Lung Cancer Staging

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Epidemiology

- Leading cause of cancer death in the United States.
- An estimated of 228,820 new cases will be diagnosed in 2020 and 135,720 deaths.
- Only 19% of cases with lung cancer are alive 5 years or more after diagnosis including small and non-small cell lung cancer.
- If eligible for targeted therapy 5 year survival rates range from 15% to 50% depending on the biomarker.


Risk Factors

- Smoking tobacco. (85%-90% of cases are caused by smoking).
- Exposed non-smokers have an increased relative risk (RR=1.24).
- Exposition to asbestos and radon gas.
- Exposition to other carcinogens: arsenic, chromium, nickel, coal smoke, soot, cadmium, beryllium, silica and diesel fumes.

Risk assessment.

- Recommended for high risk groups LDCT:

  Group 1:
  - Age 55-77 years and
  - ≥ 30 pack-year history of smoking.
  - Smoking cessation < 15 years.

  Group 2:
  - ≥ 50 years and
  - ≥ 20 pack-year history of smoking and
  - Additional risk factors.

Decreased mortality rate by 20%


Clinical presentation:

- Cough
- Hemoptysis
- Dyspnea
- Weight loss
- Chest pain

Importance of Staging:

- Prognosis.
- Intent of the treatment (Curative vs Palliative).
- Treatment strategy: multimodality vs chemoradiation vs systemic therapy alone.

Case study:

- 80 y.o female with PMH of COPD and 35 pack years history of smoking who presented with cough in 2018 treated several times as a COPD exacerbation with antibiotics and steroids.
- In January 2019 a CXR showed a lung nodule → referred to interventional pulmonology.
- CT Chest revealed mediastinal adenopathy (subcarinal lymph node measured 2.1 x 3.1 cm.) and LUL 2.1 cm mass.
**Initial evaluation:**

- CT chest and upper abdomen with contrast.
- Biopsy and Pathological Review.
- CBC, CMP
- PFT and stress test in certain situations when surgery is considered.

**Initial evaluation:**

- FDG-PET/CT scan and CT Chest and abdomen including adrenal glands.
- Positive distant disease → need pathological confirmation.
- Positive mediastinum → needs pathological confirmation.
- Pathological mediastinal evaluation with bronchoscopy (EBUS/EUS), (intraoperative if possible), mediastinoscopy, CT guided biopsy depending on the case.
- Brain imaging (MRI with contrast or CT head with contrast).

**Pretreatment assessment:**

<table>
<thead>
<tr>
<th>Mediastinal Assessment:</th>
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<tbody>
<tr>
<td>Mediastinal evaluation (N2) prior to surgery is required.</td>
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<tr>
<td>CT/PET:</td>
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<tr>
<td>Solid nodule &lt;1 cm or purely nonsolid nodule &lt; 3cm and LNs not PET avid → biopsy optional. → surgery + LN sampling/dissection.</td>
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<td>Otherwise mediastinal LN sampling recommended.</td>
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<td>Mediastinal LN positive → neoadjuvant/induction or definitive non-surgical treatment.</td>
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<td>Preoperatively, mediastinoscopy remains the gold standard.</td>
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<td>Bronchoscopy with EBUS ± EUS commonly used.</td>
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**Case study: CT chest with contrast:**

![CT chest with contrast images]
PET/CT scan results:

- In 20 (of 102 pts), 29 hot spots outside the mediastinum were detected.
- In 11 patients distant metastasis were found not otherwise seen by standard methods.
- 9 false positive (4 colon, 2 lung, 1 adrenal, liver, rib).
- 20 patients down staged.
- 64 patients upstaged.

<table>
<thead>
<tr>
<th>Method</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
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<tbody>
<tr>
<td>CT</td>
<td>75% (60-90)</td>
<td>66% (55-77)</td>
<td>69% (60-78)</td>
</tr>
<tr>
<td>PET</td>
<td>81% (81-100)</td>
<td>86% (78-94)</td>
<td>87% (80-94)</td>
</tr>
<tr>
<td>CT and PET</td>
<td>94% (86-100)</td>
<td>86% (78-94)</td>
<td>88% (82-94)</td>
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PET/CT scan results:

Results of PET staging

- PET (and preferably integrated PET/CT) improves mediastinal staging.
- PET and PET/CT may also pick up additional unsuspected metastatic lesions.
- This technique does NOT supplant mediastinoscopy or biopsy.
- Early data suggests that PET may predict clinical response.

Which diagnostic technique to use?

- Depends on:
  - Size and location of the tumor.
  - Presence of mediastinal or distant disease.
  - Patient characteristics such as baseline pulmonary pathologies or other significant comorbidities.
  - Local experience and expertise.
  - Invasiveness and risks of the procedures.

