Fundamentals of Lung Cancer Staging

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Author's disclosures of potential conflicts of interest are found at the end of this article.

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https://doi.org/10.6004/jadpro.2017.8.5.13

Abstract

Lung cancer is the leading cause of cancer-related mortality in the United States and the world. The treatment of non–small cell lung cancer (NSCLC) is dependent on adequate staging of disease at diagnosis. Computed tomography (CT) and positron emission tomography-computed tomography (PET/CT) provide noninvasive evaluation of the extent of disease. These may be the extent of staging in the case of stage IV disease. However, earlier stages of NSCLC require more extensive surgical staging evaluation. In the past 10 years, minimally invasive procedures utilizing endoscopic and video-assisted techniques have provided the ability to obtain precise staging, with a decrease in cost and morbidity associated with prior invasive procedures, such as mediastinoscopy. Each technique provides information needed for full classification and staging. The American Joint Committee on Cancer tumor-node-metastasis (TNM) staging system is updated regularly to estimate prognosis and selection of appropriate therapy. This review will discuss the staging techniques and classifications necessary to guide the management of patients with newly diagnosed lung cancer.

J Adv Pract Oncol 2017;8:25–34

Accurate staging for non–small cell lung cancer (NSCLC) is essential to management, treatment planning, and prognosis. It is one of the most important prognostic factors that drive the selection of therapy, as optimal treatment is stage-specific (National Comprehensive Cancer Network [NCCN], 2017). The NCCN (2017), American College of Chest Physicians (Silvestri et al., 2013), and the European Society of Medical Oncology (Novello et al., 2016) have developed clinical practice guidelines to guide the diagnosis, staging, and management of patients with suspected NSCLC. Timely diagnosis and staging are recommended so that appropriate treatment can proceed and improve overall outcomes (NCCN, 2017; Novello et al., 2016; Ost, Yeung, Tanoue, & Gould, 2013; Silvestri et al., 2013).

All patients with suspected lung cancer should undergo a thorough evaluation including a history and physical exam, with attention to symptoms that might suggest the extent of disease. Physical examination and laboratory evaluation can predict the likelihood of metastasis (Silvestri, Littenberg, & Colice, 1995). Laboratory tests should include complete

blood cell count, electrolytes, calcium, alkaline phosphatase, alanine transaminase, aspartate transaminase, total bilirubin, and creatinine. Although a chest radiograph is typically the first image that provides preliminary information about the presence of a tumor, it is not adequate for staging. A computed tomography (CT) scan with contrast of the chest and upper abdomen should be done to confirm the presence of a lung tumor (NCCN, 2017; Silvestri et al., 2013). The initial phase of evaluation is to determine if the patient has disease confined to the chest or if distant metastasis is present. A total-body positron emission tomography (PET)/CT scan should be done to assess for mediastinal involvement and distant metastatic spread (NCCN, 2017). If disease is localized to the chest, evaluation of mediastinal nodes is essential to determine if treatment with curative intent is possible. Surgical resection may be possible for those with stage IA, IB, IIA, and IIB disease. Those with more advanced disease—stages IIIA, IIIB, and IV—are not usually surgical candidates and therapy is multimodality, systemic, and/or palliative.

