Master Class: Fundamentals of Lung Cancer

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OUTLINE-Lung Cancer Basics

A. The scope of the problem and causes of lung cancer.
B. Clinical presentation and diagnosis of lung cancer.
C. Management and Treatment
D. Reading of Lung Cancer Screening
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Let’s talk about All Cancers

In America, 180,000 men will get Prostate Cancer this year.

How many will die?
Let’s talk about All Cancers

10,000 men
Let’s talk about All Cancers

How many women will get Breast Cancer this year?
Let’s talk about All Cancers

178,000 women
Let’s talk about All Cancers

How many women will die from Breast Cancer this year?
Let’s talk about All Cancers

30,000 women
Let’s talk about All Cancers

How many people will get Colon Cancer this year?
Let’s talk about All Cancers

178,000 people
Let’s talk about All Cancers

How many people will die from Colon Cancer this year?
Let’s talk about All Cancers

50,000 people
Let’s talk about All Cancers

How many people will get Lung Cancer this year?
Let’s talk about All Cancers

172,000 people
Let’s talk about All Cancers

How many people will die from Lung Cancer this year?
Let’s talk about All Cancers

160,000 people
Lung Cancer Basics

Age-Adjusted Cancer Death Rates in US

Males

Females

Lung

Stomach

Colon & Rectum

Prostate

Pancreas

Breast

Stomach

Ovary

Uterus

Pancreas

Rate per 100,000 male population

Rate per 100,000 female population


0 20 40 60 80


0 20 40 60 80
What Causes Most Lung Cancers?

- SMOKING CIGARETTES
- What age do most people start smoking who get lung cancer?
- 15-20 years old
- If don’t smoke by 25, probably never will smoke
What should you do if you smoke?

STOP!
Stop Smoking

- Basic and important message
- Incredibly difficult for some
- Very easy for others
- Ripe area for investigation
Etiology

- Tobacco Smoking – Sir Richard Doll
- Non-smokers – 12% at Hopkins
- What else could cause lung cancer?
- Second Hand Tobacco Smoke
- Air Pollution-Living in a Big City
- Indoor Radon Gas
- Working Around Carcinogens-asbestos in houses, arsenic, chromium, nickel, PAH, vinyl
- H/o TB, Lung Scarring
WHO Histological Classifications

- **2 Main Types**
  - Small Cell Lung Cancer (SCLC) \(\approx 12\%*\)
  - Non-Small Cell Lung Cancer (NSCLC) \(\approx 88\%*\)
Lung Cancer:
Non-small Cell Cancer

- MAIN TYPE OF LUNG CANCER
- Cancers grow at different rates in different people and how widespread a cancer is in the body at time of diagnosis is known as its STAGE
- Show up to a doctor with a cancer, not all cancers have just started growing and the cancer is diagnosed early
Lung Cancer:
Non-small Cell Cancer

- Are most lung cancers found early or late?
- In fact, 70% present with late lung cancer
- How long does cancer usually grow before a doctor can pick it up on a X-ray?
- Tumor has been growing in our bodies for about 7-10 years usually without symptoms
Lung Cancer: Non-small Cell Cancer

- What does advanced lung cancer mean?
  - Means that the cancer is no longer in the lung and has spread to other parts of the body.
  - All cancer in the body is STAGED in this way.
    - STAGING is a statement about how widespread a cancer is in a certain patient.
Non-Small Cell Lung Cancer: Staging

- Staging System: way cancer is thought to spread

  $T = \text{Main Tumor}$

  $N = \text{Regional Nodes}$

  $M = \text{Distant Metastasis}$
<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
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<tbody>
<tr>
<td>N0</td>
<td>No tumor spread to regional lymph nodes</td>
</tr>
<tr>
<td>N1</td>
<td>Spread detected in nodes close to the tumor</td>
</tr>
<tr>
<td>N2</td>
<td>Spread found in nodes in middle of chest</td>
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TNM Staging: Primary Tumor (T)

Based on Size of Tumor – bigger more chance of breaking off and spreading

T1  ≤3 cm diameter
T2  >3 cm diameter
TNM Staging: Distant Metastasis

- **M0**: No spread or metastasis outside of chest
- **M1**: Spread or metastasis present outside of chest, for example in brain or bone or liver
NSCLC: Staging and Prognosis

NSCLC: Stage I and Stage II*

Stage I

T2 NO MO
Involving mainstem bronchus >2 cm distal to carina

T2 NO MO
Involving visceral pleura

T1 NO MO
≤3 cm peripheral “coin” lesion

Mediastinal parietal pleura

Stage II

T2 N1 MO
Involving visceral pleura and peribronchial and hilar lymph nodes

T1 N1 MO
≤3 cm involving peribronchial lymph nodes (by direct extension)

T2 N1 MO
Involving main bronchus and hilar lymph nodes

T3 NO MO

Mediastinal parietal pleura

* Adapted from Mountain CF. A new international staging system for lung cancer. *Chest.* 1986;89(suppl 4):225S-233S.
NSCLC: Stage IIIA and Stage IIIB*

