Complete Summary

GUIDELINE TITLE

Invasive mediastinal staging of lung cancer: ACCP evidence-based clinical practice guidelines. (2nd Edition)

BIBLIOGRAPHIC SOURCE(S)

Detterbeck FC, Jantz MA, Wallace M, Vansteenkiste J, Silvestri GA, American College of Chest Physicians. Invasive mediastinal staging of lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition). Chest 2007 Sep;132(3 Suppl):202S-20S. [112 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Detterbeck FC, DeCamp MM Jr, Kohman LJ, Silvestri GA. Lung cancer. Invasive staging: the guidelines. Chest 2003 Jan;123(1 Suppl):167S-75S.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Lung cancer

GUIDELINE CATEGORY

Diagnosis

CLINICAL SPECIALTY

Family Practice
Oncology
Pulmonary Medicine
Radiation Oncology
Thoracic Surgery

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Health Care Providers
Nurses
Patients
Physicians
Psychologists/Non-physician Behavioral Health Clinicians
Social Workers

GUIDELINE OBJECTIVE(S)

To discuss the performance characteristics of the various invasive staging tests for the mediastinum, how to select a test, and how to interpret the results

TARGET POPULATION

Patients with a strong suspicion of lung cancer

INTERVENTIONS AND PRACTICES CONSIDERED

1. Mediastinoscopy
2. Endoscopic ultrasound-guided needle aspiration (EUS-NA)
3. Transbronchial needle aspiration (TBNA)
4. Endobronchial ultrasound needle aspiration (EBUS-NA)
5. Transthoracic needle aspiration (TTNA)
6. Video-assisted thoracic surgery (VATS) staging
7. Chamberlain procedure
8. Extended cervical mediastinoscopy

MAJOR OUTCOMES CONSIDERED

- Sensitivity and specificity of invasive staging tests
- Negative predictive value (NPV) of invasive staging tests
- Positive predictive value (PPV) of invasive staging tests

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Overview

The American College of Chest Physicians (ACCP) chose the Duke University Center for Clinical Health Policy Research to perform formal systematic reviews of the current evidence in the five new non-small cell lung cancer (NSCLC) topic areas, as well as to provide a search for the existing guidelines, systematic reviews, and meta-analyses in all of the topics areas. In addition, the Agency for Healthcare Quality and Research) AHRQ agreed to fund the BlueCross BlueShield Association Technology Evaluation Center to perform the formal systematic review of literature on small cell lung cancer (SCLC). The Health Outcomes Research Group of the Department of Epidemiology and Biostatistics at Memorial Sloan-Kettering Cancer Center conducted a full-scale review of the literature since the first set of guidelines in the area of screening for lung cancer to assist that particular writing group.

The formal systematic reviews of the five new topic areas were guided by the appropriate chapter editors and their writing committees, in concert with the Executive Committee of the panel.

The two EPC research teams conducted a variety of systematic computerized bibliographic database searches including the following: (1) a search for systematic reviews, guidelines, and meta-analyses published since the last ACCP lung cancer guideline (MEDLINE, The Cochrane Library, National Guidelines Clearinghouse); (2) targeted searches for reviews in each of five selected treatment sections (solitary pulmonary nodules, stage I and II, stage IIIA, stage IIIB, stage IV); these searches, run in OVID version of MEDLINE, were performed in July and August 2005 and were limited to publication years since 1995, English language, and human subjects; and (3) searches related to SCLC are described in the evidence chapter on SCLC.

Search terms included the medical subject heading terms lung neoplasms (exploded) and bronchial neoplasms for the lung cancer concept. Each topic search utilized key words specific to the key questions of interest (complete search strategies are available on request from the authors).

Strategy Specific for Invasive Mediastinal Staging of Lung Cancer

The data presented here are based on a systematic search and evaluation of the published literature from January 1980 through June 2006. Articles published prior to July 2001 were identified according to the criteria laid out in the previous version of the American College of Chest Physicians lung cancer guidelines. Subsequent literature was identified by the authors using the same search strategy and selection criteria (briefly, studies published in the English language, peer-reviewed, nonoverlapping, having at least 20 patients, containing an adequate assessment of the true nodal status, and with the ability to calculate performance characteristics).

