LUNG CANCER PATIENT SUPPORT ECHO SESSION 5
TREATMENT PLANNING: OVERCOMING LACK OF CONCORDANCE
WITH STAGING AND MANAGEMENT GUIDELINES
GERARD SILVESTRI, MD, MS
M. PATRICIA RIVERA, MD
JOHN RUCKDESCHEL, MD (FACILITATOR)
SEPTEMBER 27, 2018
9:00 AM ET
TODAY’S AGENDA

<table>
<thead>
<tr>
<th>Time</th>
<th>Presentation</th>
<th>Presenter(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:00-9:10</td>
<td>Welcome, roll call, housekeeping</td>
<td>John Ruckdeschel, MD</td>
</tr>
<tr>
<td>9:10-9:45</td>
<td>Didactic Presentation: ECHO Session 5</td>
<td>Gerard Silvestri, MD, MS M. Patricia Rivera, MD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>John Ruckdeschel, MD</td>
</tr>
<tr>
<td>9:45-10:00</td>
<td>Q &amp; A/Discussion</td>
<td>Facilitated by John Ruckdeschel, MD</td>
</tr>
<tr>
<td>10:00-10:15</td>
<td>Program/Case Presentation:</td>
<td>Gerard Silvestri, MD, MS</td>
</tr>
<tr>
<td>10:15-10:25</td>
<td>Q &amp; A/Discussion</td>
<td>Facilitated by John Ruckdeschel, MD</td>
</tr>
<tr>
<td>10:25-10:30</td>
<td>Conclusion/Next session</td>
<td>John Ruckdeschel, MD</td>
</tr>
</tbody>
</table>

*Sessions will be recorded.
*Please mute phones when not speaking. Mute cell phones and try to reduce extraneous noise.
*Remember to e-mail Octavia Vogel by 9/31 if you are requesting CME/CEU credit.
DISCLOSURE

- UNM CME policy, in compliance with the ACCME Standards of Commercial Support, requires that anyone who is in a position to control the content of an activity disclose all relevant financial relationships they have had within the last 12 months with a commercial interest related to the content of this activity.

- The following planners and faculty disclose that they have no financial relationships with any commercial interest.
Facilitator: John Ruckdeschel, MD  
Director, University of Mississippi Cancer Institute

Speaker/Case Presenter: Gerard Silvestri, MD, MS  
Professor of Medicine  
Medical University of South Carolina

Speaker: Patricia Rivera, MD  
Professor of Medicine  
University of North Carolina, Chapel Hill
Evidence shows that for each stage at diagnosis, a significant fraction of patients do not receive guideline appropriate diagnostic workup, staging and management.

Upon completion of this session participants will demonstrate:

- Knowledge of key points for guideline appropriate diagnostic workup, staging and management of lung cancer
- Knowledge of reasons for lack of concordance with guidelines
- Knowledge of clinical practices strategies for improving clinic concordance
The Importance of Appropriately Staging Lung Cancer Prior to Treatment

Gerard A. Silvestri MD,MS
Professor of Medicine
Medical University of South Carolina
Charleston, SC

M. Patricia Rivera, MD
Professor of Medicine
University of North Carolina
Chapel Hill, NC
Outline

• Background
• Tools For staging
• Mediastinum
• Evidence for effective staging
• Cases
Staging

• Accurate staging is critical
  • Treatment options are stage dependent
  • Prognosis is based upon stage
  • Enrollment in clinical trials by stage
  • Provides a common language when discussing cases
  • Allows for study of large cohorts of patients
Overview of NSCLC Treatment

Stage I
- Surgery (Radiation if inoperable)
- Radiation
- With Chemotherapy
- – Adjuvant Immunotherapy
- Chemotherapy
- Targeted Therapy
- Immunotherapy
- Supportive care

Stage II
- Surgery With Adjuvant Chemotherapy

Stage III
- Radiation With Chemotherapy – Adjuvant Immunotherapy

Stage IV or Recurrent Disease
- Chemotherapy
- Targeted Therapy
- Immunotherapy
- Supportive care
Staging for Lung Cancer

Non-invasive Staging
- CT
- PET

Invasive Staging
- Non-surgical
  - EUS
  - EBUS
- Surgical
  - Mediastinoscopy
  - Anterior Mediastinotomy (Chamberlain procedure)
  - VATS
Methods for Staging Non-small Cell Lung Cancer

Diagnosis and Management of Lung Cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

Gerard A. Silvestri, MD, FCCP; Anne V. Gonzalez, MD; Michael A. Jantzi, MD, FCCP; Mitchell L. Margolis, MD, FCCP; Michael K. Gould, MD, FCCP; Lynn T. Tanoue, MD, FCCP; Loren J. Harris, MD, FCCP; and Frank C. Detterbeck, MD, FCCP

Isn’t CT, PET good enough?

