

A NEW INTERNATIONAL STAGING OF LUNG CANCER

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Abstract

New recommendations for staging lung cancer using the TNM system for description of the primary tumor (T), the regional lymph nodes (N), and distant metastases (M) have been adopted by the American Joint Committee on Cancer and the Union Internationale Contre le Cancer. Revisions in TNM definitions and stage grouping rules were made in response to the needs of investigators throughout the world for staging that is consistent in meaning among all specialties and among all countries. The new international system has five stage groups, 0, I, II, IIIa, IIIb and IV, that provide for classification of six levels of disease extent. A number of elements used in prior staging recommendations have been retained; however, new descriptors for the degree of progression in tumors with extrapulmonary extension and for the levels of regional lymph node metastasis have been structured. The new system allows for specific definition of «limited» and «extensive» disease categories that can be reproduced and compared. It meets the goal of providing an internationally acceptable staging system for lung cancer that is useful for estimating prognosis, reporting end results and selection of appropriate treatment.

Introduction

The new International System for Staging Lung Cancer is a classification for the extent of disease that has consistent meaning among specialists and countries throughout the world. This descriptive nomenclature was developed to meet the need for a staging system responsive to requirements for contemporary treatment planning, as well as for estimating prognosis and reporting end results. The Union Internationale Contre le Cancer (UICC), the American Joint Committee on Cancer (AJCC), the International Association for the Study of Lung Cancer, the Spanish Society of Respiratory Pathology, and the Japanese Cancer Committee have adopted the International System as the official staging nomenclature for lung cancer.

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Relevance of Staging Principles

It is generally accepted that the extent of disease at the time of diagnosis is a harbinger of survival in patients with lung cancer. Present treatment modalities are limited in their potential for cure by this element. Therefore, precise and accurate description of the extent or stage of the disease in a way that is readily communicated and reproduced is of major importance.

Focus of classification problems

For a number of years investigators in many countries have used the recommendations of the UICC¹ and the AJCC² for staging lung cancer. Variations in the use of these systems were made that reflected individual needs and the survival experience of specialized practice. We studied the variations reported in the literature and the recommendations expressed by treatment specialty groups. A number of staging problems were identified that argued for revision of the TNM definitions and stage grouping rules to provide a system that could be universally accepted and used. This work was parallel to the careful evaluation of problems in staging lung cancer accomplished by the Work Group on Bronchogenic Carcinoma Classification of the Spanish Respiratory Pathology Society (SEPAR). The similarity of their approach and the findings of the SEPAR group were an invaluable resource for confirming the validity of the new system.

Stage Grouping and TNM Descriptors

The study of staging problems revealed substantial differences in the survival characteristics of TNM subsets within stage groups. For example, in the large experience of the Japanese Cancer Committee³ the reported end results for patient with T1 N1 M0 disease were closer to those of the Stage II patients, T2 N1 M0, than to the end results for patients in the other Stage I subsets, T1 N0 and T2 N0 M0 disease.



Problems with the TNM descriptors related to classification of (1) tumors with extrapulmonary extension and (2) regional lymph nodes. The T3 category included a wide range of disease situations, from limited invasion of the parietal pleura to extensive involvement of mediastinal structures. All patients with pleural effusion were classified T3, whether or not malignant cells were identified. The N2 definition included both ipsilateral and contralateral mediastinal lymph nodes. Supraclavicular or scalene nodes were classified in the M1 category with distal metastatic sites; however, these nodes are designated «regional» by the radiation oncologist and the treatment approach for regional disease is different from that for distant metastases⁴. The common designations of «limited» and «extensive» disease categories for patients within the AJCC Stage III group were inconsistently defined. Need for more precise and standard description of these levels of disease extent was noted, particularly by physicians involved with the treatment of small cell carcinoma⁵.

