact treatment response and outcome (6,7), it will be of great value to find a way to incorporate these findings into the purely anatomy based TNM classification. Nevertheless, we shall congratulate the achievement made by the authors and we are looking forward to the 8th edition of TNM classification to be published in 2016 and enacted in 2017.

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Footnote

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