Lung Cancer Screening

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Lung Cancer Screening.....

“...the opportunity to realize the greatest single reduction of cancer mortality in the history of the war on cancer.”

James Mulshine, MD
Associate Provost and Vice President for Research
Rush University Medical Center
Cancer Statistics, 2018

American Cancer Society
Cancer Facts & Figures, 2018
Estimated Cancer Cases, Florida, 2018

Screening tests routine

Breast
Lung & bronchus
Prostate
Colorectal
Melanoma
Urinary bladder
Lymphoma
Leukemia
Screening tests routine
History of Lung Cancer Screening

- Chest x-ray: Negative
- Sputum cytology: Negative
- Chest CT: ?
The Mayo Lung Project

A Perspective

Robert S. Fontana, M.D.

Department of Medicine, Mayo Clinic, Rochester, Minnesota.

BACKGROUND. The Mayo Lung Project (MLP) was a randomized, controlled, clinical trial designed to determine whether intensive radiologic and cytologic screening for lung carcinoma could reduce lung carcinoma mortality significantly.

METHODS. Half the MLP population was encouraged (and reminded) to undergo free chest X-rays and free sputum cytology tests every 4 months for 6 years.

1971 – 1983
N = 9211 men, heavy smokers

Randomized:

CxR + sputum q 4 months

CxR + sputum annually

Cancer, 2000
Mayo Lung Project: Results

Lung Ca Survival

Cumulative Lung Ca Deaths
Screening by Chest Radiograph and Lung Cancer Mortality
The Prostate, Lung, Colorectal, and Ovarian (PLCO) Randomized Trial

Martin M. Oken, MD
William G. Hocking, MD
Paul A. Kvale, MD
Gerald L. Andriele, MD
Saundra S. Buys, MD

Context: The effect on mortality of screening for lung cancer with modern chest radiographs is unknown.

Objective: To evaluate the effect on mortality of screening for lung cancer using radiographs in the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial.

Design, Setting, and Participants: Randomized controlled trial that involved 154,901 participants.

1993 – 2001
N = 154,901
Age: 55 – 74 years

Randomized:

Annual CxR (77,445)
Usual care (77,456)
PLCO: Results

Stage of discovered NSCLCs:

Number

Screened | Control
---|---
I | II | III | IV
0 | 200 | 400 | 600 | 800 | 1000 | 1200 | 1400 | 1600
PLCO: Results

Cumulative Lung Cancer Deaths
Early Lung Cancer Action Project: overall design and findings from baseline screening

Claudia I Henschke, Dorothy I McCauley, David F Yankelevitz, David P Naidich, Georgeann McGuinness, Olli S Miettinen, Daniel M Libby, Mark W Pasmantier, June Koizumi, Nasser K Altorki, James P Smith

Summary

Background The Early Lung Cancer Action Project (ELCAP) is designed to evaluate baseline and annual repeat screening by low-radiation-dose computed tomography (low-dose CT) in people at high risk of lung cancer. We report the baseline experience.

Methods ELCAP has enrolled 1000 symptom-free volunteers, aged 60 years or older, with at least 10 pack-years of cigarette smoking and no previous cancer, who were medically fit to undergo thoracic surgery. After a structured interview and informed consent, chest radiographs and low-dose CT were done for each participant. The diagnostic

Interpretation Low-dose CT can greatly improve the likelihood of detection of small non-calcified nodules, and thus of lung cancer at an earlier and potentially more curable stage. Although false-positive CT results are common, they can be managed with little use of invasive diagnostic procedures.

Lancet 1999; 354: 99-105
See Commentary page

Introduction

In the USA in 1998, there were an estimated 160 000 deaths from lung cancer and an estimated 172 000 new cases detected. The cure rate for lung cancer is 18%.

N = 1000
Age 60 and over
10 pack-year smoking history
CxR + low dose Chest CT

Lancet, 1999
## ELCAP: Results

### Discovered Lung Cancers:

<table>
<thead>
<tr>
<th>Stage</th>
<th>CT</th>
<th>CxR</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>23</td>
<td>4</td>
</tr>
<tr>
<td>II</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>III</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>
Problems with Screening Trials:

• *Overdiagnosis*
  Diagnosis of cancers that would have never become clinically significant

• *Lead-time bias*
Lead-time bias:
Lead-time bias:
Lead-time bias:
Lead-time bias:
Lead-time bias:

3-year survival "advantage"
“The USPSTF concludes that the evidence is insufficient to recommend for or against screening asymptomatic persons....”