Recommendations for Revisions in Staging

My approach for making recommendations to resolve these problems was to assemble a collective data base of 3,753 cases of primary lung cancer treated in a contemporary time frame. This data was contributed from two sources: (1) Sequential patients treated at the University of Texas M.D. Anderson Hospital and Tumor Institute from 1975-1980, only surgical patients 1981-1982 and, (2), patients treated at 45 general and teaching hospitals participating in the United States National Cancer Institute Lung Cancer Study Group (LCSSG) Adjuvant Trials Program. The LCSSG cases were submitted to the Reference Center for Anatomic and Pathologic Classification of Lung Cancer from 1977-1982 for confirmation of histological cell type and stage. A study of survival of patients in each of the TNM subsets, classified according to the AJCC 1979 staging recommendations, showed that a number of different combinations were rational for revision of stage grouping rules. The subsets could be grouped several ways, providing from three to five stages, each stage composed of TNM subsets with similar outcomes and each with a unique survival rate. One such revision of stage grouping rules was published⁶. However, revision of stage grouping rules, would not resolve the problem of staging that could be related to contemporary treatment planning, or of providing reproducible descriptors for «limited» and «extensive» disease.

To meet this challenge new definitions for the primary tumor were structured that would discriminate patients with limited, extrapulmonary extension from those with more widespread mediastinal involvement. Survival analysis supported the

separation of these groups into T3 and T4 categories. We followed the same procedure for classification of regional lymph nodes. New definitions for categories of N2 and N3 disease were structured to differentiate patients with metastases confined to the ipsilateral mediastinal and subcarinal nodes, N2, from those with more extensive lymph node involvement. The contralateral mediastinal and hilar lymph nodes and the ipsilateral and contralateral supraclavicular/scalene nodes were defined as N3. The survival rate for patients with metastases to supraclavicular/scalene lymph nodes was not statistically significantly better than that of patients with metastasis to a single distant site. However, this description is consistent with radiotherapy treatment planning requirements. Survival studies according to these definitions supported the rationale for their use.

If a staging system is to be universally used, it must be easily remembered and applied. This stipulation places limitations on the development of any classification scheme. A large number of prognostic groups could be identified by both data and clinical observations; however, a system that discriminated all of them would be unmanageable. The clinical components that had major impact on the selection of treatment programs and on survival rates were chosen for incorporation in the International Staging System.

International agreement

The new International System for Staging Lung Cancer was derived from the integrated studies and recommendations of the international TNM committees of the UICC and the Task Force on the Lung of the AJCC. My studies and recommendations were reviewed by the Task Force members, along with their own end results⁷⁻¹⁰, the end results of many other investigators¹¹⁻¹⁵, and the recommendations of the UICC TNM study groups. The Task Force then made recommendations for revision of the 1979 AJCC staging system for lung cancer that were consistent with international objectives. The UICC made recommendations for modification of their system and the TNM definitions and the stage grouping rules, shown in Tables I, II, III, were agreed on by all of the international representatives¹⁶.

The new system retains valid and useful components of prior recommendations and has new elements to meet the needs of treatment specialists for staging that is related to therapeutic options—as well as to prognosis and reporting of end results.

TNM definitions

Selected new T and N descriptors are illustrated in Figs. 1-6.



TABLA I
International Staging System for Lung Cancer
TNM Definitions

Primary Tumor (T)	
TX	Tumor proven by the presence of malignant cells in bronchopulmonary secretions but not visualized roentgenographically or bronchoscopically, or any tumor that cannot be assessed as in a retreatment staging.
TO	No evidence of primary tumor.
TIS	Carcinoma in situ
T1	A tumor that is 3.0 cm or less in greatest dimension, surrounded by lung or visceral pleura, and without evidence of invasion proximal to a lobar bronchus at bronchoscopy.*
T2	A tumor more than 3.0 in greatest dimension, or a tumor of any size that either invades the visceral pleura or has associated atelectasis or obstructive pneumonitis extending to the hilar region. At bronchoscopy, the proximal extent of demonstrable tumor must be within a lobar bronchus or at least 2.0 cm distal to the carina. Any associated atelectasis or obstructive pneumonitis must involve less than an entire lung.
T3	A tumor of any size with direct extension into the chest wall (including superior sulcus tumors), diaphragm, or the mediastinal pleura or pericardium without involving the heart, great vessels, trachea, esophagus or vertebral body, or a tumor in the main bronchus within 2 cm of the carina without involving the carina.
T4	A tumor of any size with invasion of the mediastinum or involving heart, great vessels, trachea, esophagus, vertebral body or carina presence of malignant pleural effusion.*
Nodal Involvement (N)	
NO	No demonstrable metastasis to regional lymph nodes.
N1	Metastasis to lymph nodes in the peribronchial or the ipsilateral hilar region, or both, including direct extension.
N2	Metastasis to ipsilateral mediastinal lymph nodes and subcarinal lymph nodes.
N3	Metastasis to contralateral mediastinal lymph nodes, contralateral hilar lymph nodes, ipsilateral or contralateral scalene or supraclavicular lymph nodes.
Distant Metastasis (M1)	
MO	No (know) distant metastasis.
M1	Distant metastasis present - Specify Site (s)