After excluding distant metastatic disease, stage I or II, it is critical to evaluate for regional spread of tumor in the mediastinum with tissue confirmation, especially if there is strong clinical suspicion of N2 or N3 nodal disease (NCCN, 2017; De Leyn et al., 2014; Silvestri et al., 2013). Mediastinal staging should be done on all central tumors, peripheral tumors larger than 3 cm, CT scan lymph nodes greater than 1 cm, N1 lymph node involvement on PET, and PET maximum standard uptake value (SUVmax) greater than 2 (NCCN, 2017; Silvestri et al., 2013). Understating or missed mediastinal lymph node involvement will result in inadequate therapy. Identification of mediastinal node involvement provides the foundation to avoid futile surgical resection. Patients with no nodal involvement are candidates for potentially curative resection. Those with ipsilateral N2 nodal metastasis or contralateral mediastinal metastasis (N3) are not candidates for surgical resection. However, patients with stage IIIA disease may receive concurrent chemotherapy and radiation therapy followed by resection. Invasive mediastinal evaluation is not recommended if the primary tumor is less than 2 to 3 cm with no abnormal hypermetabolic uptake in the mediastinal nodes on PET/CT (Fernandez et al., 2015). In patients with imaging findings suggestive of metastasis to one site, tissue sampling is recommended to pathologically confirm the mass is consistent with primary lung cancer. However, this is not necessary if there is overwhelming radiographic evidence of metastatic disease in multiple sites (NCCN, 2017; Silvestri et al., 2013). Thoracentesis and/or thoracoscopic evaluation of the pleura should be considered in the setting of a pleural effusion before initiating therapy with curative intent.

There are several strategies available for mediastinal lymph node evaluation. The most important considerations in the selection are sensitivity, specificity, that adequate tissue volume be obtained for diagnosis and molecular testing, and least invasive (NCCN, 2017). Additionally, the procedure selected should be readily available, well tolerated, safe, inexpensive, and highly reliable (Gamliel, 2016). A multidisciplinary team of thoracic experts, including a thoracic radiologist, interventional radiologist, pulmonologist, oncologist, and a board-certified thoracic surgeon, should be involved in the decision about the patient's initial evaluation and optimal diagnostic procedures (NCCN, 2017). In addition, consideration should be made to have procedures done by physicians with specialized experience and skill who perform the procedures frequently and who specialize in thoracic malignancies. Success rates of each procedure are operator dependent.

NONINVASIVE STAGING DIAGNOSTIC TESTS

A CT scan of the chest is used to determine the presence and size of a tumor. It should include visualization of the liver and adrenal glands. Intravenous contrast enhancement provides better evaluation of the mediastinum and blood vessels. Sensitivity ranges from 42% to 86% and specificity of 84% to 100% in detecting primary lung tumors, with less sensitivity (40% to 65%) and specificity (54% to 90%) for assessing nodal involvement, as nodes must be larger than 1 cm for detection (De Wever, Verschakelen, & Cooen, 2014; Novello et al., 2016; Tsim, O'Dowd, Milroy, & Davidson, 2010; Silvestri et al., 2013).

Positron emission tomography–computed tomography is used to evaluate the extent and presence of distant metastasis (Novello et al., 2016; Silvestri et al., 2013). This nuclear medicine imaging is obtained by injecting fluorine-18 (F-18) fluo-

rodeoxyglucose (FDG) and scanning for uptake by metabolically active glucose–using tissue. There is normal uptake in the brain, heart, and urinary tract (Sarji, 2006). The accuracy for diagnosing mediastinal disease is 97.7% sensitivity and 56% to 86% specificity (Brocken et al., 2014; Paul et al., 2012; Silvestri et al., 2013; Ung et al., 2007). It has improved sensitivity (93%) and specificity (80% to 90%) in determining nodal involvement over CT scan (Kim et al., 2015; Novello et al., 2016; Paul, Ley, & Metson, 2012), and distant metastasis sensitivity of 82% to 90% and specificity of 90% to 98% (Ung et al., 2007). Positron emission tomography results are presented as SUVmax, a measurement of metabolic activity noted in tumors. There is variability in interpretation of SUVmax uptake in mediastinal nodes among institutions (Serra-Fortuny et al., 2016). Therefore, despite negative PET scan results (i.e., no evidence of lymph node involvement), a biopsy of mediastinal nodes is still necessary to adequately stage patients at high risk for local extension (Serra-Fortuny et al., 2016). False-positive PET scan results may be seen with infectious or inflammatory conditions, leading to over-diagnosis of the extent of lung cancer involvement. Positron emission tomography scans are a valuable noninvasive procedure to help guide evaluation and staging, but they should not be the sole guide to determine potential surgical resection (Murgu, 2015; Pak et al., 2015). Positron emission tomography/MRI and delayed PET imaging have been investigated as potential imaging strategies. Positron emission tomography/MRI has similar accuracy to PET/CT, with higher cost and limited availability (Gross, Guimaraes, Chojniak, & Lima, 2014; Huellner et al., 2016). Delayed PET imaging takes into consideration that cancers continue to increase FDG uptake over 1.5 to 5 hours, so an increase over time may suggest cancer etiology. The concept has not demonstrated improved sensitivity or specificity. In addition, patients with diabetes mellitus or high blood glucose levels are more likely to have false-negative studies.