The data abstraction was performed for patients suspected of having lung cancer (e.g., non-small cell lung cancer [NSCLC] and small cell lung cancer [SCLC]). Patients suspected of a diagnosis other than lung cancer were excluded from the

study, where possible. A definite diagnosis of any lung cancer in the mediastinal tissues was considered to be positive, while other diagnoses (e.g., benign disease or lymphoma) were coded as negative for lung cancer. Equivocal test results were considered to be negative. Biopsies that were aborted or yielded insufficient tissue are included as negative findings and are counted as such in the statistics. The reported feasibility of the test is also reported (i.e., the proportion of patients undergoing the test in whom an adequate biopsy was able to be obtained) in order to have an assessment of the technical success rate. The calculation of the subtotal or total summary performance characteristics was accomplished by the calculation of an average of the values (e.g., of sensitivity and specificity) from each study; in other words, no weighting according to study size was performed. This was chosen for simplicity, and because a comparison of the results using both methods revealed minimal differences (i.e., 1 to 2 percentage points).

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus
Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

High - Randomized controlled trials (RCTs) without important limitations or overwhelming evidence from observational studies*

Moderate - RCTs with important limitations (inconsistent results, methodologic flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies*

Low or very low - Observational studies or case series

*Although the determination of magnitude of the effect based on observational studies is often a matter of judgment, the guideline developers offer the following suggested rule to assist this decision: a large effect would be a relative risk >2 (risk ratio < 0.5) [which would justify moving from weak to moderate], and a very large effect is a relative risk > 5 (risk ratio < 0.2) [which would justify moving from weak to strong]. There is some theoretical justification in the statistical literature for these thresholds (the magnitude of effect that is unlikely or very unlikely to be due to residual confounding after adjusted analysis). However, once the decision is made, authors should be explicit in justifying their decisions.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Quality of evidence is scored in three categories with high-quality evidence obtained from randomized controlled trials (RCTs) without important methodologic limitations based on the study design, the consistency of the results, and the directness of the evidence. In extraordinary circumstances, significant and consistent evidence from observational studies could also be ranked as high quality. RCTs with important methodologic limitations or flaws, inconsistent results, or indirect or imprecise results would be scored as medium quality, as well as exceptionally strong evidence from observational studies. Other observational studies or case-series data would fall into the low quality of evidence category. It is the interface of the quality of the evidence and the balance of benefits to harms or burdens that determines the strength of the recommendation, with a 1A recommendation being the strongest and 2C the weakest.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus
Informal Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Writing committees studied the evidence and summary tables or reviewed the literature for their assigned topics, developing their arguments for the recommendations and suggested grading of those recommendations that were put forth for early drafts. The Executive Committee of the panel, composed of the Chair, Vice-Chair, methodologist, and both project managers, reviewed drafts of each chapter of the manuscript during the writing process. Sections that were determined to be potentially overlapping were shared among the appropriate chapter editors, and conference calls were organized to coordinate the placement of these sections and to confirm that there would be no conflicting information or recommendations.

A conference of the panel was convened in July 2006, prior to which time all panelists, including representatives from the invited organizations, were requested to review the complete manuscript and identify recommendations for which the proposal, wording, or grading were determined to be controversial or could be interpreted as controversial by others, incorrectly evolved from the evidence, disagreement existed with regard to the proposal or the grading, or required full panel discussion and further review for any reason. When the panelists who were present were not in unanimous agreement with the proposed recommendations or the grading of the recommendations, informal group consensus techniques were employed. After the meeting, a series of conference calls were convened to finish the discussions and finalize the recommendations. There were a few chapters for which there was insufficient time for full dialogue during the meeting; in the interest of ensuring that the recommendations followed the evidence, the conference calls were necessary. This process ensured the "buy-in" of the panelists and was deemed to be a worthwhile effort.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grade of Recommendations Scale