Lung Cancer Screening Recommendations (2004)
Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

The National Lung Screening Trial Research Team*

33 Sites
$300,000,000
National Lung Screening Trial

- Age 55-75 years
- >30 pack-year smoking history
- Enrolled between 2002-2004
- Annual scans (T0, T1 and T2)
- >4 mm considered positive test

<table>
<thead>
<tr>
<th>Modality</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest CT*</td>
<td>26,722</td>
</tr>
<tr>
<td>Chest x-ray</td>
<td>26,732</td>
</tr>
</tbody>
</table>

NEJM, June, 2011
• 20% reduction in deaths from lung cancer
• 20% reduction in deaths from lung cancer

• 6.6% reduction in overall mortality
Cumulative Lung Cancers

Cumulative Deaths from Lung Cancer
NLST: Stage Shift

Stage at Diagnosis:

<table>
<thead>
<tr>
<th>Number</th>
<th>CxR</th>
<th>CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-200</td>
<td>400</td>
<td>600</td>
</tr>
<tr>
<td>201-400</td>
<td>300</td>
<td>400</td>
</tr>
<tr>
<td>401-600</td>
<td>200</td>
<td>500</td>
</tr>
<tr>
<td>601-800</td>
<td>100</td>
<td>200</td>
</tr>
<tr>
<td>801-1000</td>
<td>50</td>
<td>300</td>
</tr>
<tr>
<td>1001-1200</td>
<td>20</td>
<td>500</td>
</tr>
</tbody>
</table>

Legend:
- I
- II
- III
- IV
Lung cancer incidence = 645/100,000 person-years
96% of positive findings were not cancer
LUNG CANCER SCREENING

By Bruce S. Pyenson, Marcia S. Sander, Yiding Jiang, Howard Kahn, and James L. Mulshine

An Actuarial Analysis Shows That Offering Lung Cancer Screening As An Insurance Benefit Would Save Lives At Relatively Low Cost

ABSTRACT Lung cancer screening is not established as a public health practice, yet the results of a recent large randomized controlled trial showed that screening with low-dose spiral computed tomography reduces lung cancer mortality. Using actuarial models, this study estimated the costs and benefits of annual lung cancer screening offered as a commercial insurance benefit in the high-risk US population ages 50–64. Assuming current commercial reimbursement rates for treatment, we found that screening would cost about $1 per insured member per month in 2012 dollars. These results differ somewhat from those of previous analyses.

Age 50-64 years, >30 pack-year smoking history

Health Affairs, April 2012
## Cost per Life-year Saved

<table>
<thead>
<tr>
<th>Type of Cancer</th>
<th>Screening Technique</th>
<th>Cost per life-year saved (2012 dollars)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical</td>
<td>Pap smear</td>
<td>50,162</td>
</tr>
<tr>
<td>Colorectal</td>
<td>Colonoscopy</td>
<td>18,705</td>
</tr>
<tr>
<td>Breast</td>
<td>Mammography</td>
<td>31,309</td>
</tr>
<tr>
<td>Lung</td>
<td>Low-dose chest CT</td>
<td>11,708 – 26,016</td>
</tr>
</tbody>
</table>

Health Affairs, April, 2012
NELSON Lung Screening Trial

- Randomized European trial
- 10 year results presented at IASLC 2018 meeting
- N = 15,792

<table>
<thead>
<tr>
<th>Modality</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest CT</td>
<td>7,900</td>
</tr>
<tr>
<td>No screen</td>
<td>7,892</td>
</tr>
</tbody>
</table>
• LDCT
• Indeterminate: 2 month f/u for volume doubling time
NELSON Lung Screening Trial

Results:

- Follow-up at 10 years for 93.7% of participants
- 86% compliance rate
- False positive rate = 59.4%

Overall lung cancer detection rate = 3.2%

<table>
<thead>
<tr>
<th>Time</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>0.9%</td>
</tr>
<tr>
<td>1 year</td>
<td>.08%</td>
</tr>
<tr>
<td>3 years</td>
<td>1.1%</td>
</tr>
<tr>
<td>5 ½ years</td>
<td>0.8%</td>
</tr>
</tbody>
</table>
NELSON Lung Screening Trial