The NCCN recommends MRI of the brain for stages II, III, or IV disease (NCCN, 2017), with a sensitivity of 97.7% and a specificity of 100% (Kim et al., 2005). However, the American College of Chest Physicians guidelines recommend conducting brain MRI only in patients with clinical stage III or IV disease (Silvestri et al., 2013). Several studies have found that preoperative brain MRI is of low diagnostic value and support, forgoing brain MRI in asymptomatic patients with early disease (Backhus et al., 2014; Novello et al., 2016; Vernon et al., 2016).

INVASIVE STAGING DIAGNOSTIC TESTS

Endobronchial ultrasound–fine-needle aspirate (EBUS-FNA) and endoscopic ultrasound—fine needle-aspirate (EUS-FNA) have emerged as the preferred routes of biopsy, depending on the node of interest. Prior to the development of EBUS and EUS, patients who were candidates for resection of suspected or diagnosed lung cancer often required staging with mediastinoscopy to evaluate for potential lymph nodes in the mediastinum. However, mediastinoscopy is associated with a higher complication rate and more importantly is unable to sample certain lymph nodes such as hilar (stations 10, 11, and 12), para-aortic (station 6), or aortopulmonary window (station 5) lymph nodes (Table 1; Figures 1 and 2).

Table 1. Summary of Nodal Stations by Biopsy Method

Biopsy method	Accessible nodes
EBUS-FNA	1, 2R, 2L, 3P, 4R, 4L, 7, 10, 11, 12R, 12L
EUS-FNA	2R, 2L, 3P, 4L, 5, 7, 8, 9; celiac axis, left lobe of liver, and left adrenal gland
Cervical mediastinoscopy	1, 2R, 2L, 3, 4R, 4L, anterior 7
Anterior mediastinoscopy	5, 6
VATS	2R, 2L, 3A, 3P, 4R, 4L, 5, 6, 7, 8, 9, 10, 11; ipsilateral hilar and mediastinal lymph nodes

Note. EBUS-FNA = endobronchial ultrasound–fine-needle aspirate; R = right; L = left; 3P = retrotracheal; EUS-FNA = endoscopic ultrasound–fine-needle aspirate; VATS = video-assisted thorascopic surgery. Information from Hegde & Liberman (2016).

