



Updates on the Version 9 American Joint Committee on Cancer Staging System for Lung Cancer

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The tumor, node, metastasis (TNM) classification is the global system that reflects the anatomic extent of cancer. The American Joint Committee on Cancer (AJCC) and Union for International Cancer Control (UICC) have played a principal role in publishing and revising the international TNM classifications. The AJCC has engaged expert panels for each disease site to review and publish updates to the TNM classification for cancers based on evidence, in consultation with the UICC.

The TNM classification for lung cancer was first described in the UICC book, *TNM Classification of Malignant Tumours*, published in 1968.¹ The revised version was subsequently incorporated into the second edition of the UICC *TNM Classification of Malignant Tumours* published in 1975 and the first edition of the *Manual for Staging of Cancer* published by the AJCC in 1977.^{2,3} The revisions were repeated afterward with the efforts of Dr. Clifton Mountain and colleagues, who had collected a lung cancer database of more than 5,000 patients for that purpose. The international staging system for lung cancer was implemented and accepted worldwide. As the TNM classification became more widely used, the limitations of its database, which exclusively included patients treated surgically in North America, became more apparent. To collect more extensive data from around the world, the International Association for the Study of Lung Cancer (IASLC),

the only global organization dedicated to the study of lung cancer, was suggested to take over the role of proposing the new revision of the TNM classification. In 1997, the IASLC established a multidisciplinary International Staging Committee, now known as the Staging and Prognostic Factors Group (SPFG), to begin the first phase of the IASLC International Staging Project to revise and improve the TNM classification of lung cancer.

The first phase of the IASLC International Staging Project collected data from 100,869 lung cancer cases diagnosed between 1990 and 2000 from 45 sources in 20 countries in Europe, North America, Asia, and Australia. The data were analyzed to revise the TNM classification. Recommendations for changes to the TNM classification of lung cancer were submitted to and accepted by the UICC and AJCC as their seventh edition of the staging classifications for lung cancer, which were enacted in 2010.^{4,5}

The second phase of the IASLC International Staging Project began in 2009 and resulted in a new database containing 94,708 cases of lung cancer diagnosed between 1999 and 2010 from 35 sources in 16 countries in Europe, Asia, North America, Australia, and South America. Proposed recommendations for revising the TNM classification were adopted by the UICC and AJCC as their eighth edition of the TNM classification for lung cancer.^{6,7} The changes between the seventh and eighth editions included segmentation of the T categories and an emphasis on the size of the solid component on computed tomography and the invasive component on pathologic examination.^{8,9} The eighth edition of the TNM classification has been implemented worldwide since 2017, except in North America, where it was delayed until 2018.

For the third phase of the IASLC International Staging Project, a new database of lung cancer cases diagnosed

FIG. 1 Eighth edition and Version 9 anatomic stages. The changes in Version 9 stages result from the subdivision of the N2 category into N2a and N2b and their different prognoses. The subdivision of M1c into M1c1 and M1c2 did not result in any changes because both remain in stage IVB

8th Edition TNM Categories and Stages

8 th Edition TNM Categories					
T/M	Label	N0	N1	N2	N3
T1	T1a	IA1	IIB	IIIA	IIIB
	T1b	IA2	IIB	IIIA	IIIB
	T1c	IA3	IIB	IIIA	IIIB
T2	T2a	IB	IIB	IIIA	IIIB
	T2b	IIA	IIB	IIIA	IIIB
T3	T3	IIB	IIIA	IIIB	IIIC
	T4	IIIA	IIIA	IIIB	IIIC
M1	M1a	IVA	IVA	IVA	IVA
	M1b	IVA	IVA	IVA	IVA
	M1c	IVB	IVB	IVB	IVB

Version 9 TNM Categories and Stages

Version 9 TNM Categories					
T/M	Label	N0	N1	N2	N3
T1	T1a	IA1	IIA	IIB	IIIA
	T1b	IA2	IIA	IIB	IIIA
	T1c	IA3	IIA	IIB	IIIA
T2	T2a	IB	IIB	IIIA	IIIB
	T2b	IIA	IIB	IIIA	IIIB
T3	T3	IIB	IIIA	IIIA	IIIB
T4	T4	IIIA	IIIA	IIIB	IIIC
M1	M1a	IVA	IVA	IVA	IVA
	M1b	IVA	IVA	IVA	IVA
	M1c1	IVB	IVB	IVB	IVB
	M1c2	IVB	IVB	IVB	IVB

between January 2011 and December 2019 was established. The newly formed database was composed of 124,581 cases. The data came from 25 countries and 75 unique sites, including Asia/Australia (69,749 cases, 56.0%), Europe (30,827 cases, 24.7%), North America (19,608 cases, 15.7%), South/Central America (4,225 cases, 3.4%), and Africa and the Middle East (172 cases, 0.1%).¹⁰ After cleaning the contents of the dataset, analyses were performed based on the anatomical extent of the disease and the patient's survival status. The results were proposed to the UICC and AJCC as the ninth edition of the TNM classification for lung cancer. The recommendations were accepted, with the AJCC publishing them as the Version 9 of the cancer staging system at the end of 2024 and becoming effective for implementation in January of 2025.¹¹

