The IASLC Lung Cancer Staging Project: The New Database to Inform the Eighth Edition of the TNM Classification of Lung Cancer

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Abstract: The analyses of the retrospective database of the International Association for the Study of Lung Cancer (IASLC), consisting of more than 81,000 evaluable patients diagnosed with lung cancer between 1990 and 2000, formed the basis of recommendations to the Union for International Cancer Control and the American Joint Committee on Cancer for the revision of the sixth edition of the tumor, node, and metastasis (TNM) classification of lung cancer. However, despite the large number of patients, not all descriptors could be validated. This prompted a new collection of retrospective and prospective data to overcome the limitations of the original retrospective database. The new IASLC database has information on 94,708 new patients diagnosed of lung cancer between 1999 and 2010. They originated from 35 sources in 16 countries, and 4,667 were submitted via the online electronic data capture system. Europe contributed 46,560 patients, Asia: 41,705, North America: 4,660, Australia: 1,593, and South America: 190. After exclusions, 77,156 (70,967 with nonsmall cell lung cancer and 6,189 with small cell lung cancer) remained for analysis. This database will be analyzed according to established objectives for the T, the N, and the M components to inform the eighth edition of the TNM classification of lung cancer due to be published in 2016. The IASLC hopes for the continuing contribution of our partners around the world to improve the classification of anatomical extent of disease, but also to create prognostic groups in a parallel project of the IASLC Staging and Prognostic Factors Committee.

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The call for action launched during the International Workshop on Intrathoracic Staging, that took place in London, United Kingdom, in October 1996[1] to revise and improve the tumor, node, and metastasis (TNM) classification of lung cancer, resulted in an unprecedented response from groups and institutions around the world. By 2005, data on 100,869 patients diagnosed of lung cancer between 1990 and 2000 were submitted to the International Association for the Study of Lung Cancer (IASLC) database at Cancer Research And Biostatistics (CRAB). These data originated from 46 different sources in 20 countries of Europe, North America, Asia, and Australia. After exclusions, 81,495 patients were available for analyses: 68,463 with nonsmall cell lung cancer (NSCLC) and 13,032 with small cell lung cancer (SCLC).[2] From the analyses of these data, a series of research articles on the T,[3] the N,[4] and the M[5] components of the TNM classification were peer-reviewed and published in the *Journal of Thoracic Oncology* for public discussion. In a similar manner, a revised stage grouping was proposed,[6] the new findings were internally and externally validated,[7] and the TNM classification was tested and validated for SCLC[8,9] and, for the first time in the history of the anatomical staging of malignant tumors, for broncho-pulmonary carcinoids.[10] In addition, a new lymph node map, resulting from an international and multidisciplinary consensus and reconciling the differences of the previous ones, was proposed for prospective validation;[11] and a new definition of visceral pleura invasion was agreed based on the published data.[12] The nonanatomic information included in the database was used to create prognostic groups before and after surgical treatment based on the combination of anatomic staging and very simple clinical variables, such as age, gender, and performance status.[13,14] The recommendations for changes in the TNM classification of lung cancer derived from the analyses of the IASLC database (Table 1) were submitted

to the Union for International Cancer Control (UICC) and the American Joint Committee on Cancer (AJCC), and were accepted and subsequently published in the seventh edition of their staging manuals.[15,16] At the same time, the IASLC produced the *Staging Handbook in Thoracic Oncology* and the *Staging Manual in Thoracic Oncology* including the TNM classifications of lung cancer and mesothelioma, the general rules of the TNM classification, site-specific rules for lung cancer and mesothelioma, and complementary chapters on survival analyses, prognostic factors, frequently asked questions and the history of the TNM classification since its inception by Pierre Denoix in the mid 20th century.[17,18] With this contribution, the IASLC became the primary source of database-based evidence to revise subsequent editions of the UICC and the AJCC TNM classifications of thoracic malignancies.

Despite the vastness of the IASLC database, not all descriptors of the T, the N, and the M components of the anatomical classification could be validated. The main reason was that many of the original datasets of the contributing databases had not been designed to study the TNM classification. The resulting lack of detailed data prevented the analyses of many descriptors. For the T component, only could tumor size, additional tumor nodule(s) and pleural effusion be analyzed reliably. For the N component, the present categories could be validated in the clinical and pathological staging. However, the

TABLE 1. Innovations Introduced in the seventh Edition of the Tumor, Node, and Metastases Classification of Lung Cancer

Descriptor/TNM	Category/Stage in the sixth Edition	Category/Stage in the seventh Edition
Tumor size ≤ 2 cm	T1	T1a
Tumor size > 2 cm but ≤ 3 cm	T1	T1b
Tumor size > 3 cm but ≤ 5 cm	T2	T2a
Tumor size > 5 cm but ≤ 7 cm	T2	T2b
Tumor size > 7 cm	T2	T3
Additional tumor nodule(s) in the same lobe of the primary tumor	T4	T3
Additional tumor nodule(s) in another ipsilateral lobe	M1	T4
Pleural dissemination (malignant pleural effusion and separated pleural nodules)	T4	M1a
Pericardial dissemination (malignant pericardial effusion and separated pericardial nodules)	N/A	M1a
Intrathoracic metastases	M1	M1a
Extrathoracic metastases	M1	M1b
T2b N0 M0	IB	IIA
T2a N1 M0	IIB	IIA
T4 N0-1 M0	IIIB	IIIA

TABLE 2. Number of Cases Submitted by Each Data Source, by Continent

Region	Data Source	EDC Source	N
Asia	EDC	Guangdong General Hospital, China	739
		Shanghai Lung Tumor Clinical Medical Center, China	51
	Japan 1999		13,344
	Japan 2002		14,695
	Japan 2004		10,889
	South Korea		1,987
Australia	EDC	Peter MacCallum Cancer Centre	4
	Prince Charles		229
	Sydney		1,360
Europe	Belgrade, Serbia		88
	Denmark		33,949
	EDC	Athens School of Medicine, Greece	39
		Clinical Center of Serbia, Serbia	40
		GCCB-S, Spain	2,362
		L'Institut Mutualiste Montsouris, France	120
		Military Medical Academy, Serbia	20
		Antwerp University Hospital, Multidisciplinary Oncological Centre Antwerp (MOCA), Belgium	195
		University Hospital Ghent, Belgium	85
		University of Torino, Italy	4
	Norway		2,354
	Turkey		7,304
North and South America	EDC	Alexander Fleming Institute, Argentina	6
		Clinica y Maternidad Suizo Argentina, Argentina	3
		Fundación Clínica Valle del Lili, Colombia	2
		Good Samaritan Hospital, USA	10
		Hospital Británico de Buenos Aires, Argentina	68
		Hospital Universitario Austral, Argentina	46
		Hospital Universitario-Fundación Favaloro, Argentina	36
		Hospital de Rehabilitación Respiratoria, Argentina	14
		Mayo Clinic Rochester, USA	47
		New York University Langone Medical Center and Cancer Center, USA	688
		Penrose Cancer Center, USA	73
		University of Sao Paulo Medical School, Brazil	15
	MDACC, USA		2,415
	MSKCC, USA		1,427
Global Total			94,708

GCCB-S, Grupo Cooperativo de Carcinoma Broncogénico de la Sociedad Española de Neumología y Cirugía Torácica; NYU, New York University; MDACC, M. D. Anderson Cancer Center; MSKCC, Memorial Sloan-Kettering Cancer Center.