Lung Cancer Screening

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Case Presentation

- 67 year old male
- Hypertension, but otherwise healthy
- Smokes 7-8 cigarettes per day, >50 pack year history
- Here for routine health maintenance
- Should you screen for lung cancer?
Case Presentation

• Our patient was not screened for lung cancer.
• But he developed pneumonia.
• CXR raised the possibility of a nodular lesion.
• A CT was obtained.
Case Presentation

- FDG-PET showed avid uptake
- VATS right upper lobe resection
- Stage IA adenocarcinoma

PACS BIDMC, courtesy Dr. Petkovska
ACS recommendations

• American Cancer Society (ACS) position for early detection: “At present neither the ACS, nor any other medical/scientific organization, recommends testing for early lung cancer detection in asymptomatic individuals.”
Epidemiology

- 2nd most common cancer in the U.S. 221,000 new cases of lung cancer (2010).

- Most common cause of cancer death, >150,000 per year

Epidemiology

- 5 year survival rate for stage I disease is 60%
- 5 year survival rate for stage IV disease is <5%
- 75% of patients have incurable locally advanced or metastatic disease by diagnosis
- 15% of patients survive >5 years

Epidemiology

- Cigarette smoking is a major cause of lung cancer
- >80% of lung cancers occur in persons with tobacco exposure (RR 20-25, AR 85%-90%)
- 1 in 9 smokers eventually develop lung cancer
- 20.6% of Americans >18 years old smoke

Rationale for Screening

- Lung cancer is common
- Most lung cancer is diagnosed at advanced stages at which the prognosis is poor
- Early intervention save lives
- High risk cohort that we can target for screening (smokers)
- **Key point:** Given the lethality and high incidence of lung cancer, an effective screening test is needed
Screening Goals

- Detection of stage I disease
- Target high risk groups
- Decrease disease-related mortality
Screening Test Criteria

- High sensitivity (especially for early stage disease)
- High specificity (reduce false positives and number of people needing diagnostic evaluation)
- High positive predictive value
- Low cost
- Safety
Screening Modalities

• Chest radiography/Sputum
• Low dose computed tomography
Chest radiography

- Projection image
- Good resolution but poor contrast
- Fast
- Inexpensive
- Low radiation
Low Dose CT

- 3D imaging
- Good resolution and contrast
- High sensitivity
- Fast - 15 seconds during a single breath hold
- More expensive than radiograph
- Low radiation (1/9th radiation of conventional CT)
Early trials

- No difference in mortality rate between screened and control group
  - Used survival as an endpoint rather than mortality reduction
  - Lead-time bias- screening test appears to increase survival by detecting cancer early
  - Length-time bias- screening test may detect slow-growing tumors more often and thereby show an improvement in survival rates
  - Overdiagnosis bias- diagnoses disease that may never have caused symptoms
Radiograph & Sputum

- **U.S. National Cancer Institute 1970’s**
  - 3 Randomized control trials in males smokers
    - Memorial Sloan-Kettering Study
    - Johns Hopkins Study
    - Mayo Lung Project

- **Czechoslovakian Study**
  - Randomized control trial

- **No reduction in lung cancer mortality**
Chest Radiograph

- Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO)
  - RCT of 155,000 subjects aged 55-74
  - Subjects randomized to standard care or annual screening with chest radiograph
  - **Findings:** Annual screening did not reduce lung cancer mortality compared with usual care
Computed Tomography

- CT screening detects more lung cancers compared with CXR but does not reduce lung cancer deaths

Low Dose CT

• National Lung Screening Trial (NLST)- Study Design
  • Largest RCT to date consisting of 53,464 subjects
  • Aged 55-74 years
  • At least 30 pack year history (if former smoker, quit within the past 15 years)
  • Randomized to undergo baseline and 2 annual screenings by either low dose CT or CXR

http://www.cancer.gov
Low Dose CT

- National Lung Screening Trial - Results
  - 649 cancers detected by CT screening compared with 279 cancers by CXR
  - Of lung cancers diagnosed with CT 63% were stage I and 29.8% were stage III or IV compared with 47.6%, 43.2% respectively in the CXR arm
  - 20.0% relative reduction in mortality from lung cancer with low-dose CT
  - Number needed to treat was 320
Low Dose CT

- National Lung Screening Trial - Results Cont.
- Rate of positive screening tests
  - CT: 24.2%; Radiography: 6.9%
  - 90% had further diagnostic evaluation
- False positive results
  - CT: 96.4%; Radiography: 94.5%
CT: Potential Problems

- False-positive scans
- Benign nodule resections
- Overdiagnosis
- Patient anxiety
- Radiation
- Cost
CT: Potential Problems

- High false positive rate
  - Benign nodule resection
  - Expensive diagnostic workup
- Response to high false positive rate
  - Many researchers call a scan “negative’ if the largest nodule is <4-5 mm.
    - Decreases false positive rate, but increases the false negative rate
    - Caution: McWilliams et al. (2006) 18% of cancers were first detected when less than 4 mm
CT: Potential Problems

Progressive growth of a **nodule** in the left upper lobe. (A) baseline (B) 1 year (C) 2 years

CT: Potential Problems

• Benign nodule resection
  • Diederich et al. 20% of resections
  • DANTE study 22% of resections
  • NLST study 27% of resections

• Overall CT-screening reports benign nodules resection rates between 15-30%

• Surgical series report benign nodules resection rates between 50-86%
CT: Potential Problems

- How can we reduce the number of benign nodules resections?
  - Careful review of old images
  - Serial examinations
  - Evaluating larger nodules with needle biopsy or PET
CT: Potential Problems

- Radiation risk
  - NLST: radiation risk from screening 55 year old smokers results in 1-3 lung cancer deaths per 10,000 screened and 0.3 new breast cancer per 10,000 women screened.
  - Highlight importance of having proven mortality benefit before implementing screening

www.wikimedia.org/wikipedia/commons/thumb/0/0b/Radiation_warning_symbol
Future

• NLST: Awaiting quality of life, smoking behavior, health care use, and cost-effectiveness of screening reports. Who will pay for screening and follow up?

• UK Lung Screen trial- RCT using CT screening, designed to determine the appropriate population to screen
Conclusions

• Lung cancer is a common and lethal disease and therefore patients would benefit from early detection and intervention.

• NLST demonstrates that low dose CT screening saves lives.

• Reports regarding cost-effectiveness are pending.

• Currently, routine screening is not recommended. In the meantime, the decision to screen for lung cancer should be evaluated on a case by case basis with discussion of the risks and benefits.

• Primary prevention is still paramount!
References