Grade	Recommendation
1A	Strong
1B	Strong
1C	Strong
2A	Weak
2B	Weak
2C	Weak

Relationship of Strength of the Supporting Evidence to the Balance of Benefits to Risks and Burdens

Balance of Benefits to Risks and Burdens				
Quality of Evidence	**Benefits Outweigh Risks/Burdens**	**Risks/Burdens Outweigh Benefits**	**Evenly Balanced**	**Uncertain**
High	1A	1A	2A	
Moderate	1B	1B	2B	
Low or very low	1C	1C	2C	2C

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Following final chapter revisions and incorporation of these ultimate recommendations and grading, a concluding review was conducted by the guideline panel Executive Committee. The guidelines were then submitted for review and approval to the American College of Chest Physicians Health and Science Policy Committee (ACCP HSP) Committee, as well as the Thoracic Oncology Network of the college.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the strength of evidence and recommendation grades (1A-2C) follow the recommendations.

1. For patients with extensive mediastinal infiltration of tumor (and no distant metastases), radiographic (CT scan) assessment of the mediastinal stage is

usually sufficient without invasive confirmation. **Grade of recommendation, 2C**

2. For patients with discrete mediastinal lymph node enlargement (and no distant metastases), invasive confirmation of the radiographic stage is recommended (regardless of whether the findings of a positron emission tomography [PET] scan of the mediastinal nodes are positive or negative). **Grade of recommendation, 1B**
3. For patients with discrete mediastinal lymph node enlargement (and no distant metastases), many invasive techniques for confirmation of the N2,3 node status are suggested as reasonable approaches (mediastinoscopy Endoscopic ultrasound-guided needle aspiration (EUS-NA), Transbronchial needle aspiration (TBNA), Endobronchial ultrasound needle aspiration (EBUS-NA) Transthoracic needle aspiration (TTNA) given the availability of personnel with appropriate experience and skill. **Grade of recommendation, 1B**
4. For patients with discrete mediastinal lymph node enlargement (and no distant metastases), a nonmalignant result from a needle technique (e.g., EUS-NA, TBNA, EBUS-NA, or TTNA) should be further confirmed by mediastinoscopy (regardless of whether the findings of a PET scan of the mediastinal nodes are positive or negative). **Grade of recommendation, 1C**
5. For patients with a radiographically normal mediastinum (determined by CT scan) and a central tumor or N1 lymph node enlargement (and no distant metastases), invasive confirmation of the radiographic stage is recommended (regardless of whether the findings of a PET scan of the mediastinal nodes are positive or negative). **Grade of recommendation, 1C**
6. For patients with a central tumor or N1 lymph node enlargement (and no distant metastases), invasive staging is recommended. In general, mediastinoscopy is suggested, but EUS-NA or EBUS-NA may be a reasonable alternative if nondiagnostic results are followed by mediastinoscopy. **Grade of recommendation, 2C**
7. For patients with a peripheral clinical stage I tumor in whom a PET scan shows uptake in the mediastinal nodes (and no distant metastases), invasive staging is recommended. In general, mediastinoscopy is suggested, but EUS-NA or EBUS-NA may be a reasonable alternative if nondiagnostic results are followed by mediastinoscopy. **Grade of recommendation, 1C**
8. For patients with a peripheral clinical stage I tumor, invasive confirmation of the mediastinal nodes is not needed if the findings of a PET scan of the mediastinum are negative. **Grade of recommendation, 1C**
9. For patients with an LUL cancer in whom invasive mediastinal staging is indicated, as defined by the previous recommendations, it is suggested that invasive mediastinal staging include the assessment of the aortopulmonary window (APW) nodes (via Chamberlain procedure, thoracoscopy, extended cervical mediastinoscopy, EUS-NA, or EBUS-NA) if other mediastinal node stations are found to be uninvolved. **Grade of recommendation, 2C**

Definitions:

Quality of Evidence Scale

High - Randomized controlled trials (RCTs) without important limitations or overwhelming evidence from observational studies*

