Lumping, Splitting, and Sorting

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A staging system is an evolutionary process, and it requires periodic revision. This issue reports the proposed latest revision of the lung cancer staging system with respect to the definition of the T component. Distinct strengths of this revision are the remarkable size of the database that has been compiled, the sophistication of the analysis, and the attention to validation of the proposed new definitions. It is based on 100,869 patients, gleaned from multiple registries, centers, and series representing Europe, North America, Asia, and Australia, and it includes patients with all stages and histologic types of lung cancer. In contrast, the previous iteration of the staging system was based on 5319 patients who were exclusively from North America; it included few patients with SCLC, and it underrepresented nonsurgical patients.

The purposes of a staging system are to establish a common terminology, to define prognosis, to define cohorts with similar treatment strategies, and, lastly, to group patients by the biologic behavior of their tumors. The primary focus chosen by the staging committee is prognostication; therefore, the emphasis is on postresection pathologic classification. Nevertheless, clinicians will want to use this system to guide clinical management decisions, most of which are made before treatment. We must be careful in extrapolating the data from the pathologic stage to the pretreatment situation. What we would really like, of course, is to predict a tumor’s biologic behavior and group patients accordingly. Unfortunately, our ability to do this is limited, although there is hope that the evolving genetic characterization of tumors will provide this.

It is good that the proposed T staging system emphasizes tumor size, because this can be easily determined before treatment. Nevertheless, because treatment strategies also evolve, it will be important to keep track of details in addition to the T classification. For example, adjuvant chemotherapy trials should record the actual size of the tumors—not just whether they are T2a or T2b.

The issue of the underlying biologic behavior is best illustrated by the difficulties in trying to classify an additional focus of cancer in the lung parenchyma separate from the primary mass. A reasonable amount of data suggest that an additional focus in the same lobe represents a form of local spread; indeed, prognosis and treatment strategy are not altered in a major way by a same-lobe satellite nodule. A second focus in a different lobe, nevertheless, is more problematic. Is this evidence of field cancerization (a second primary), an unusual form of intrapulmonary spread, or a solitary distant metastasis that happens to be in the lung? Understanding this would have significant implications for the treatment. Simply grouping according to observed prognosis (which may be highly dependent on the treatment strategy chosen) may be purely arbitrary and misleading. Furthermore, this area is complicated by the possibility of ethnic and environmental differences. The incidence of separate foci of cancer seems to be higher in Asia, and it may represent a different tumor biology than on other continents (i.e., higher incidence of adenocarcinoma or a higher rate of response of endothelial growth factor receptor inhibitors). Again, authors reporting results in these patients should detail specific subgroups rather than pooling all T4 patients together, so that we can learn how we should be thinking about these patients.
Grouping patients purely by prognosis is problematic because it is a moving target. As treatments evolve, outcomes change. Furthermore, it is becoming increasingly clear that a diagnosis of lung cancer is not a black and white matter; there are shades of gray along a spectrum of biologic aggressiveness. Importantly, the spectrum of disease identified (and, therefore, the prognosis) changes as technology advances. Lung cancers that are associated with 10- and 20-year survival without treatment are being recognized, perhaps because of a proliferation of computed tomography imaging. We must be careful to develop systems that can adjust to changes, because the pace of change can only be expected to increase.

Like any good scientific study, the proposed staging revision leaves at least as many questions open to future investigation as it answers. What is the best size criterion to distinguish between T1 and T2 subgroups? Should this be based on the overall size or on the size of the solid components in patients with a ground-glass periphery? Should the T classification be the same for different tumor types, and should it be the same for patients on different continents? The proposed classification system is particularly strong because it is derived from an international cohort and because it has been internally and externally validated. It gives us a common language to speak. But we must be careful to go beyond the system in describing populations that are potentially grouped more arbitrarily. As our knowledge evolves, particularly with molecular genetic analysis, we may define distinctions that are not yet clearly apparent. I look forward to challenges and refinements as the thoracic oncology community deliberates the proposed new staging classification.

REFERENCES