American Joint Committee on Cancer

Lung Cancer Staging

7th EDITION

Classifications

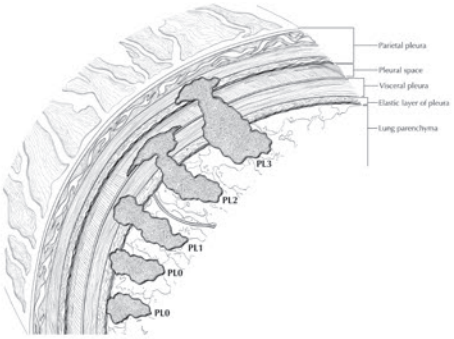
Primary Tumor (T) Classification

- **TX** Primary tumor cannot be assessed, or tumor proven by the presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy
- **T0** No evidence of primary tumor
- **Tis** Carcinoma in situ
- **T1** Tumor 3 cm or less in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus
- **T1a** Tumor 2 cm or less in greatest dimension
- **T1b** Tumor more than 2 cm but 3 cm or less in greatest dimension
- **T2** Tumor more than 3 cm but 7 cm or less or tumor with any of the following features (T2 tumors with these features are classified T2a if 5 cm or less): involves main bronchus, 2 cm or more distal to the carina; invades visceral pleura (PL1 or PL2); associated with atelectasis or obstructive pneumonitis that extends to the hilar region but does not involve the entire lung
- **T2a** Tumor more than 3 cm but 5 cm or less in greatest dimension
- **T2b** Tumor more than 5 cm but 7 cm or less in greatest dimension
- **T3** Tumor more than 7 cm or one that directly invades any of the following: parietal pleural (PL3), chest wall (including superior sulcus tumors), diaphragm, phrenic nerve, mediastinal pleura, parietal pericardium; or tumor in the main bronchus less than 2 cm distal to the carina[1] but without involvement of the carina; or associated atelectasis or obstructive pneumonitis of the entire lung or separate tumor nodule(s) in the same lobe
- **T4** Tumor of any size that invades any of the following: mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina, separate tumor nodule(s) in a different ipsilateral lobe

Distant Metastasis (M) Classification

- **M0** No distant metastasis
- **M1** Distant metastasis
- **M1a** Separate tumor nodule(s) in a contralateral lobe, tumor with pleural nodules or malignant pleural (or pericardial) effusion
- **M1b** Distant metastasis (in extrathoracic organs)

ANATOMIC STAGE/PROGNOSTIC GROUPS			
Occult Carcinoma	TX	N0	M0
Stage 0	Tis	N0	M0
Stage IA	T1a	N0	M0
	T1b	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T2b	N0	M0
	T1a	N1	M0
	T1b	N1	M0
	T2a	N1	M0
Stage IIB	T2b	N1	M0
	T3	N0	M0
Stage IIIA	T1a	N2	M0
	T1b	N2	M0
	T2a	N2	M0
	T2b	N2	M0
	T3	N1	M0
	T3	N2	M0
	T4	N0	M0
	T4	N1	M0
Stage IIIB	T1a	N3	M0
	T1b	N3	M0
	T2a	N3	M0
	T2b	N3	M0
	T3	N3	M0
	T4	N2	M0
	T4	N3	M0
Stage IV	Any T	Any N	M1a
	Any T	Any N	M1b



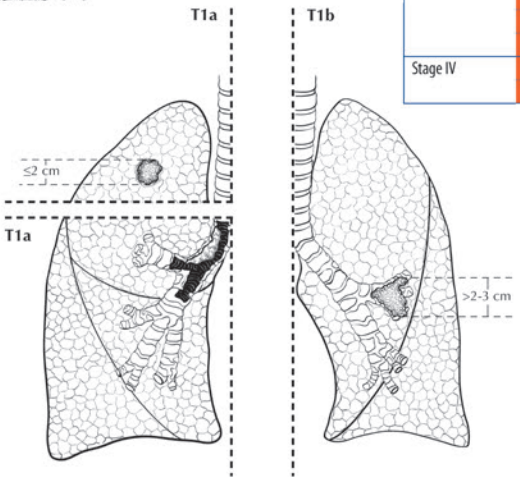


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Figure 1. Lung cancer staging: Classifications. Used with permission from the American Joint Committee on Cancer.