TABLA II
Explanatory Footnote to TNM Definitions

T1*
The uncommon superficial tumor of any size with its invasive component limited to the bronchial wall which may extend proximal to the main bronchus is classified as T1.
T4*
Most pleural effusions associated with lung cancer are due to tumor. There are, however, some few patients in whom cytopathological examination of pleural fluid (on more than one specimen) is negative for tumor, the fluid is non-bloody and is not an exudate. In such cases where these elements and clinical judgment dictate that the effusion is not related to the tumor, the patients should be staged T1, T2 or T3, excluding effusion as a staging element.

TABLA III
International Staging System for Lung Cancer

STAGE GROUPING	
OCCULT CARCINOMA	
TX NO MO	
STAGE 0	
Carcinoma in situ	
STAGE I	
T1 NO MO	
T2 NO MO	
STAGE II	
T1 N1 MO	
T2 NO MO	
STAGE IIIa	
T3 NO MO	
T3 N1 MO	
T1-3 N2 MO	
STAGE IIIb	
Any T	Any N3 MO
T4	Any N MO
STAGE IV	
Any T	Any N M1

T-primary tumor

Four distinct levels of tumor progression are identified by the T1, T2, T3 and T4 descriptors that have different implications for treatment selection and prognosis, depending on the presence or absence of lymph node or distant metastases. The *T1* category identifies tumors less than or equal to 3 cm with no invasion of the main stem bronchus or pleura. The footnote shown in Table I has been added to the *T1* definition to aid in the classification of the uncommon superficial tumor with the invasive component limited to the bronchial wall, which may spread along the main bronchus. *T2* designates tumors larger than 3 cm or those involving the visceral pleura or main bronchus, regardless of size, and those with atelectasis or obstructive pneumonitis extending to the hilar region. The *T3* category discriminates tumors with limited, circumscribed, extrapulmonary extension involving the chest wall, the proximal main bronchus, mediastinal pleura or pericardium (Fig. 1). Included are tumors originating in the superior sulcus that have no accompanying Pancoast's syndrome or invasion of the vertebral body (Fig. 2). *T4* identifies those tumors with extensive extrapulmonary extension involving the mediastinum, major vessels, nerves, or, in the case of Pancoast's tumors, the vertebral body (Figs. 3-4).

Pleural effusion

To resolve the question of the implications of the presence of pleural effusion, a footnote has been included with the definitions. In patients with lung cancer pleural effusion is usually related to the malignancy and is a poor prognostic sign. In a few patients, however, cytopathological examina-

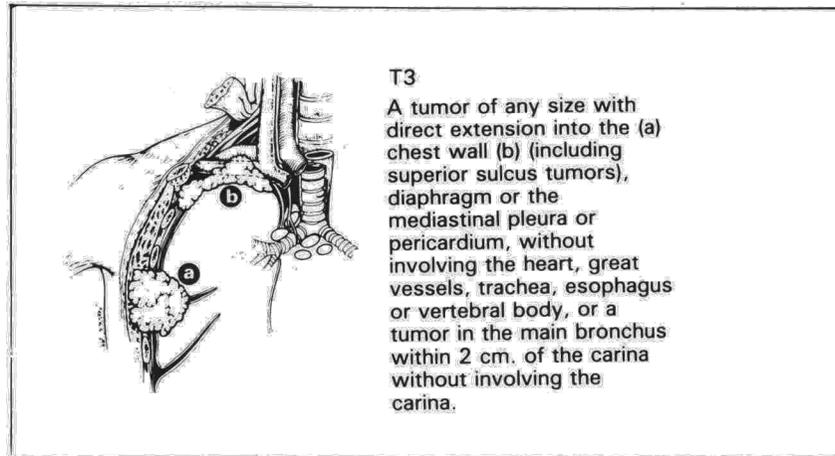
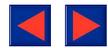


Fig. 1. T3: A tumor of any size with direct extension into the (a) chest wall (b) including superior sulcus tumors.