Results – Lung Cancer Deaths:

214 study arm vs. 157 control arm

LC mortality rate-ratio:

• Men = 0.74 (p = 0.0003)
• Women = 0.61 (p = 0.0054)
Low-dose Spiral Chest CT

- Single breath-hold
- No iv contrast
## Radiation Exposure

<table>
<thead>
<tr>
<th>Test</th>
<th>Radiation (mSv)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transatlantic flight</td>
<td>0.1</td>
</tr>
<tr>
<td>Mammogram</td>
<td>0.7</td>
</tr>
<tr>
<td><strong>LDCT</strong></td>
<td><strong>&lt;1</strong></td>
</tr>
<tr>
<td>Lumbar Spine series</td>
<td>2</td>
</tr>
<tr>
<td>Diagnostic chest CT</td>
<td>10</td>
</tr>
<tr>
<td>CT Abd/pelvis</td>
<td>25</td>
</tr>
<tr>
<td>Background/yr</td>
<td>3</td>
</tr>
<tr>
<td>Background /yr– Colorado</td>
<td>4.5</td>
</tr>
<tr>
<td>Occupational Exposure</td>
<td>50</td>
</tr>
</tbody>
</table>

“Risks of medical imaging at effective doses below 50 mSv are too low to be detectable and may be non-existent.”

*Am Assoc of Physicists in Medicine*
NCCN Guidelines - 2018

• Age 55 – 74 y, and
• ≥ 30 pack-year history of smoking, and
• Smoking cessation < 15 years

or

• Age > 50 y, and
• ≥ 20 pack-year history of smoking, and
• Additional risk factors*

* Risk factors
  • Personal cancer history
  • Family history of lung cancer
  • Chronic lung disease (COPD, ILD)
  • Carcinogen exposure (Asbestos, radon, arsenic, etc.)
Screening for Lung Cancer: U.S. Preventive Services Task Force Recommendation Statement

Summary of Recommendation and Evidence

The U.S. Preventive Services Task Force (USPSTF) recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in persons at high risk for lung cancer based on age and smoking history.

This is a Grade B recommendation.
Screening for Lung Cancer: U.S. Preventive Services Task Force Recommendation Statement

Virginia A. Moyer, MD, MPH, on behalf of the U.S. Preventive Services Task Force*

Description: Update of the 2004 U.S. Preventive Services Task Force (USPSTF) recommendation on screening for lung cancer.

Methods: The USPSTF reviewed the evidence on the efficacy of low-dose computed tomography, chest radiography, and sputum cytologic evaluation for lung cancer screening in asymptomatic persons who are at average or high risk for lung cancer (current or former smokers) and the benefits and harms of these screening tests and of surgical resection of early-stage non-small cell lung cancer. The USPSTF also commissioned modeling studies to provide information about the optimum age at which to begin and end screening, the optimum screening interval, and the relative benefits and harms of different screening strategies.

Population: This recommendation applies to asymptomatic adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years.

Recommendation: The USPSTF recommends annual screening for lung cancer with low-dose computed tomography in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery. (B recommendation)

Ann Intern Med. For author affiliation, see end of text.
* For a list of the members of the USPSTF, see the Appendix (available at www.annals.org).
This article was published online first at www.annals.org on 31 December 2013.
MHS Lung Cancer Screening Program

2013 – ACR Accreditation
2018 – Formal program launched

- FTE ARNP
- Shared decision making visit
- Letters to patients/physicians
- “Open” program
MHS Lung Cancer Screening Program

Annual Volume

- 2017: 170
- 2018: 238
## MHS Lung Cancer Screening Program

<table>
<thead>
<tr>
<th>Interval</th>
<th>Lung-RADS 3</th>
<th>Lung-RADS 4</th>
<th>Positive Biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/2018 – 12/2018</td>
<td>4</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>1/2019 – 2/2019</td>
<td>4</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>
Challenges:

- Legal – HIPAA
- “Open” program makes management difficult
The bottom line....

Screening for lung cancer saves lives...

Needs to be done in a well-organized program, and

...along with smoking cessation.
“...the opportunity to realize the greatest single reduction of cancer mortality in the history of the war on cancer.”

James Mulshine, MD
Associate Provost and Vice President for Research
Rush University Medical Center