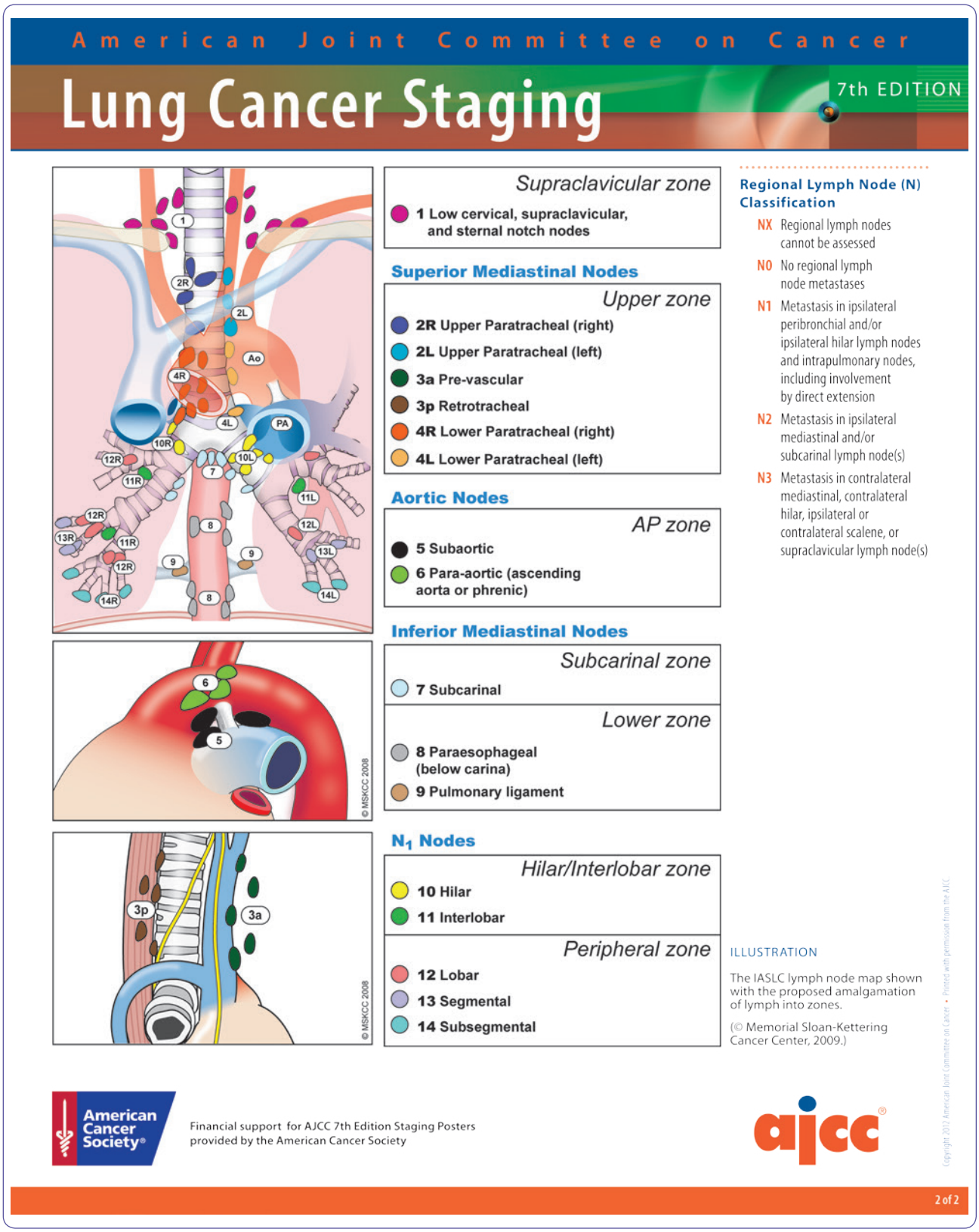

Figure 2. Lung cancer staging: Lymph node stations. Used with permission from the American Joint Committee on Cancer.

Endobronchial ultrasound–fine-needle aspirate is a minimally invasive technique that complements mediastinoscopy by ability to access lymph node stations 1, 2, 3, 4, 7, 10, 11, and 12. If suspicious lymph nodes are identified in level 5 or 6, EBUS will not be sufficient. Endobronchial ultrasound is a bronchoscopic technique that utilizes ultrasound to identify and permit real-time ultrasound-guided needle biopsy of paratracheal, hilar, and interlobar lymph nodes. The scope has a video component and transducer at the tip, which provides the ability to use suction or to pass a needle for biopsy.