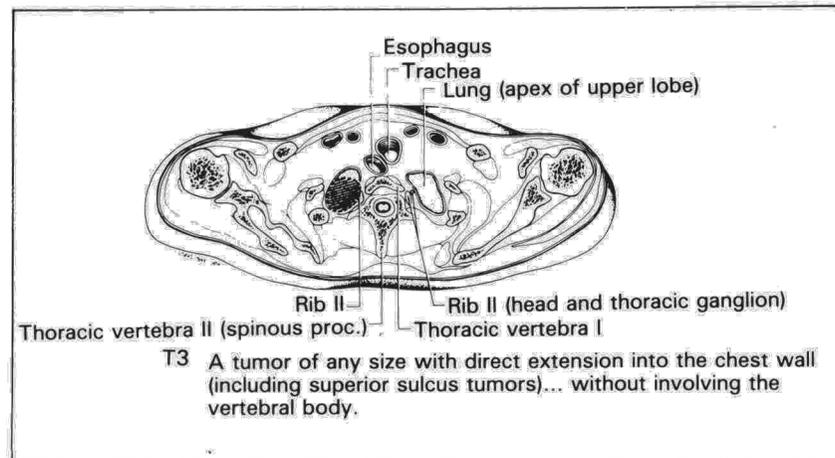


Fig. 2. T3: Superior sulcus tumor with no involvement of the vertebral body.

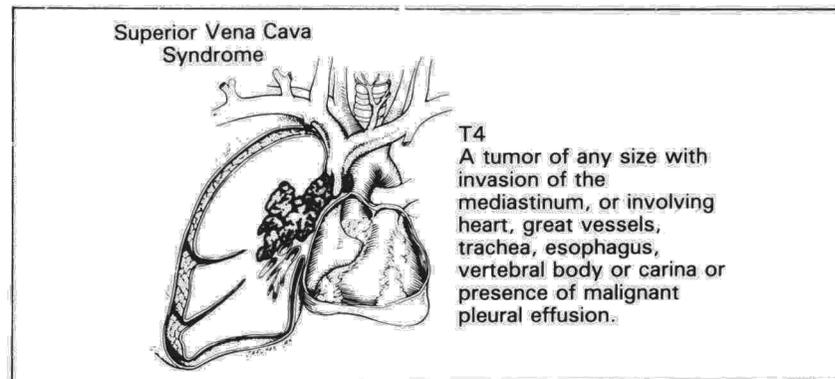


Fig. 3. T4: Superior vena cava syndrome-tumor involving great vessels.

tion of the pleural fluid —on more than one specimen— is negative for tumor, is nonbloody and is not an exudate. If these findings and clinical judgment confirm that the effusion is the result of another disease and not caused by the lung cancer, the patient should be staged T1, T2 or T3, excluding effusion as a staging element. Patients with malignant pleural effusion, as determined clinically or from cytologic examination of the fluid are classified T4.

N-regional lymph nodes

The N1 descriptor identifies metastasis or direct extension involving intrapulmonary lymph nodes. Metastases to the ipsilateral mediastinal and subcarinal lymph nodes is classified N2 (Fig. 5). Metastases to the contralateral mediastinal, contralateral hilar or ipsilateral and contralateral supraclavicular/scalene lymph nodes is N3 disease (Fig. 6).