Silvestri et al. CHEST 2013; 143(5)(Suppl):e211S–e250S
### Accuracy of CT and PET Staging Mediastinal Lymph Nodes

Summary of 43 (CT) and 45 (PET) trials

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CT</strong></td>
<td>55%</td>
<td>81%</td>
</tr>
<tr>
<td>N=7,368</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PET</strong></td>
<td>80%</td>
<td>88%</td>
</tr>
<tr>
<td>N=4,105</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Silvestri et al. *CHEST 2013; 143(5)(Suppl):e211S–e250S*
## Accuracy of Staging Tests in Lung Cancer Patients

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Number of Studies</th>
<th>N</th>
<th>Sens</th>
<th>Spec</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mediastinoscopy</td>
<td>35</td>
<td>10,648</td>
<td>81</td>
<td>100</td>
</tr>
<tr>
<td>EUS</td>
<td>26</td>
<td>2,443</td>
<td>89</td>
<td>100</td>
</tr>
<tr>
<td>EBUS</td>
<td>26</td>
<td>2,756</td>
<td>89</td>
<td>100</td>
</tr>
<tr>
<td>EBUS/EUS</td>
<td>7</td>
<td>811</td>
<td>91</td>
<td>100</td>
</tr>
</tbody>
</table>

ACCP Recommendations for CT and PET-2007

- In patients with enlarged discrete mediastinal lymph nodes on CT scans further evaluation of the mediastinum should be performed.
- In patients with an abnormal result on FDG-PET scans, further evaluation of the mediastinum with sampling of the abnormal lymph node should be performed.

Silvestri et al. Chest 2007;132:178s
Recommendations

• ACCP guidelines 2007: Many invasive techniques for the confirmation of the N2,3 node status are suggested as reasonable approaches (eg, mediastinoscopy, EUS-NA, TBNA, EBUS-NA, or TTNA)

• ACCP guidelines 2013: In patients with high suspicion of N2,3 involvement, either by discrete mediastinal lymph node enlargement or PET uptake (and no distant metastases), a needle technique (EBUS-NA, EUS-NA or combined EBUS/EUS-NA) is recommended over surgical staging as a best first test

Detterbeck F et al. ACCP 2 guidelines Chest 2007
Silvestri et al. CHEST 2013; 143(5)(Suppl):e211S–e250S
Methods of Obtaining Tissue

• Mediastinoscopy
• Mediastinotomy
• Thoracoscopy
• Trans bronchial needle aspirate
• EUS with FNA
• EBUS with FNA
Mediastinoscopy
Left anterior Mediastinotomy (Chamberlain Procedure)
Patterns of Surgical Care of Lung Cancer Patients

- Survey with chart abstraction- 729 hospitals
- 40,000 patients, 11,668 surgeries
- Staging:
  - Preoperative Mediastinoscopy was performed in only 27% of patients
  - Of those less than ½ had a biopsy taken
  - Thus of 11,668 patients operated upon, tissue was obtained from the mediastinum in only 1,480 patients

Real-Time Endobronchial Ultrasound-Guided Transbronchial Lymph Node Aspiration

Brad D. Vincent, MD, Ezzat El-Bayoumi, MD, Brenda Hoffman, MD, Peter Doelken, MD, John DeRosimo, MD, Carolyn Reed, MD, and Gerard A. Silvestri, MD, MS

Departments of Pulmonary, Critical Care and Sleep Medicine, Thoracic Surgery, and Gastroenterology and Hepatology, Medical University of South Carolina, Charleston, South Carolina
Real-Time EBUS TBNA

- Retrospective analysis of 152 patients
- Cancer was identified in 113 patients
  - NSCLC 59% cases
- 20 underwent surgical resection
- Compared with radiologic staging EBUS-TBNA
  - Down-staged 18 of 113 (15.9%)
  - Up-staged 11 (9.7%)
- Sensitivity 98.7%
- Specificity 100%