Endoscopic ultrasound—fine-needle aspirate is a minimally invasive ultrasound-based technique that uses an esophagogastroendoscopy to sample paraesophageal lymph nodes. They include paratracheal (station 4), aortopulmonary window (station 5), posterior subcarinal (station 7), paraesophageal (station 8), and pulmonary ligament (station 9). This approach also provides access to the left lobe of the liver and left adrenal gland. Endoscopic ultrasound complements both EBUS and mediastinoscopy.

Negative results with EBUS or EUS cannot exclude mediastinal nodes (Dooms, 2015), and additional staging is recommended with confirmatory mediastinoscopy prior to proceeding to surgical resection, particularly for patients in whom there is a high suspicion of N2 disease (Defranchi et al., 2010; De Leyn et al., 2014; Nasir, Yasufuku, & Liberman, 2017; Silvestri et al., 2013). It is suggested to analyze all lymph nodes greater than 0.5 cm and at least three to four lymph node stations (DeLeyn, 2014).

Bronchoscopy with biopsy and transbronchial needle aspiration may be utilized with CT scan for evaluation of the major airways. A flexible scope is inserted into the airway to examine for the presence and extent of suspected endobronchial involvement and central masses. This procedure allows for the placement of fiducial markers around a lung nodule to guide stereotactic radiation. Successful biopsy assumes the scope is positioned correctly for placement of the fiducial markers.

Cervical and anterior mediastinoscopy has been and remains the "gold standard" for surgical staging. An incision is made at the base of the neck above the suprasternal notch. A mediastinoscope is inserted along the length of the trachea to permit sampling of paratracheal lymph nodes (stations 1, 2, 3, and 4) and anterior subcarinal lymph nodes. An extended cervical mediastinoscopy allows access to para-aortic lymph nodes (station 6). Anterior mediastinoscopy (Chamberlain procedure) permits evaluation of aortopulmonary window lymph nodes. In this procedure, an incision is made at the level of the second or third intercostal space to the left of the sternum and a mediastinoscope is inserted to visualize nodes and biopsy. There are two adapted mediastinoscopy procedures: video-assisted mediastinoscopic lymphadenectomy (VAMLA) and transcervical extended mediastinal lymphadenectomy (TEMLA). These procedures are open procedures assisted by videomediastinoscopy or video thoracoscope. The VAMLA explores all mediastinal nodes from the supraclavicular to the paraesophageal; however, it cannot reach the subaortic or parasortic region. The TEMLA explores the right and left paratracheal, subaortic, and subcarinal nodes. The benefit of VAMLA and TEMLA is that they allow the complete removal of mediastinal nodes and surrounding tissue instead of just a biopsy (Call et al., 2016). All mediastinoscopy approaches require general anesthesia and cannot be performed repeatedly. Complications of mediastinoscopy approaches include temporary or permanent laryngeal nerve palsies, pneumothorax, and hemorrhage (Call et al., 2016).

Video-assisted thorascopic surgery (VATS) or thoracoscopy permits the surgeon to evaluate the pleural space, ipsilateral nodes, and direct visualization of T4 lesions. It requires general anesthesia, and there is a risk of prolonged air leak during and following the procedure.

A thoracentesis is recommended for patients who present with a pleural effusion. A temporary catheter is inserted to remove pleural fluid for cytology diagnostic evaluation. A negative cytology does not exclude pleural involvement. Additional evaluation of the pleura should be done before the start of curative intent surgical resection (NCCN, 2017). The procedure may provide palliation of symptoms. However, there is a risk of pneumothorax with the procedure, particularly if repeat procedures are performed.

