

Regional Lymph Node Classification for Lung Cancer Staging*

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Recommendations for classifying regional lymph node stations for lung cancer staging have been adopted by the American Joint Committee on Cancer (AJCC) and the Union Internationale Contre le Cancer. The objective was to unify the two systems that have been in common use for the past 10 years; that is, the schema advocated by the AJCC, adapted from the work of Tsuguo Naruke, and the schema advocated by the American Thoracic Society and the North American Lung Cancer Study Group. Anatomic landmarks for 14 hilar, intrapulmonary, and mediastinal lymph node stations are designated. This classification provides for consistent, reproducible, lymph node mapping that is compatible with the international staging system for lung cancer. It is applicable for clinical and surgical-pathologic staging. (CHEST 1997; 111:1718-23)

Key words: lung cancer; lymph node classification; lymph node mapping; lymph nodes; staging; survival rates

Abbreviations: AJCC=American Joint Committee on Cancer; ATS=American Thoracic Society; cN=status of lymph nodes according to all diagnostic and evaluative information obtained prior to the institution of treatment or decision for no treatment; LCSG=Lung Cancer Study Group (National Cancer Institute North American Cooperative Lung Cancer Study Group); N=regional lymph nodes; pN=status of lymph nodes according to surgical-pathologic information obtained from resected specimens; TNM=subset describing the extent of disease in terms of the T compartment, primary tumor, the N compartment, regional lymph nodes, and the M compartment, distant metastasis

The status of regional lymph nodes is a major factor for staging, assigning treatment, and evaluating treatment efficacy in patients with lung cancer. Consistent, reproducible classification or map-

ping of these lymph nodes is essential for designing clinical research studies that are needed to fully understand the implications of lymphatic metastasis. Comparative studies of prognostic factors that influence the metastatic process will be reliable only if they are based on reproducible classification. The objective of the present recommendations for classifying mediastinal, hilar, and intrapulmonary lymph nodes was to combine the features of two systems^{1,2} used over the past 10 years into a single schema that is compatible with internationally accepted staging

definitions for the TNM (T=primary tumor, N=regional lymph nodes, M=distant metastasis) categories.^{3,4}

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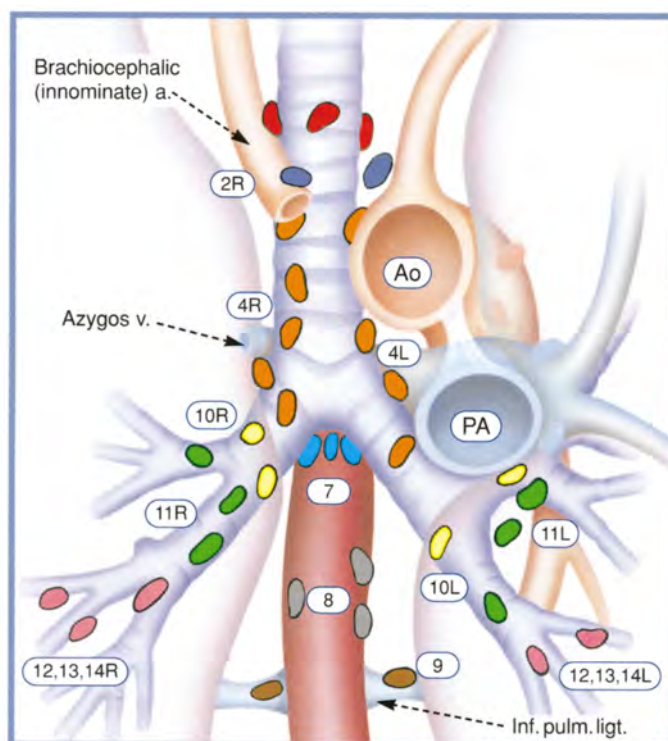
LYMPH NODE MAPPING

The recommendations for classifying regional lymph nodes for lung cancer staging are shown in Figure 1 with accompanying definitions in Table 1. This schema was adopted by the American Joint Committee on Cancer (AJCC) and the Prognostic Factors TNM Committee of the Union Internationale Contre le Cancer at the 1996 annual meetings of each of these organizations (see Appendix for participants and organizational representation). The diagram and definitions unify in a single system the features of the lymph node classification developed by Naruke and coworkers,⁵⁻⁷ which was based on data and was approved by the AJCC, and the schema advocated by the American Thoracic Society and the North American Lung Cancer Study Group (ATS/LCSG).⁸⁻¹⁰ Differences in classifying the lymph node stations according to the two systems resulted in confusion in the interpretation of end results.¹¹ The AJCC and ATS lymph node classifications are similar, except for the ATS stations 10L (designated left peribronchial nodes), and 10R (designated right tracheobronchial nodes) vs Naruke station 10 (designated hilar nodes) and Naruke station 4 (designat-