REVISIONS IN THE AJCC VERSION 9 FOR LUNG CANCER

For Version 9 of the lung cancer staging, no changes were made to the T definitions of the T categories in the eighth edition. One hypothesis was stated that patients with tumors with obvious chest wall invasion or parietal pleura involvement (PL 3) had a worse prognosis compared with patients with tumors characterized by the other single T3 definitions. Although pathologic chest wall or PL 3 invasion yielded a lower survival rate compared with the other T3 definitions, this difference was not observed for clinical chest wall or PL 3 tumors. Because of these inconsistent findings, no reallocation of chest wall or PL 3 tumors was made. In Version 9 of the AJCC *Cancer Staging System*, certain specific descriptions were added to the T categories, including the following: the invasion of an adjacent lobe is T2a; the pericardium, with no distinction between parietal and visceral, phrenic nerve, azygos vein, thoracic nerve roots, and stellate ganglion are T3 category; and thymus, vagus nerve, supra-aortic arteries

and brachiocephalic veins, subclavian vessels, lamina, spinal canal, cervical nerve roots, and brachial plexus are T4.

An important change was made to the N category in Version 9. N2, which indicates metastasis in the ipsilateral mediastinal and/or subcarinal lymph node(s), was split into N2a and N2b.¹³ N2a denotes metastasis limited to a “single” ipsilateral mediastinal or subcarinal station, whereas N2b denotes metastases in “multiple” mediastinal or subcarinal stations. Because survival analyses demonstrated a clear and consistent prognostic difference between single and multiple N2 station involvement in both clinical and pathologic stages, this change was adopted in Version 9. No changes were made to the N1 and N3 categories.

Another important revision was made to the M category. M1c, which indicates multiple extrathoracic metastases in a single or multiple organ system[s], was divided into M1c1 and M1c2.¹⁴ M1c1 denotes multiple extrathoracic metastases in a single organ system, whereas M1c2 denotes multiple extrathoracic metastases in several organ systems. No changes were made to the M1a and M1b categories. Stratified multivariable analyses revealed progressively worse survival for patients with tumors involving the Version 9 M1 categories (M1a/1b, M1c1, and M1c2). Each of these comparisons demonstrates statistical significance after adjusting for potentially confounding factors.

The stage groups were reassigned according to the prognostic analyses by using the new N and M categories¹⁵ (Fig. 1). Consequently, T1N2a was assigned to stage IIB and T1N1 was reassigned from stage IIB to stage IIA. T2N2b was newly assigned to stage IIIB, while T3N2a was newly assigned to stage IIIA. Although N2 disease had been assigned to stage III in the previous TNM classifications, T1N2a was newly assigned to stage IIB in the AJCC Version 9. The survival curves of the AJCC Version 9 edition stage groups demonstrated strong discrimination between the adjacent stages. Although M1c was split into

M1c1 and M1c2, no changes of stage assignment were made to M1 diseases.

FUTURE DIRECTIONS

The revisions between the eighth edition and Version 9 of the TNM classification of lung cancer were based on the prognostic impact of the anatomic extent of disease analyzed in the IASLC database, which included lung cancer cases submitted from around the world. Careful consideration was given to balancing high specificity in prognostic characterization with global ease of application. The development of Version 10 will address some remaining gaps in anatomic classification and will also focus on nonanatomic factors (e.g., molecular biomarkers) that may support the development of prognostic groups. Available data were insufficient to incorporate nonanatomic factors in Version 9.

CONCLUSIONS

The AJCC Version 9 of the TNM classification of lung cancer was established through the global efforts led by the IASLC. Although no changes were made to the T categories, N2 was split into N2a and N2b, while M1c was divided into M1c1 and M1c2. N2a denotes metastasis limited to a “single” ipsilateral mediastinal or subcarinal station and N2b denotes metastases in “multiple” mediastinal or subcarinal stations. M1c1 denotes multiple extrathoracic metastases in a single organ system, and M1c2 denotes multiple extrathoracic metastases in several organ systems. For the stage groups, T1N2a was assigned to stage IIB. T1N1 was downstaged from stage IIB to stage IIA. T2N2b was assigned to stage IIIB, and T3N2a was assigned to stage IIIA. This new version of the TNM classification is based on the analyses of overall survival according to the anatomic extent of the disease within an international dataset.

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