Stage IIIA

- T3 N1 MO
  - Peripheral tumor involving chest wall and intrapulmonary lymph nodes

- T2 N2 MO
  - >3 cm tumor involving ipsilateral hilar and mediastinal lymph nodes

Stage IIIB

- T4 N3 MO
  - Involvement of mediastinum, (ipsilateral and contralateral mediastinal lymph nodes, contralateral hilar nodes, supraclavicular lymph nodes

* Adapted from Mountain CF. A new international staging system for lung cancer. Chest. 1986;89(suppl 4):225S-233S.
Approximately 138,000 New NSCLC cases/year

34,000 (24%) Stage I
12,000 (8%) Stage II
38,000 (28%) Stage III
54,000 (40%) Stage IV

Source: Plan A Cancer Populations
## Survival of Patients with NSCLC by Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>Proportion Alive after Diagnosis 5 years</th>
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<tbody>
<tr>
<td>I</td>
<td>64%</td>
</tr>
<tr>
<td>II</td>
<td>35%</td>
</tr>
<tr>
<td>III</td>
<td>15%</td>
</tr>
<tr>
<td>IV</td>
<td>5%</td>
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</table>
JHH: 5-Year Survival by Year of Diagnosis (4 intervals) Stages Combined (I, II-III A, IIIB-IV), N=

*based on 3-year survival rates
The Problem

- Surgery (that is cutting out the lung cancer) is the best chance of cure, but only can be done if cancer is early stage.

- Another problem: Even when cut out cancer early:
  
  A third of the time it comes back often spread to other parts of the body.
The Problem

- Even patients with Stage 1 disease who are completely resected (and should be tumor free after surgery), have unacceptable rates of distant recurrence.

- Why might that be?
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Patient

- 62 year old smoker presents with a CXR lesion as follows:
Doctors – help me?

- What is the first question?
- Yes – is this a cancer?
- What’s best way of finding out?
- ASK the Patient
History-What should we ask the patient?

- Previous CXR
- If CXR more than 2 years ago and not changed- maybe benign?
- Smoking history
- Cough
- Spitting up of blood
- Hoarseness
- Previous malignancy - r/o mets
Doctors – help me?

- OK- It’s a cancer. What’s the best way to cure it?

- CUT to CURE!

- What’s the next question?
- How far has it spread? CAN it be cut out! OR –
- What is the CANCER’s STAGE?
Doctors – help me?

- How can I figure out how far a cancer has spread?
Physical Exam

- What is another test to do?
PET-Positron Emission Test

- PET positive tumor based on metabolic activity of glucose analogue
Tests

- So, it looks like we can take it out
- What else do we need to do?
- Now, can the patient tolerate surgery?
- More tests needed to make sure the patient can live after we take out part of their lungs
- Treatment
OUTLINE - Lung Cancer Basics

A. Causes of lung cancer and the scope of the problem.

B. Clinical presentation and diagnosis of lung cancer.

C. Management and Treatment

D. Reading of Lung Cancer Screening
TREATMENT Basics-SURGERY
Surgery

- Complete and total resection of the tumor
- All surgical margins must be negative
- All lymph nodes sampled
- Complications of the surgical procedure
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Screening for Lung Cancer

Hypothesis: That if we screen HIV smokers with sensitive CT scans, we would detect the cancer earlier and can maybe cure it.

Photo by Michael Geminder. Creative Commons BY-NC-ND
Spiral CT Screening

- Multiple Studies Performed and Underway Internationally

- Early Lung Cancer Action Project – ELCAP

- Most prominent National Lung Cancer Screening Trial in USA
Spiral CT Screening

- ELCAP

- 1000 Patients – how many nodules?

- 233 non-calcified nodules

- How many cancers found?

- 27
Screening Studies for Lung Cancer

- Most important finding

- The proportion of early stage disease that is detected is significantly increased to 80%
Spiral CT Screening

- 26 out of the 27 had surgery
- Remember, surgery is the best chance of cure for these patients
Biases

- Lead Time Bias
- Length and Overdiagnosis Bias
- Non-randomized cohort: need a randomized cohort to prove reduction in mortality
- Would take 14 years to complete
- Chest x-ray lung study showed no significant difference
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Road Ahead – Lots to Discover

• What is certain about science is that this is the tip of the iceberg
• All this work is just getting started
• Heart attacks still kill, AIDS is still deadly and lung cancer kills more people than all the other cancers combined
• Discovering new ideas is fun and if you’re lucky you can help someone when you are done
Elcap vs. Mayo Study

- Box of what ELCAP and Mayo Lung share
- ELCAP not randomized and unable to answer question about decrease in mortality
- Mayo did and it was not significant - technology was not good enough
The Will Rodgers Effect

- While commenting on geographic migration during the economic depression of the 1930s, the American humorist Will Rogers is alleged to have said "When the Okies left Oklahoma and moved to California, they raised the average intelligence levels in both states".

- An analogous phenomenon, stage migration, occurs with more careful staging of cancer.

- If a population of patients is more accurately staged it will improve the survival of all stages because patients with subtle advanced disease will be upstaged.