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Superior Mediastinal Nodes

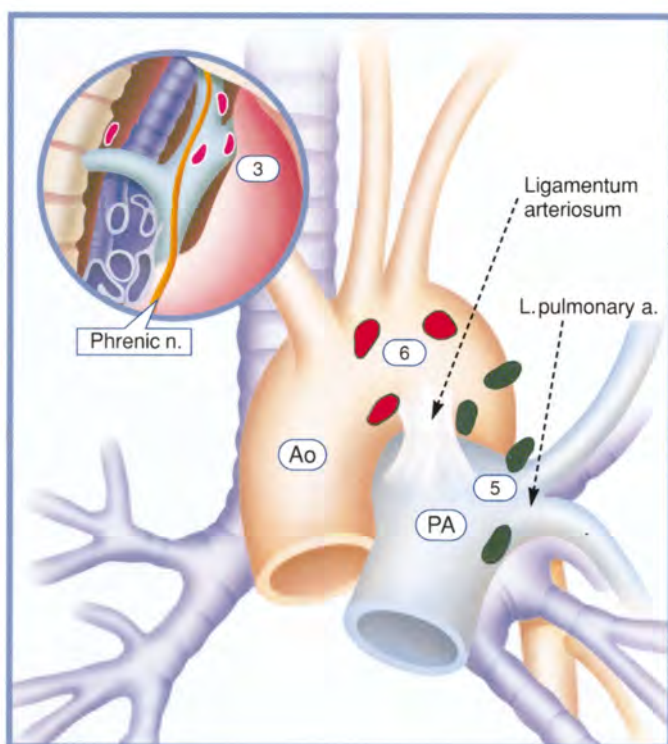
- 1 Highest Mediastinal
- 2 Upper Paratracheal
- 3 Pre-vascular and Retrotracheal
- 4 Lower Paratracheal (including Azygos Nodes)

N_2 = single digit, ipsilateral

N_3 = single digit, contralateral or supraclavicular

Aortic Nodes

- 5 Subaortic (A-P window)
- 6 Para-aortic (ascending aorta or phrenic)



Inferior Mediastinal Nodes

- 7 Subcarinal
- 8 Paraesophageal (below carina)
- 9 Pulmonary Ligament

N_1 Nodes

- 10 Hilar
- 11 Interlobar
- 12 Lobar
- 13 Segmental
- 14 Subsegmental

(Mountain/Dresler modifications from Naruke/ATS-LCSG Map)

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FIGURE 1. Regional lymph node stations for lung cancer staging. Adapted from Naruke et al.⁶ and the ATS/North American LCSG² (copyright 1996, Mountain and Dresler; may be reproduced for educational purposes without permission).

Table 1—Lymph Node Map Definitions

Nodal Station	Anatomic Landmarks
N2 nodes—All N2 nodes lie within the mediastinal pleural envelope	
1 Highest mediastinal nodes	Nodes lying above a horizontal line at the upper rim of the brachiocephalic (left innominate) vein where it ascends to the left, crossing in front of the trachea at its midline
2 Upper paratracheal nodes	Nodes lying above a horizontal line drawn tangential to the upper margin of the aortic arch and below the inferior boundary of No. 1 nodes
3 Prevascular and retrotracheal nodes	Prevascular and retrotracheal nodes may be designated 3A and 3P; midline nodes are considered to be ipsilateral
4 Lower paratracheal nodes	The lower paratracheal nodes on the right lie to the right of the midline of the trachea between a horizontal line drawn tangential to the upper margin of the aortic arch and a line extending across the right main bronchus at the upper margin of the upper lobe bronchus, and contained within the mediastinal pleural envelope; the lower paratracheal nodes on the left lie to the left of the midline of the trachea between a horizontal line drawn tangential to the upper margin of the aortic arch and a line extending across the left main bronchus at the level of the upper margin of the left upper lobe bronchus, medial to the ligamentum arteriosum and contained within the mediastinal pleural envelope Researchers may wish to designate the lower paratracheal nodes as No. 4s (superior) and No. 4i (inferior) subsets for study purposes; the No. 4s nodes may be defined by a horizontal line extending across the trachea and drawn tangential to the cephalic border of the azygos vein; the No. 4i nodes may be defined by the lower boundary of No. 4s and the lower boundary of No. 4, as described above
5 Subaortic (aorto-pulmonary window)	Subaortic nodes are lateral to the ligamentum arteriosum or the aorta or left pulmonary artery and proximal to the first branch of the left pulmonary artery and lie within the mediastinal pleural envelope
6 Para-aortic nodes (ascending aorta or phrenic)	Nodes lying anterior and lateral to the ascending aorta and the aortic arch or the innominate artery, beneath a line tangential to the upper margin of the aortic arch
7 Subcarinal nodes	Nodes lying caudal to the carina of the trachea, but not associated with the lower lobe bronchi or arteries within the lung
8 Paraesophageal nodes (below carina)	Nodes lying adjacent to the wall of the esophagus and to the right or left of the midline, excluding subcarinal nodes
9 Pulmonary ligament nodes	Nodes lying within the pulmonary ligament, including those in the posterior wall and lower part of the inferior pulmonary vein
N1 nodes—All N1 nodes lie distal to the mediastinal pleural reflection and within the visceral pleura	
10 Hilar nodes	The proximal lobar nodes, distal to the mediastinal pleural reflection and the nodes adjacent to the bronchus intermedius on the right; radiographically, the hilar shadow may be created by enlargement of both hilar and interlobar nodes
11 Interlobar nodes	Nodes lying between the lobar bronchi
12 Lobar nodes	Nodes adjacent to the distal lobar bronchi
13 Segmental nodes	Nodes adjacent to the segmental bronchi
14 Subsegmental nodes	Nodes around the subsegmental bronchi

