

Diagnosing and Staging Lung Cancer Involving the Mediastinum

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The purpose of this article is to provide an update on evidence-based methods for mediastinal staging in patients with lung cancer. This is a review of the recently published studies and a summary of relevant guidelines addressing the role of CT scan, PET scan, endobronchial ultrasound transbronchial needle aspiration (EBUS-TBNA), and mediastinoscopy as pertinent to lung cancer staging and restaging. The focus is on how these diagnostic methods fit into the best algorithm for patients with chest imaging abnormalities suspected of malignant disease. Several studies, meta-analyses, and systematic reviews specifically targeted the role of PET scan, EBUS-TBNA, and mediastinoscopy for detecting mediastinal lymph node involvement in patients suffering from lung cancer. Based on the recommendations from the currently published guidelines, algorithms of care are proposed for staging and restaging of the mediastinum. CHEST 2015; 147(5):1401-1412

ABBREVIATIONS: APW = aortopulmonary window; ATS = American Thoracic Society; EBUS = endobronchial ultrasound; ECM = extended cervical mediastinoscopy; EUS = esophageal ultrasound; FNA = fine-needle aspiration; IASLC = International Association for the Study of Lung Cancer; LUL = left upper lobe; MD-ATS = Mountain Dressler-American Thoracic Society; NPV = negative predictive value; NSCLC = non-small cell lung cancer; SBRT = stereotactic body radiation therapy; SEPAR = Spanish Society for Pulmonology and Thoracic Surgery; TBNA = transbronchial needle aspiration; VATS = video-assisted thoracic surgery

In patients with non-small cell lung cancer (NSCLC), accurate mediastinal staging is relevant to determine treatment options, estimate prognosis, and provide a common language when communicating about patients and enrolling them in clinical trials. For the last 4 decades, several lymph node maps have been used to define the clinical and pathologic lymph node involvement in patients with lung cancer by labeling intrathoracic lymph node regions using either anatomic descriptions (eg, right lower paratracheal) or numerical levels (eg, 4R). These maps include those by

Naruke, American Thoracic Society (ATS), and Mountain Dressler-ATS (MD-ATS), a modification of the ATS map. The Naruke map had been used by Japanese surgeons and oncologists, whereas the MD-ATS was widely adopted in North America. The International Association for the Study of Lung Cancer (IASLC) has proposed a revision of the TNM staging system in which the N descriptors reconcile the discrepancies between the Naruke and the MD-ATS maps. The most striking discrepancy between the two systems was that level 7 subcarinal lymph nodes in the MD-ATS map corresponded

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to levels 7 and 10 in the Naruke map. Thus, some tumors were staged as N2 (stage IIIA) according to the MD-ATS map, but they were N1 (stage II) by the Naruke map.

Data analyses, treatment options, and outcomes therefore were significantly affected by the choice of a particular lymph node map. This discrepancy illustrates the relevance of having a unified staging system. For mediastinal staging, this is now offered by the IASLC map.

Relevance and Impact of Adequate Staging

The distinct treatment options and prognosis for any given tumor stage make accurate staging the most relevant step in the management of patients with lung cancer. Staging sequence and completeness prior to curative-intent treatment remain suboptimal. In one study, single (CT scan), bimodality (CT scan plus PET scan or CT scan plus invasive), or trimodality (CT scan, PET scan, and invasive) tests were used to assess for mediastinal metastases. Only 30% of patients had bimodality and 5% had trimodality staging, despite the guidelines recommending for bimodality or trimodality strategies, which have a significantly lower risk of death.¹

The Institute of Medicine recommends that patient care should be “STEEEP”: safe, timely, effective, efficient, equitable, and patient-centric. For efficiency, access, and timeliness of an initial procedure in the management of patients with suspected lung cancer, concomitant diagnosis and staging is beneficial because it avoids additional procedures. It is preferable to perform a biopsy at the site that would confer the highest stage (ie, to perform a biopsy of a suspected metastasis or mediastinal lymph node rather than the primary pulmonary lesion).² Timely staging is relevant, as negative outcomes result from delaying therapy. Distant metastases may become evident on serial CT scans or PET scans in 3% of untreated patients at 4 weeks and in 13% at 8 weeks. Complete restaging, therefore, should be considered if therapy is delayed for 4 to 8 weeks after the diagnosis.³

Safety and effectiveness can be ensured by adherence to the guidelines, which recommend mediastinal lymph node sampling as the first invasive test in patients with suspected lung cancer and mediastinal lymph node involvement without distant metastases. Guideline-consistent care with initial mediastinal sampling results in fewer tests and complications.⁴ One study compared outcomes of diagnostic strategies in patients with lung cancer with regional spread without distant metastases.⁴ If the first invasive test involved mediastinal sampling, patients were classified as guideline consistent; otherwise, they were classified as inconsistent. Only 21% of

patients had guideline-consistent diagnostic evaluations, and 44% never had mediastinal sampling. Patients who had guideline-consistent care required fewer tests than patients with guideline-inconsistent care, including thoracotomies and CT scan-guided biopsies, although they had more transbronchial needle aspirations. As a consequence, patients with guideline-consistent care had fewer pneumothoraces, chest tubes, hemorrhages, and respiratory failure events.⁴ Three quality gaps are in fact identified in the care of patients with lung cancer: failure to sample the mediastinum first, failure to sample the mediastinum at all, and overuse of thoracotomy. Furthermore, out of the seven process of care quality indicators related to the evaluation of patients with lung cancer, four are related to staging alone and include mediastinal sampling prior to curative-intent surgery for stage IB or higher.⁵ Performing a safe, timely, efficient, effective, and patient-centric staging requires a coordinated effort. Guidelines recommend a multidisciplinary lung cancer team involvement early in a patient’s care, which coordinates the optimal approach to staging and specimen acquisition to expedite diagnostic and molecular testing.^{2,6,7}

Normal and Pathologic Mediastinum on CT Scan and PET Scan: Implications for Staging

Contrast-enhanced chest and upper abdominal CT scan is recommended as an initial step for all patients with suspected or confirmed diagnosis of lung cancer suitable for treatment.⁷⁻¹⁰ The revised IASLC system is clinician oriented and should be used for staging,⁸ as it unifies previously used systems and defines the borders of the mediastinal, hilar, and interlobar lymph nodes based on CT scan landmarks.¹¹ To further help clinicians in their routine practice, the American College of Chest Physicians proposed that patients with lung cancer be separated into four categories with respect to the radiographic characteristics of the primary tumor and the lymph nodes based on CT scan findings¹² (Fig 1). For group A, tissue diagnosis suffices, as mediastinal involvement is implied. Group B patients need pathologic confirmation of their lymph nodes prior to curative-intent treatment. Groups C and D involve patients with normal mediastinal nodes on CT scan. In group C, the presence of a central tumor or suspected N1 disease on CT scan or PET scan (hilar, interlobar nodes) makes the risk of mediastinal (N2, 3) nodal involvement high (20%-25%) despite normal-sized mediastinal nodes negative on PET scan; thus, further tissue confirmation is needed for this group. For group D, invasive staging is currently not routinely recommended prior to thoracotomy

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