Diagnostic modalities:

- Central masses and suspected endobronchial involvement:
  - Bronchoscopy +/- EBUS/EUS.

- Peripheral nodules:
  - Transthoracic needle aspiration.
  - Navigational bronchoscopy and radial EBUS.
  - VATS and open surgical biopsy.

- Suspected nodal disease:
  - EBUS, EUS.
  - Navigational bronchoscopy, or mediastinoscopy.

- Associated pleural effusion:
  - Thoracentesis with cytology.
  - If negative, repeat thoracentesis and/or VATS before starting curative intent therapy.

Case study

- Patient underwent rigid bronchoscopy with biopsy and mechanical debulking of the left mainstream tumor.
- Endobronchial ultrasound was used to examined mediastinal lymph nodes and station 7 (subcarinal) was biopsied.
- Left lung mass biopsy: adenosquamous carcinoma.
- Station 7 lymph node: positive for adenocarcinoma of possible lung primary with rare squamous differentiation.

Pathological review:

- Histology and immunohistochemistry stains:
  - Adenocarcinoma: TTF-1, Napsin A.
  - Squamous cell carcinoma: p40, p63.
  - Small cell lung cancer: TTF-1, chromogranin and synaptophysin and high K67 proliferative marker.
  - Typical and atypical carcinoid tumors: chromogranin and synaptophysin and intermediate to low Ki67.
Pathological review:

- PD-L1 testing: Tumor proportion score of 99%.

- Molecular testing for actionable mutations:
  1. EGFR, ALK, ROS, BRAF, NTRK gene alterations.
  2. Other: RET, MET, ERBB2.

TNM Staging System:

- T→ denotes the size and extent of the primary tumor.
- N→ denotes the spread pattern to the nearby lymph nodes.
- M→ denotes the spread to distant sites.

Primary Tumor or T:

TX: primary tumor cannot be assessed.

T0: No evidence of primary tumor

Tis: Carcinoma in situ

T1 ≤ 3cm and no invasion into the main bronchus.

T2 > 3cm but ≤ 5cm or
  • Involves main bronchus
  • Visceral pleural invasion
  • Associated atelectasis or obstructive pneumonitis extending to hilar region.

Primary Tumor or T:

T3 > 5cm but ≤ 7cm or invading:

  • Parietal pleura.
  • Chest wall (including superior sulcus tumors).
  • Phrenic nerve.
  • Parietal pericardium.
  • Separate tumor nodule(s) in the same lobe as the primary.
Primary Tumor or T:

- **T4 > 7cm or any size invading one or more of the following:**
  - Diaphragm.
  - Mediastinum, heart and/or great vessels.
  - Trachea and carina.
  - Esophagus.
  - Recurrent laryngeal nerve.
  - Vertebral body.
  - Separate tumor nodules in an ipsilateral lobe different from that of the primary.

Lymph Nodes or N:

- **NX:** Regional lymph nodes cannot be assessed.
- **N0:** No regional lymph node metastasis.
- **N1:** Ipsilateral peribronchial, ipsilateral hilar lymph node(s) and intrapulmonary.
- **N2:** Ipsilateral mediastinal or subcarinal lymph node(s)
- **N3:** Contralateral mediastinal, hilar, or ipsilateral or contralateral scalene or supraclavicular lymph nodes.

Distant metastasis or M:

- **M1a:** Separate tumor nodule(s) in a contralateral lobe; tumor with pleural or pericardial nodules or malignant pleural or pericardial effusion.
- **M1b:** Single extrathoracic metastases in a single organ.
- **M1c:** Multiple extrathoracic metastases in a single or multiple organs.

Case study:

- **cT2, N2, M0.**
  - Subcarinal lymph node measures right side 2.1 x 3.1 cm and left side 1.6 x 1.6 cm.
  - Considered non-surgical candidate due to N2 bulky lymphadenopathy and multi-station involved.
  - Referred to Radiation Oncology for definitive concurrent chemoradiation with carboplatin and paclitaxel – durvalumab.
MRI brain with contrast:

- NCCN guidelines recommend evaluation of brain with MRI (~25% of patients either have or will develop brain metastasis):
  - Symptomatic suspicion
  - Stage Ib: optional
  - Stage ≥2: mandatory
Conclusions:

- A multidisciplinary approach is important to better decide diagnostic and staging strategies.

- Typical staging testing includes:
  - CT chest abdomen and pelvis with contrast.
  - PET/CT which aides with bone disease identification +/- MRI
  - Brain MRI with contrast (CT head with contrast)
  - Mediastinal evaluation if no distant disease.
  - Pathological review including: IHC for histology subtypes, PD-L1 and molecular alteration (NGS, PCR, FISH, IHC).