ed lower paratracheal, including azygos nodes). The recommended schema resolves the problem by using anatomic landmarks that identify all lymph node stations within the mediastinal pleural reflection as N2 nodes, and anatomic landmarks that identify all lymph node stations distal to the mediastinal pleural reflection and within the visceral pleura as N1 nodes.

Regional Lymph Nodes for Lung Cancer Staging

The international staging system for lung cancer defines the regional lymph nodes, the N component, as follows.^{1,3,4} N0=no lymph node metastasis; 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; and N3=metastasis to contralateral mediastinal lymph nodes, contralateral hilar lymph nodes, ipsilateral or contralateral scalene or supraclavicular lymph nodes.

The descriptors for the N category were derived from analysis of a collected database of information representing patients treated for primary lung cancer from 1975 to 1982.¹² This series was updated through 1988, and survival patterns according to the N descriptors, by clinical and surgical-pathologic criteria, are shown in Figure 2. Erosion of survival expectations with disease progression from N0 to N1 to N2 to N3 disease confirms that the definitions

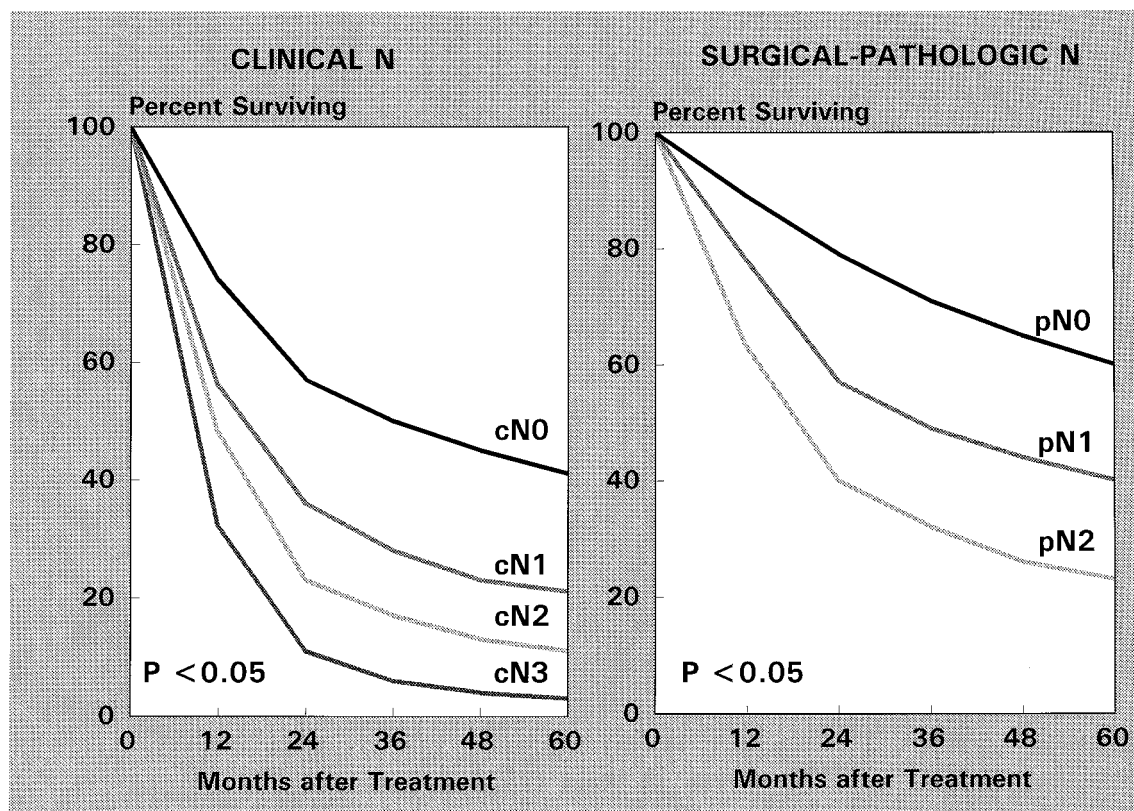


FIGURE 2. Cumulative percent of patients surviving ≥ 5 years after treatment according to the status of lymph nodes. By clinical criteria: cT1-4 N0M0, no evidence of metastasis ($n=2,177$); cT1-4 N1M0, hilar and intrapulmonary metastasis ($n=408$); cT1-4 N2M0, ipsilateral mediastinal lymph node metastasis ($n=659$); cT1-4 N3M0, contralateral mediastinal, contralateral hilar, ipsilateral and contralateral supraclavicular/scalene lymph node metastasis ($n=572$). By surgical-pathologic criteria (small cell carcinoma excluded), pT1-4 N0M0 ($n=1,179$), pT1-4 N1M0 ($n=429$), pT1-4 N2M0 ($n=354$). Collected database: M.D. Anderson Cancer Center 1975 to 1988 ($n=4,351$); Reference Center for Anatomic and Pathologic Classification of Lung Cancer (patients treated by the North American LCSG and submitted to the Reference Center for Anatomic and Pathologic Classification of Lung Cancer for confirmation of staging and histology, 1977 to 1982, $n=968$). Comparison of survival experience according to the method of Gehan;²⁵ operative deaths excluded.