CLASSIFICATION

The tumor, node, metastasis (TNM) staging system is the internationally accepted system to describe the extent of disease. The TNM staging system is the foundation that guides treatment recommendations and the most important prognostic factor in predicting survival and recurrence. T is the description of tumor size by greatest dimension as measured on CT imaging. In most cases, this reflects the solid component of a tumor. T also describes the effect on or invasion of tumor into nearby structures. N is the extent and region of nodal involvement. M describes the presence or absence of metastatic spread of lung cancer outside of lung tissue or distant-site disease. Stage I disease describes tumors 4 cm or less with no nodal or metastatic involvement. Stage IIA describes tumors greater than 4 cm and less than 5 cm with no nodal or metastatic involvement. Stage IIB includes tumors ranging in size from less than 1 cm to 7 cm or less with nodal involvement in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension. Stages IIIA, IIIB, and IIIC are the largest and most heterogeneous stages of lung cancer. Tumors may be small with extensive nodal involvement to larger tumors with more extensive nodal invasion. Stage IV includes disease of any size tumor and nodal involvement with evidence of distant metastasis (Table 2).

Staging will likely be assessed at several time points. Clinical stage (cTNM) refers to staging based on physical exam, diagnostic imaging, biopsy, and surgical staging prior to treatment. Pathologic staging (pTNM) is based on information obtained from surgical resection. Staging done after a recurrence of disease or at autopsy is denoted by rTNM and aTNM, respectively.

The American Joint Committee on Cancer TNM staging classification is updated periodically, usually every 5 to 7 years. The eighth edition of the classification will replace the previous edition beginning January 1, 2018. Until then, all new cases will be staged using the seventh edition (Amin et al., 2017). The revision incorporates retrospective analysis of survival data that permits sharper distinction between the subsets compared to the seventh edition. Tumor size, nodal involvement, and areas of metastasis are categorized in more detail, which reflect updated prognosis and improve accuracy and efficacy of staging (Detterbeck et al., 2016; Goldstraw et al., 2015). There are four different clinical presentations of multifocal lung involvement that are challenging: second primary tumor, intrapulmonary metastasis, multifocal lung adenocarcinoma with ground glass/lepidic features, and pneumonic-type lung adenocarcinoma. The updated guidelines state that:

- Tumors are considered a second primary tumor if they have different histology or different radiographic appearance, metabolic uptake, growth pattern, or biomarkers. In this case, each tumor must be staged separately per the TNM staging.
- Tumors are considered intrapulmonary metastasis if there is an exact genetic matching and similar clinical features of radiographic appearance, growth pattern, or significant nodal and systemic metastasis (Detterbeck et al., 2016).

The TNM eighth edition continues to have some limitations, including lack of guidance on which image to measure the long axis of the tumor, measurement of lesions with ill-defined borders, cavity or consolidative lesions, or imaging to use to distinguish primary lung cancer from post-obstructive atelectasis or pneumonia. It does not distinguish multiple nodes within a group from those in multiple groups, nodes with irregular borders, or nodes in other regions. This updated edition does not provide classification for lymphangitic spread (Betancourt-Cuellar, Carter, Palacio, & Erasmus, 2015; Carter, Godoy, Wu, Erasmus, & Truong, 2016).

SUMMARY

Staging is one of the key factors in determining prognosis and treatment of lung cancer. All patients with suspected lung cancer should undergo a CT scan of the chest and upper abdomen to evaluate for the extent of disease. The scan evaluates metastasis to the liver and adrenal glands. Patients with local regional disease require evaluation of the mediastinum to determine if they are candidates for curative surgical resection.

Disclosure

Dr. Davies has served on the speakers bureaus for AstraZeneca, Bristol-Myers Squibb, Genentech,

Table 2. T, N, and M Descriptors From the Eighth Edition of TNM Classification for Lung Cancer