Moderate - RCTs with important limitations (inconsistent results, methodologic flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies*

Low or very low - Observational studies or case series

*Although the determination of magnitude of the effect based on observational studies is often a matter of judgment, the guideline developers offer the following suggested rule to assist this decision: a large effect would be a relative risk > 2 (risk ratio < 0.5) [which would justify moving from weak to moderate], and a very large effect is a relative risk > 5 (risk ratio < 0.2) [which would justify moving from weak to strong]. There is some theoretical justification in the statistical literature for these thresholds (the magnitude of effect that is unlikely or very unlikely to be due to residual confounding after adjusted analysis). However, once the decision is made, authors should be explicit in justifying their decisions.

Grade of Recommendations Scale

Grade	Recommendation
1A	Strong
1B	Strong
1C	Strong
2A	Weak
2B	Weak
2C	Weak

Relationship of Strength of the Supporting Evidence to the Balance of Benefits to Risks and Burdens

Balance of Benefits to Risks and Burdens				
Quality of Evidence	**Benefits Outweigh Risks/Burdens**	**Risks/Burdens Outweigh Benefits**	**Evenly Balanced**	**Uncertain**
High	1A	1A	2A	
Moderate	1B	1B	2B	
Low or very low	1C	1C	2C	2C

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate use of invasive mediastinal staging of lung cancer
- The invasive procedures are often needed to more accurately confirm the presumptive mediastinal stage, but they are also sometimes used simply to confirm the diagnosis of malignancy.

POTENTIAL HARMS

- *Endobronchial ultrasound–needle aspiration (EUS-NA)* of mediastinal lymph nodes through the wall of the esophagus has been performed with a negligible risk of infection or bleeding.
- Two major complications reported for *extended cervical mediastinoscopy* are stroke and aortic injury.
- There is a low risk of mortality and other complications from mediastinoscopy.
- False-negative and false-positive results.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The publication of the *Diagnosis and Management of Lung Cancer: ACCP Evidence-Based Clinical Practice Guidelines; Second Edition* in *CHEST* is the first of two dissemination vehicles. The circulation of the journal is 23,000 subscribers and libraries, including six translations and distribution to 107 countries. All subscribers received a copy of this full-text guideline. The American College of Chest Physicians (ACCP) Clinical Resource on Lung Cancer is composed of a printed publication and an accompanying CD-ROM, containing a quick reference guide for physicians and other health-care providers, patient-targeted educational materials, and a set of slides for use in educational or clinical contexts. In addition, the recommendations and grading are personal digital assistant downloadable from the clinical resource. This product is available for purchase from the ACCP. The patient education materials are accessible free of charge on www.chestnet.org.

The implementation and translation of evidence-based clinical practice guidelines facilitates knowledge uptake, critical for practice change, and should ultimately lead to better patient-focused care. The HSP Subcommittee on Implementation has proposed to collaborate with the Governors, Thoracic Oncology Network, and other groups within the ACCP to disseminate and implement the guidelines in their local communities. Residency and specialty training programs are encouraged to use the guidelines in journal clubs and grand rounds. Other organizations that were invited to send representatives to the final conference and review the proposed drafts were also requested to endorse the guidelines and market them to their membership through their own communication channels.

IMPLEMENTATION TOOLS

Patient Resources
Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Detterbeck FC, Jantz MA, Wallace M, Vansteenkiste J, Silvestri GA, American College of Chest Physicians. Invasive mediastinal staging of lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition). Chest 2007 Sep;132(3 Suppl):202S-20S. [112 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2003 Jan (revised 2007 Sep)

GUIDELINE DEVELOPER(S)

American College of Chest Physicians - Medical Specialty Society

SOURCE(S) OF FUNDING

American College of Chest Physicians

GUIDELINE COMMITTEE

American College of Chest Physicians (ACCP) Expert Panel on Lung Cancer Guidelines