identify four statistically significant prognostic groups by clinical criteria and three by surgical-pathologic criteria. The clinical survival curves reflect, primarily, the radiologist's description of normal (N0) or abnormal hilar (N1), or mediastinal lymph nodes (N2), or contralateral and scalene/supraclavicular nodes (N3). Also reflected is the clinician's assessment of the supraclavicular or scalene lymph nodes, including biopsy in some instances. Other cervical lymph nodes are classified M1. The surgical-pathologic curves reflect the accuracy of disease extent evaluation based on pathologic examination of resected specimens, as well as the improved prognosis for patients having definitive surgical treatment. Similar findings have been reported by others.^{13,14}

The Lymph Node Map

Fourteen numbered stations for classifying the status of the mediastinal (N2) and hilar and intrapul-

monary lymph nodes (N1) are shown in Figure 1. The anatomic landmarks delineating each nodal compartment are described in the accompanying Table 1. All N2 nodes are contained within the mediastinal pleural envelope; they are numbered 1 through 9, and include the superior mediastinal nodes, numbers 1 through 4; the aortic nodes, depicted in the lower part of the diagram, numbers 5 and 6; and the inferior mediastinal nodes, numbers 7 through 9. According to the location of the primary tumor, the ipsilateral nodes are designated right or left; midline prevascular and retrotracheal lymph nodes are considered ipsilateral. It should be noted that nodes sampled at mediastinoscopy are N2 nodes, as long as one does not create a pneumothorax, which would mean that the pleural reflection has been violated, and in fact, the surgeon may then be sampling N1 nodes. As an aid to the study of the effect on survival of metastasis to specific mediastinal lymph node levels, the surgical committees of Na-

tional Cooperative Study Groups suggested that researchers may wish to divide the lower peritracheal nodes into superior (No. 4s) and inferior (No. 4i) groups. Anatomic landmarks for this division are described in Table 1. All N1 nodes lie distal to the mediastinal pleural reflection and are numbered 10 through 14. The most proximal nodes in the N1 category, No. 10L and 10R, are designated hilar nodes and 11 R/L through 14 R/L as intrapulmonary nodes, with specific designations related to the location on or between the bronchi.