T: Primary tumor	
Tx	Primary tumor cannot be assessed or tumor proven by presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor ≤ 3 cm in greatest dimension surrounded by lung or visceral pleura without bronchoscopic evidence of invasion more proximal than the lobar bronchus (i.e., not in the main bronchus)[a]
T1a(mi)	Minimally invasive adenocarcinoma[b]
T1a	Tumor ≤ 1 cm in greatest dimension[a]
T1b	Tumor > 1 cm but ≤ 2 cm in greatest dimension[a]
T1c	Tumor > 2 cm but ≤ 3 cm in greatest dimension[a]
T2	Tumor > 3 cm but ≤ 5 cm or tumor with any of the following features:[c] • Involves main bronchus regardless of distance from the carina but without involvement of the carina • Invades visceral pleura • Associated with atelectasis or obstructive pneumonitis that extends to the hilar region, involving part or all of the lung
T2a	Tumor > 3 cm but ≤ 4 cm in greatest dimension
T2b	Tumor > 4 cm but ≤ 5 cm in greatest dimension
T3	Tumor > 5 cm but ≤ 7 cm in greatest dimension or associated with separate tumor nodule(s) in the same lobe as the primary tumor or directly invades any of the following structures: chest wall (including the parietal pleura and superior sulcus tumors), phrenic nerve, parietal pericardium
T4	Tumor > 7 cm in greatest dimension or associated with separate tumor nodule(s) in a different ipsilateral lobe than that of the primary tumor or invades any of the following structures: diaphragm, mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, and carina
N: Regional lymph node involvement	
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
N2	Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
N3	Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)
M: Distant metastasis	
M0	No distant metastasis
M1	Distant metastasis present
M1a	Separate tumor nodule(s) in a contralateral lobe; tumor with pleural or pericardial nodule(s) or malignant pleural or pericardial effusion[d]
M1b	Single extrathoracic metastasis[e]
M1c	Multiple extrathoracic metastases in one or more organs

Note. TNM = tumor, node, metastasis; Tis = carcinoma in situ; T1a(mi) = minimally invasive adenocarcinoma. Adapted from Goldstraw et al. (2015).
[a]The uncommon superficial spreading tumor of any size with its invasive component limited to the bronchial wall, which may extend proximal to the main bronchus, is also classified as T1a.
[b]Solitary adenocarcinoma, ≤ 3 cm with a predominately lepidic pattern and ≤ 5 mm invasion in any one focus.
[c]T2 tumors with these features are classified as T2a if ≤ 4 cm in greatest dimension or if size cannot be determined, and T2b if > 4 cm but ≤ 5 cm in greatest dimension.
[d]Most pleural (pericardial) effusions with lung cancer are due to tumor. In a few patients, however, multiple microscopic examinations of pleural (pericardial) fluid are negative for tumor, and the fluid is nonbloody and not an exudate. When these elements and clinical judgment dictate that the effusion is not related to the tumor, the effusion should be excluded as a staging descriptor.
[e]This includes involvement of a single distant (nonregional) lymph node.

☞ *Table continued on next page*

Table 2. T, N, and M Descriptors From the Eighth Edition of TNM Classification for Lung Cancer (cont.)

Stage groupings			
Occult carcinoma	Tx	N0	M0
Stage 0	Tis	N0	M0
Stage IA1	T1a(mi)	N0	M0
	T1a	N0	M0
Stage IA2	T1b	N0	M0
Stage IA3	T1c	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T2b	N0	M0
Stage IIB	T1a to c	N1	M0
	T2a	N1	M0
	T2b	N1	M0
	T3	N0	M0
Stage IIIA	T1a to c	N2	M0
	T2a to b	N2	M0
	T3	N1	M0
	T4	N0	M0
	T4	N1	M0
Stage IIIB	T1a to c	N3	M0
	T2a to b	N3	M0
	T3	N2	M0
	T4	N2	M0
Stage IIIC	T3	N3	M0
	T4	N3	M0
Stage IVA	Any T	Any N	M1a
	Any T	Any N	M1b
Stage IVB	Any T	Any N	M1c

Note. TNM = tumor, node, metastasis; Tis = carcinoma in situ; T1a(mi) = minimally invasive adenocarcinoma. Adapted from Goldstraw et al. (2015).

and Merck and has received payments for the development of educational programs for BioMedical Learning Institute, PeerView, and Practicing Physicians Exchange.

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