Overtreatment of patients with clinically diagnosed early stage lung cancer

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DISCLOSURE

• The investigators have no conflicts to disclose.
Lung cancer is the most common cause of cancer mortality in the United States with 158,040 approximate deaths in 2015. Approximately 15% of new lung cancer cases are clinically localized.

Stereotactic body radiotherapy is an acceptable alternative treatment option for medically inoperable patients with early stage lung cancer at high risk for surgical morbidity or mortality.

Obtaining pathologic confirmation of a presumed lung cancer may be difficult due to poor pulmonary function, multiple comorbidities, tumor location or patient refusal. As a result, physicians often rely on a patient’s clinical history and imaging studies to identify whether a lung nodule is a presumed malignancy.
PURPOSE

• To identify the trends in the utilization of a clinical diagnosis for lung cancer using a large national registry.

• To identify whether the method of diagnosis (clinical versus pathologic diagnosis) impacts treatment outcomes (Overall Survival and Cancer Specific Survival) for patients undergoing radiotherapy for Stage I lung cancer.
MATERIALS & METHODS

• The Surveillance, Epidemiology, and End Results (SEER) program is sponsored by the National Cancer Institute and collects cancer incidence, survival, and treatment information and covers approximately 28% of the United States population.

• The database includes clinical (age, race, gender, stage, grade) and treatment (lymph nodes evaluated, type of surgery) information.

• The SEER registry does not include data on radiation technique (ie, SBRT use), radiation dose, comorbidities, performance status, margin status, or chemotherapy use.

• All data regarding treatment represents the first course of therapy and excludes treatment delivered at recurrence or progression.
## MATERIALS & METHODS

### EXCLUSION CRITERIA
- Patients undergoing surgery
- Tumors > 5 cm
- Any previous cancer diagnosis
- ≤ 1 month follow-up
- Missing treatment information
- Unknown diagnosis type

### INCLUSION CRITERIA
- 2004 to 2012
- >18 years old
- External beam radiation therapy
- Stage I lung cancer
STATISTICAL ANALYSIS

• Demographic and clinical characteristics were compared between patients diagnosed pathologically or clinically using Chi-square tests.

• Trends in rates of clinical diagnosis use over time were examined using the Chi-square test for trend.

• Survival Analysis:
  – Kaplan-Meier method with comparisons between groups via the log-rank test
  – Overall Survival multivariate analysis using the Cox proportional hazards model
  – Cancer Specific Survival multivariate analysis using Fine and Gray Competing Risk Regression
BASELINE CHARACTERISTICS

- 7,050 patients included
  - 6,399 (91%) were pathologically diagnosed, 651 (9%) were clinically diagnosed

- Patient Characteristics:
  - Median age was 75 (range, 28-98)
  - Median follow-up was 17 months (range, 2-107)
  - Most patients had clinical T1 disease (58%)

- Pathologic versus Clinical Diagnosis:
  - Patients with clinical T1 disease (p<0.001), tumors 0-1.9 cm in size (p<0.001), and upper lobe tumors (p=0.007) were more likely to be clinically diagnosed
  - No difference in age (p=0.274), gender (p=0.627), or tumor laterality (p=0.09)
  - For pathologically diagnosed patients, 2,208 (35%) had squamous cell carcinoma, 2,195 (34%) had adenocarcinoma, 1,996 (31%) had an unknown or not otherwise specified histology
RESULTS

p=0.172

% of patients diagnosed clinically


Year
## RESULTS

<table>
<thead>
<tr>
<th>Diagnosis Type</th>
<th>2 year CSS</th>
<th>5 year CSS</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathologic</td>
<td>63.1%</td>
<td>38.1%</td>
<td>&lt;0.001</td>
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<tr>
<td>Clinical</td>
<td>74.1%</td>
<td>48.8%</td>
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</table>

<table>
<thead>
<tr>
<th>Diagnosis Type</th>
<th>2 year OS</th>
<th>5 year OS</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathologic</td>
<td>50.7%</td>
<td>21.0%</td>
<td>0.026</td>
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<tr>
<td>Clinical</td>
<td>57.3%</td>
<td>21.2%</td>
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</table>
### RESULTS

<table>
<thead>
<tr>
<th>Diagnosis Type</th>
<th>Adjusted sHR* (CSS)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathologic</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Clinical</td>
<td>0.82 (95% CI 0.71-0.96)</td>
<td>0.013</td>
</tr>
</tbody>
</table>

*The following covariates were included in the model: age, race, gender, marital status, clinical T stage, laterality, tumor location, poverty level, income level, education status.*

<table>
<thead>
<tr>
<th>Diagnosis Type</th>
<th>Adjusted HR* (OS)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathologic</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Clinical</td>
<td>1.01 (95% CI 0.90-1.13)</td>
<td>0.872</td>
</tr>
</tbody>
</table>
RESULTS

Adjusted Overall Survival Curves Using Cox Proportional Hazards Model Stratified by Method of Diagnosis

\[ p = 0.872 \]
RESULTS

Cumulative Incidence Estimates of Cancer Specific Mortality Using Competing Risk Analysis Stratified by Method of Diagnosis

\[ p=0.013 \]
RESULTS

Competing Risk Regression Model for Cancer Specific Survival Stratified by Quartile Tumor Size

sHR (95% CI)

Clinical Diagnosis Better

Pathologic Diagnosis Better

- 0-1.9 cm: 0.74 (0.58-0.99)
- 2-2.7 cm: 0.78 (0.58-1.03)
- 2.8-3.7 cm: 0.80 (0.58-1.10)
- 3.8-5 cm: 1.13 (0.50-1.59)
RESULTS

Competing Risk Regression Model for Cancer Specific Survival Stratified by Clinical Stage

sHR (95% CI)

- cT1a: 0.75 (0.58-0.96)
- cT1b: 0.74 (0.55-1.00)
- cT2a: 0.99 (0.77-1.26)
CONCLUSION

- These results demonstrate an improved cancer specific survival in patients undergoing clinical versus pathologic diagnosis for Stage I lung cancer without any difference in overall survival.

- We hypothesize that the disparity in cancer specific survival between patients diagnosed clinically versus pathologically may be due to a greater number of patients in the clinical diagnosis group having benign disease which precludes them from developing a cancer related death.
CONCLUSION

• Although a certain percentage of false positive results are expected when treating non-biopsied lung cancer, careful observation and verification is needed to ensure proper management of smaller lesions in particular.

• With an increasing number of early stage lung cancers being diagnosed with the adoption of national lung screening guidelines, this becomes an increasingly important observation and potential limitation of current clinical practice.
ACKNOWLEDGEMENTS

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