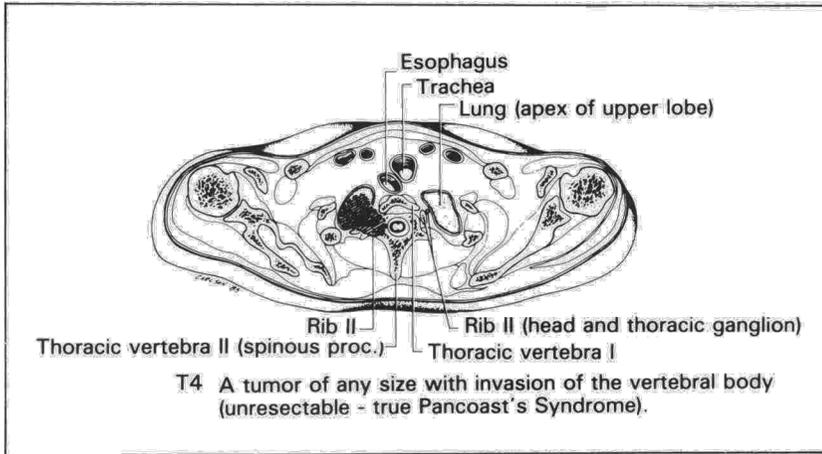
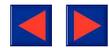


Fig. 4. T4: Tumor invading the vertebral body unresectable, produces Pancoast's syndrome.

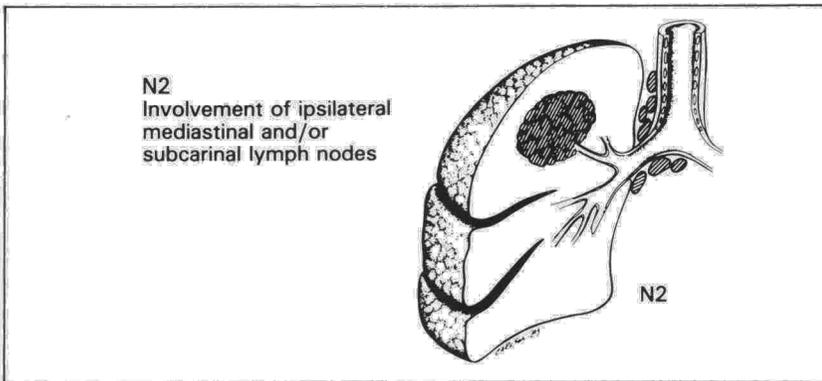


Fig. 5. N2: Involvement of ipsilateral mediastinal and/or subcarinal lymph nodes.

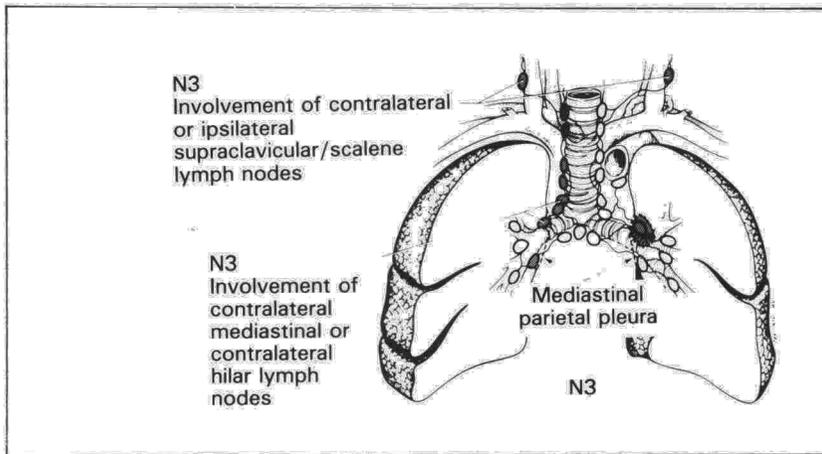


Fig. 6. N3: Involvement of contralateral or ipsilateral scalene or supraclavicular lymph nodes; contralateral mediastinal or contralateral hilar lymph nodes.

M-distant metastasis

M1 identifies metastases to distant organ or lymph node sites.