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Authors: Frank C. Detterbeck, MD, FCCP; Michael A. Jantz, MD, FCCP; Michael Wallace, MD, FCCP; Johan Vansteenkiste, MD, PhD; Gerard A. Silvestri, MD, FCCP

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Funding for both the evidence review and guideline development was supported by educational grants from AstraZeneca LP, Bristol-Myers Squibb Company, Eli Lilly and Company, Genentech, and Sanofi-Aventis. Representatives from these companies were neither granted the right of review, nor were they allowed participation in any portion of the guideline development process. This precluded participation in either conference calls or conferences. No panel members or ACCP reviewers were paid any honoraria for their participation in the development and review of these guidelines.

The ACCP approach to the issue of potential or perceived conflicts of interest established clear firewalls to ensure that the guideline development process was not influenced by industry sources. This policy is published on the ACCP Web site at www.chestnet.org. All conflicts of interest within the preceding 5 years were required to be disclosed by all panelists, including those who did not have writing responsibilities, at all face-to-face meetings, the final conference, and prior to submission for publication. The most recent of these conflict of interests are documented in this guideline Supplement. Furthermore, the panel was instructed in this matter, verbally and in writing, prior to the deliberations of the final conference. Any disclosed memberships on speaker's bureaus, consultant fees, grants and other research monies, and any fiduciary responsibilities to industry were provided to the full panel in writing at the beginning of the conference and at submission for publication.

ENDORSER(S)

American Association for Bronchology - Disease Specific Society
American Association for Thoracic Surgery - Medical Specialty Society
American College of Surgeons - Medical Specialty Society
American Society for Therapeutic Radiology and Oncology
Asian Pacific Society of Respirology - Disease Specific Society
Oncology Nursing Society - Professional Association
Society of Thoracic Surgeons - Medical Specialty Society
World Association of Bronchology - Disease Specific Society

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Detterbeck FC, DeCamp MM Jr, Kohman LJ, Silvestri GA. Lung cancer. Invasive staging: the guidelines. Chest 2003 Jan;123(1 Suppl):167S-75S.

GUIDELINE AVAILABILITY

Electronic copies: Available to subscribers of Chest - The Cardiopulmonary and Critical Care Journal.

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

Executive Summary:

- Alberts MW. Diagnosis and management of lung cancer executive summary. Chest 2007 Sep;132(3 Suppl):1S-19.

Background Articles:

- Alberts WM. Introduction: diagnosis and management of lung cancer. Chest 2007 Sep;132(3 Suppl):20S-22.
- McCrory DC, Lewis SZ, Heitzer J, Colice GL, Alberts WM. Methodology for lung cancer evidence review and guideline development. Chest 2007 Sep;132(3 Suppl):23S-28.
- Alberg AJ, Ford JG, Samet JM. Epidemiology of lung cancer. Chest 2007 Sep;132(3 Suppl):29S-55.

Electronic copies: Available to subscribers of Chest - The Cardiopulmonary and Critical Care Journal.

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

The following is also available:

- ACCP clinical resources: Diagnosis and management of lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition).

Available from the American College of Chest Physicians Web site.

PATIENT RESOURCES

The following are available:

- Lung cancer guides: lung cancer...am I at risk? Patient education guide. Northbrook (IL): American College of Chest Physicians, 2004. 12 p.
- Lung cancer guides: What if I have a spot on my lung? Do I have cancer? Patient education guide. Northbrook (IL): American College of Chest Physicians, 2004. 16 p.
- Lung cancer guides: living with lung cancer. Patient education guide. Northbrook (IL): American College of Chest Physicians, 2004. 12 p.

- Lung cancer guides: advanced lung cancer: issues to consider. Patient education guide. Northbrook (IL): American College of Chest Physicians, 2004. 12 p.

Electronic copies: Available in Portable Document Format (PDF) from the American College of Chest Physicians (ACCP) Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI on July 22, 2003. The information was verified by the guideline developer on August 18, 2003. This NGC summary was updated by ECRI Institute on November 9, 2007. The updated information was verified by the guideline developer on December 21, 2007.

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