Clinical and Surgical-Pathologic Extent of Disease

The true extent of lymph node metastasis can be determined only by complete lymph node dissection, and the extent of metastatic disease may be underestimated if an extended or total resection of all accessible nodes is not performed. Excellent descriptions of these procedures have been published, including evaluations of morbidity and the effect on survival that may be associated with the extended procedure.¹⁵⁻¹⁷ The results of pathologic assessment of pulmonary resection and lymphadenectomy specimens represent the highest order of reliability. Although most patients with lung cancer are not candidates for surgical treatment, the lymph node mapping schema is useful for clinical staging. It also is useful for other investigations of lymphatic metastasis, such as correlative studies of diagnostic and evaluative examinations—radiographs, CT, positron emission tomography, immunoscintigraphy, or trans-bronchial needle biopsy performed at bronchoscopy, or mediastinoscopy and mediastinotomy.

Prognostic Implications of Regional Lymph Node Metastasis

The prognostic implications of the absence or presence and extent of lymph node metastasis, regardless of primary tumor characteristics, are shown in Figure 2 and were discussed previously. However, within the spectrum of the N1 and N2 categories, the implications of specific patterns and characteristics of metastatic lymph node disease on survival duration are not fully understood. Reports are inconsistent regarding the relationship to prognosis of metastasis to specific lymph nodes, the number of nodes and level of nodes involved,¹⁸⁻²⁰ the influence of primary tumor characteristics and histologic features, the influence of intranodal and extranodal disease,²¹ and the influence of various biological prognostic factors.²² A unified lymph node mapping schema will provide a means for collecting data to study these patterns of metastatic spread and translate the information for useful clinical and research purposes.

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APPENDIX

American Joint Committee on Cancer Annual Meeting Scottsdale, Ariz, January 13, 1996

American Cancer Society

Myles P. Cunningham, MD
Robert J. McKenna, MD
Robert J. Schweitzer, MD*

American College of Physicians

B.J. Kennedy, MD*
Robert J. Mayer, MD*
John W. Yarbrow, MD*

American College of Radiology

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Frederick L. Greene, MD

College of American Pathologists

Gerald Nash, MD
David L. Page, MD*
Mark R. Wick, MD

National Cancer Institute

Sudhir Srivastava, PhD, MPH
Harvey I. Pass, MD
Edward L. Trimble, MD

Association of American Cancer Institutes

Stephen Edge, MD*

National Cancer Registrar's Association

Ms. Carol S. Venuti, CTR*

American Urological Association

Andrew C. von Eschenbach, MD*

American Society of Clinical Oncology

Derek Raghavan, MD

Centers for Disease Control and Prevention

Daniel S. Miller, MD, MPH

The American Society of Colon and Rectal Surgeons

Mark L. Welton, MD

The Society of Gynecologic Oncologists

Howard W. Jones III, MD

The Society of Urologic Oncology

Ian M. Thompson, MD

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William Creasman, MD*
Dean F. Bajorin, MD*
Oliver H. Beahrs, MD*
Harmon J. Eyre, MD*
Robert V.P. Hutter, MD*
Mary Lerchen, PhD*
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Clifton F. Mountain, MD*
Brian O'Sullivan, MD*
Mr. Thomas J. Terry*

UICC Representatives to the AJCC

Gerald P. Murphy, MD*
UICC Secretary General
Leslie H. Sobin, MD, Chairman,
TNM Prognostic Factors Project Committee

*Participants at Annual Meeting; 1997 revisions in staging and recommendations for lymph node mapping adopted.

*UICC-TNM-Prognostic Factors Project Committee
Meeting
Geneva, Switzerland, April 30-May 1, 1996*

Dr. Leslie Sobin (Project Chairman), Armed Forces Institute of Pathology, Washington, DC
Dr. Fausto Badellino, Istituto Nazionale per la Ricerca sul Cancro, Genova, Italy
Dr. Nikolay N. Blinov, N.N. Petrov Research Institute of Oncology, St. Petersburg, Russia
Dr. Irvin D. Fleming, Mid-South Oncology Group, PC, Memphis, Tenn
Dr. Brian O'Sullivan, Princess Margaret Hospital, Ontario, Canada
Dr. Marcel Hayat, Institut Gustave Roussy, Villejuif Cedex, France
Dr. Helmut Kasdorf, Academia Nacional de Medicina, Montevideo, Uruguay
Dr. Michael Morgan, United Kingdom
Dr. Tsuguo Naruke, National Cancer Center, Tokyo, Japan
Dr. Christian Wittekind, Institut für Pathologie der Universität, Leipzig, Germany
Dr. Robert V.P. Hutter, Representative American Cancer Society, Saint Barnabas Hospital, Livingston, NJ
Dr. Donald Henson, Representative College of American Pathologists, National Cancer Institute, Bethesda, Md

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