Stage grouping of the TNM subsets

Examples of TNM subsets in Stages I, II, IIIa and IIIb are shown in figs. 7-10. Stage I disease in-

cluded only patients with the best prognoses-those with T1 or T2 primary tumors and no evidence of metastases, the T1 N0 M0 and T2 N0 M0 subsets (Fig. 7). Stage II includes patients with T1 or primary tumors with intrapulmonary, including hilar, lymph node metastases-the T1 N1 M0 M0 and T2 N1 M0 subsets (Fig. 8). Stage III disease is divided into «a» and «b» categories to discriminate those patients with limited, circumscribed extrapulmon-

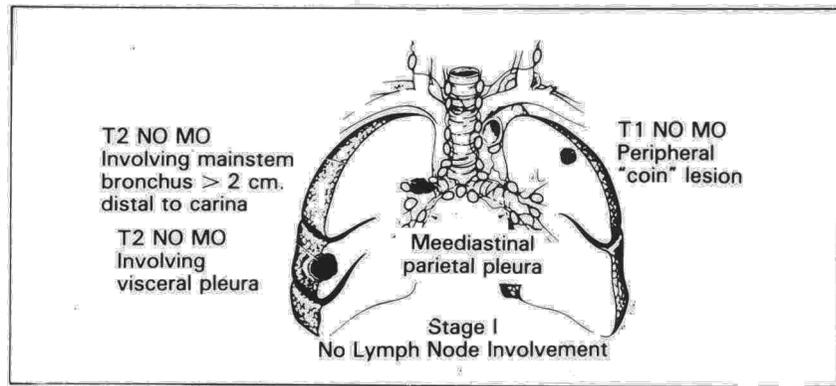
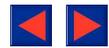


Fig. 7. Stage I disease.

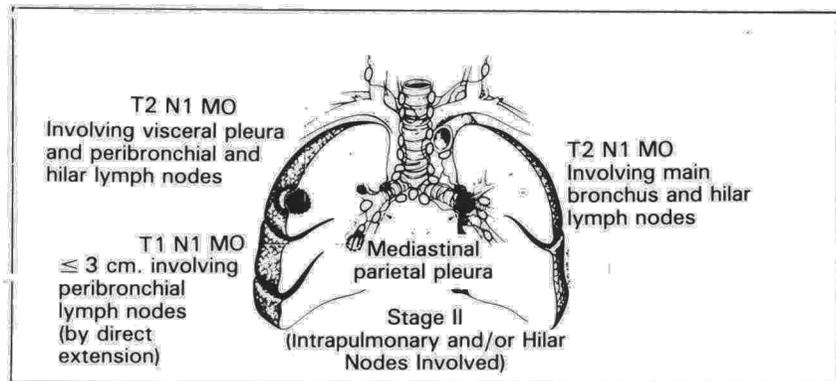


Fig. 8. Stage II disease.

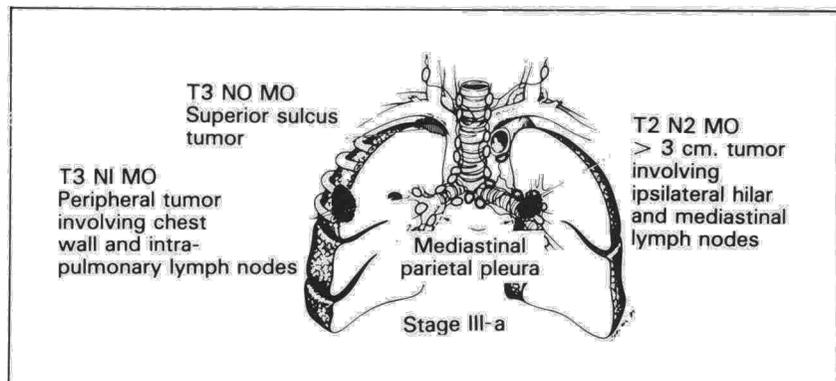


Fig. 9. Stage IIIa disease.

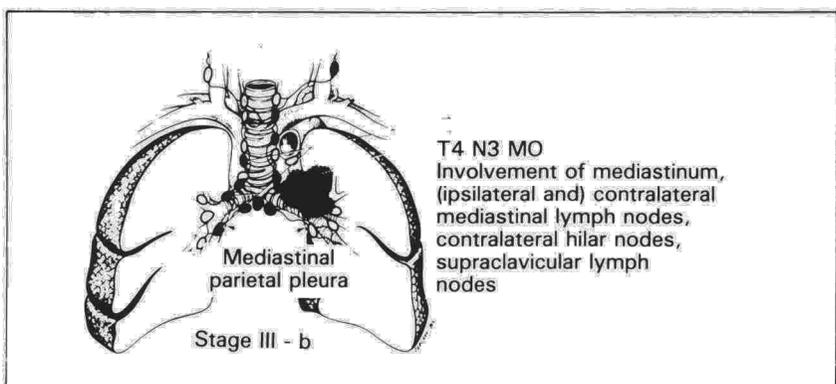


Fig. 10. Stage IIIb disease.