Frequency of Invasive Preoperative Mediastinal Staging

• Has been low

• Likely reflects:
  • Practice gaps in knowledge concerning existing recommendations
  • Practice patterns and regional variations regarding mediastinoscopy and EBUS-TBNA
Thoroughness of Mediastinal Staging in Stage IIIA Non-Small Cell Lung Cancer

Vest MT et al. JTO2012;7:188-95

• Cohort study, SEER–Medicare data from 1998 to 2005

• 7583 patients with stage IIIA NSCLC

• Only 1678 (22%) underwent invasive mediastinal staging
  • 76% with mediastinoscopy
  • 26% transbronchial needle aspiration (TBNA)
  • 1.6% Esophageal Ultrasound (EUS)
Thoroughness of Mediastinal Staging

- Predictors of thorough staging:
  - Curative intent treatment (30% vs. 9.8% (OR 3.32, 95% CI 2.78-3.95) in patients who did not receive cancer specific therapy
  - Older age (85+)

- Sex, income and race not associated with use of invasive staging

- Use of invasive staging stable throughout study period despite increase use of PET from 10% in 2000 to about 70% in 2005

- Conclusion:
  - Nearly 80% of Medicare patients with stage IIIA do not receive guideline-recommended mediastinal staging
  - Cannot be explained by patient factors or increase use of PET
Multi-Modality Mediastinal Staging for Lung Cancer Among Medicare Beneficiaries

Farjah F et al JTO; 2009:355-

- Use of non-invasive and invasive tests improves accuracy of mediastinal staging
- Unknown how frequently it is used and whether it improves health outcomes
- Cohort study using SEER data (1998-2005)
- Categorized as staged by
  - Single modality (CT)
  - Bimodality (CT & PET)
  - Trimodality (CT & PET & invasive staging)
Findings

- 42,912 patients
- Median age 75
- Overall survival over 5 years – 13%
- 77% single modality
- 21% bi-modality
- 2% tri modality
- Over time PET increased, single mode decreased and invasive staging stayed about the same
Factors Associated With Lower Odds of Receipt of Multi-Modality Staging

<table>
<thead>
<tr>
<th>Factors</th>
<th>Odds ratio</th>
<th>(99% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.97</td>
<td>(0.96–0.97)</td>
</tr>
<tr>
<td>Male</td>
<td>0.79</td>
<td>(0.74–0.84)</td>
</tr>
<tr>
<td>Race</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>0.63</td>
<td>(0.55–0.72)</td>
</tr>
<tr>
<td>Other</td>
<td>0.85</td>
<td>(0.74–0.98)</td>
</tr>
<tr>
<td>Low income</td>
<td>0.84</td>
<td>(0.77–0.93)</td>
</tr>
<tr>
<td>Low education</td>
<td>0.89</td>
<td>(0.81–0.97)</td>
</tr>
<tr>
<td>Unmarried</td>
<td>0.76</td>
<td>(0.72–0.82)</td>
</tr>
<tr>
<td>Geography</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td>West</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td>East</td>
<td>0.98</td>
<td>(0.90–1.07)</td>
</tr>
<tr>
<td>Midwest</td>
<td>0.68</td>
<td>(0.62–0.74)</td>
</tr>
<tr>
<td>South</td>
<td>1.07</td>
<td>(0.98–1.17)</td>
</tr>
<tr>
<td>Residence</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td>Metro</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>0.90</td>
<td>(0.79–1.03)</td>
</tr>
<tr>
<td>Rural</td>
<td>0.80</td>
<td>(0.71–0.91)</td>
</tr>
<tr>
<td>Prior malignancy</td>
<td>1.13</td>
<td>(1.05–1.21)</td>
</tr>
<tr>
<td>Comorbidity index</td>
<td>1.00</td>
<td>(0.97–1.03)</td>
</tr>
</tbody>
</table>

CI, confidence interval.
Stage-Based Survival by Number of Staging Modalities

- Solid line: Single modality (CT)
- Long dash: Bi-modality (CT, PET)
- Dotted: Tri-modality (CT, PET, invasive staging)
### TABLE 4. Relationship Between Mediastinal Staging and Survival