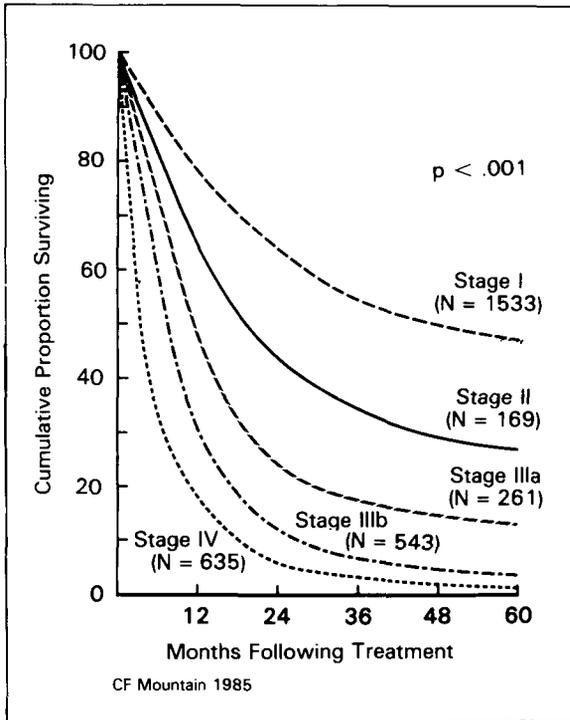
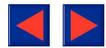


Fig. 11. Cumulative proportion of patients surviving five years by clinical stage of disease.

ary extension of the primary, *Stage IIIa*, from those with more extensive involvement of the mediastinum, *Stage IIIb*. T3 N0-N1 M0 and T1-3 N2 M0 tumors are included in *Stage IIIa* (Fig. 9). Patients with T4 or N3 tumors with no evidence of distant metastases are included in *Stage IIIb* (Fig. 10). *Stage IV* includes all patients with distant metastases, M1 disease.

End results according to the new staging proposal

When the TNM definitions and stage grouping rules are applied to a large contemporary data base, the end results shown in Fig. 11 are obtained. These survival patterns reflect CLINICAL estimates of disease extent. Each stage has a unique survival experience and relationship to treatment planning. Patients with clinical stage I, II or IIIa non-small cell lung cancer usually are candidates for definitive surgical treatment, and those with stage IIIb and stage IV disease are generally assigned to radiotherapy, chemotherapy or combined modalities. Chemotherapy or combined programs are usually the treatment of choice for patients with undifferentiated small cell carcinoma, regardless of stage; however, the proportion of patients expected to achieve the complete response necessary for long term survival varies with the stage of disease. The treatment regimen is related to the stage classification of small cell carcinoma just as it is for non-small cell lung cancer.

Conclusion

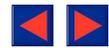
The new international proposal for staging lung cancer has five stages of disease, including a *Stage 0*, that provide for the classification of six groups of patients who have similar prognostic expectations and therapeutic options. In patients with *Stages I and II* disease all of the known cancer is confined to the ipsilateral lung. In these groups the *Stage I* patients have no lymph node extension or metastases; all of the *Stage II* patients have involvement of the intrapulmonary lymph nodes. *Stage IIIa* disease designates those patients, usually within the realm of the surgical oncologist, with extrapulmonary extension of the primary tumor and/or ipsilateral mediastinal lymph node metastasis. *Stage IIIb* includes patients with more extensive extrapulmonary involvement than is present in the *Stage IIIa* group, those with malignant pleural effusion and patients with metastases to the contralateral mediastinum, hilum, or supraclavicular and scalene lymph nodes. *Stages IV* disease is reserved for patients with metastasis to distant sites.

These new recommendations for staging fill the need for specific definitions for «limited» and «extensive» disease that can be reproduced and compared. They meet the goal of modifying present classifications to provide a universal, single staging system that is responsive to the needs of all those involved in the treatment and study of lung cancer.

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