<table>
<thead>
<tr>
<th></th>
<th>Overall survival</th>
<th>Lung cancer cause-specific survival</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hazard ratio&lt;sup&gt;a&lt;/sup&gt; (99% CI)</td>
<td>Hazard ratio&lt;sup&gt;a&lt;/sup&gt; (99% CI)</td>
</tr>
<tr>
<td>Bi- vs. single modality</td>
<td>0.58 (0.56–0.60)</td>
<td>0.56 (0.54–0.58)</td>
</tr>
<tr>
<td>Tri- vs. single modality</td>
<td>0.49 (0.45–0.54)</td>
<td>0.46 (0.42–0.52)</td>
</tr>
<tr>
<td>Tri- vs. bi-modality</td>
<td>0.85 (0.77–0.93)</td>
<td>0.83 (0.74–0.93)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Adjusted for age, sex, race, income, education, marital status, geography, area of residence, history of prior malignancy, and comorbidity index.

CI, confidence interval.
Comparing the magnitude of survival benefit...

* LACE Clin Oncol (Meeting Abstracts) 2006; 24:7008
** ECOG 4599 Sandler A, NEJM 2006; 355:2542-2550
*** Data taken from a SEER-Medicare (1998-2005) analysis. Results are adjusted for all significant factors.6
Quality Gaps and Comparative Effectiveness in Lung Cancer Staging and Diagnosis


- SEER-Medicare and Texas registry data from 1995-2007

- Cohort of 15,316 patients with NSCLC with regional metastasis

- **Guideline-consistent care:**
  - If first test involved mediastinal sampling

- Compared number of tests performed

- Multivariate logistic regression to compare frequency of complications
Quality Gaps and Comparative Effectiveness in Lung Cancer Staging and Diagnosis

• Results:
• 21% of patients underwent guideline recommended care with invasive mediastinal staging as the first diagnostic modality

• 44% of patients never underwent mediastinal staging
Quality Gaps and Comparative Effectiveness in Lung Cancer Staging and Diagnosis

- Patients who had guideline consistent care:
  - Required fewer tests ($P < .0001$) including less thoracotomies (49% vs. 80%, $p < .001$) and CT-guided biopsies (9% vs. 63%, $p < .001$)
  - Fewer complications

<table>
<thead>
<tr>
<th>Table 4—Cumulative Incidence of Complications During the Entire Diagnostic Evaluation Per Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evaluation Consistent With Guidelines, Mediastinal Sampling Done First</td>
</tr>
<tr>
<td>NSCLC Present, Mediastinal Sampling Performed Second or Later</td>
</tr>
<tr>
<td>Complication</td>
</tr>
<tr>
<td>---------------</td>
</tr>
<tr>
<td>No. patients</td>
</tr>
<tr>
<td>Pneumothorax</td>
</tr>
<tr>
<td>Pneumothorax requiring chest tube</td>
</tr>
<tr>
<td>Hemorrhage</td>
</tr>
<tr>
<td>Respiratory failure</td>
</tr>
</tbody>
</table>

$P$ Value$^a$:
- $< .001$
- $< .001^b$
CASE PRESENTATION

GERARD SILVESTRI, MD, MS
Patient 1

- 62 y/o WW with >20 pack year tobacco
- CT for abnormal CXR prior to LE surgery
EBUS Mediastinum – 4R (11mm)

- Simultaneously diagnosed & staged
  - Adenocarcinoma stage IIIA
  - Patient went from surgical candidate to unresectable
Patient 2

- 76 y/o never smoker
- CT chest during evaluation of abd pain
CT – 4R
Patient 2 PET – 4R
Pre-EBUS T1N2M0 (stage 3a) -> Post-EBUS T1N0M0 (stage IA)
RLL resection confirmed stage IA adenocarcinoma
Summary

• Stage dictates treatment options and prognosis
• Treatment varies significantly by stage
• Confirmation of stage by whatever mode provides the best quality care
• A simple quality indicator should be receipt of multi-modality staging in newly diagnosed patients with lung cancer
You may email questions to: Octavia.vogel@cancer.org
THANK YOU!

You may email questions to:
Octavia.vogel@cancer.org
JOIN US NEXT MONTH FOR LUNG CANCER PATIENT SUPPORT
ECHO SESSION 6
DISPARITIES IN RECEIPT OF CURATIVE-INTENT SURGERY FOR EARLY STAGE NSCLC
OCTOBER 25, 2018
9:00 AM ET

Presenters:
Elizabeth David, MD, MAS (Thoracic Surgeon)
University of Southern California
Douglas Wood MD (Thoracic Surgeon)
University of Washington

Case Presentation:
TBD