Lung Cancer Screening: Management of Incidental Findings

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Lung cancer screening: Management of incidental findings

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Incidental findings at lung screening CT

• additional costs
• patient anxiety
• iatrogenic injury

potential benefit to patient

Should we look for incidental findings?
Should we report incidental findings?
Should we recommend further investigation?

Causes of mortality in the NLST

Significant causes of mortality in the lung cancer screening population

- Cardiovascular disease
- COPD
- Other cancers

Significant causes of mortality in the lung cancer screening population

- Other cancers
Coronary artery calcium can predict all-cause mortality and cardiovascular events on LDCT screening for lung cancer

- NELSON trial
- Case-cohort design
- 150 cases (death, cardiac event), 808 random sample
- Excluded subjects with history of CVD
- 4 level risk stratification based on Agatston score:
  - 0, 1 - 100, 101 - 1,000, > 1,000

NELSON trial

Case-cohort design

150 (death, cardiac event), 808 random sample

Excluded subjects with history of CVD

4 level risk stratification based on Agatston score:

Annualized Event Rates for Coronary Artery Calcium (CAC) Risk Categories

<table>
<thead>
<tr>
<th>CAC Risk Category</th>
<th>All-cause mortality (ACM)</th>
<th>CVD endpoint</th>
<th>CHD endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.08</td>
<td>0.7</td>
<td>0.3</td>
</tr>
<tr>
<td>1 - 100</td>
<td>0.2</td>
<td>1.5</td>
<td>0.4</td>
</tr>
<tr>
<td>101 – 1,000</td>
<td>0.6</td>
<td>1.7</td>
<td>1.0</td>
</tr>
<tr>
<td>&gt; 1,000</td>
<td>1.1</td>
<td>6.1</td>
<td>3.2</td>
</tr>
</tbody>
</table>

CAC is an independent predictor of all-cause mortality, fatal and nonfatal cardiovascular events, and fatal and nonfatal coronary events in a lung cancer screening population.


Annualized Event Rates for Coronary Artery Calcium (CAC) Risk Categories

CAC on LDCT

- A visual assessment of CAC can be used for risk prediction of CHD death and all-cause mortality using non-gated LDCT for lung cancer screening, and is comparable to Agatston scoring.
- Simplest scoring system of none/mild/moderate/heavy calcification is adequate for risk assessment.
- Patients who are aware of high CAC scores are more likely to be treated with statins as a lipid-lowering intervention, and to initiate aspirin therapy, dietary changes, and increased exercise.

COPD

- Underdiagnosed disease
- 4th leading cause of death
- Infrequently self-reported even in older, heavy smokers in screening trials
- An earlier diagnosis of COPD can improve patient management and result in fewer exacerbations
- Independent risk factor for lung cancer

Significant causes of mortality in the lung cancer screening population

- Cardiovascular disease
- COPD
- Other cancer
Imaging phenotypes in COPD

- Emphysema-predominant COPD
  - Qualitative assessment
  - Quantitative assessment
    - emphysema index = % of all lung voxels <950 HU (affected by reconstruction algorithm, section thickness, inpiration level, scanner, gravity, and radiation dose)
  - Airway-predominant COPD
    - Qualitative assessment
    - wall thickness, luminal narrowing
    - Quantitative assessment
      - software analysis of average wall thickness, total wall area, inner perimeter length, wall area percentage

COPD exacerbations in COPDGene

- Emphysema-predominant group
  - total percentage of emphysema ≥ 35%
  - segmental bronchial wall thickness < 1.75 mm.
- Airway-predominant group
  - <35% emphysema
  - segmental bronchial wall thickness ≥1.75 mm.
- COPD exacerbations related to both emphysema severity and airway wall thickness
  - At lower levels of emphysema, airway wall thickness became the predominant factor.

Identification of COPD at lung cancer screening (NELSON)

- 1140 men
- PFTs and inspiratory/expiratory CT on same date
- PFT diagnosis
  - COPD = FEV1/FVC of < 70%
  - Air trapping = RV/TLC > 95th predicted value
- CT diagnosis
  - emphysema = % of voxels < 950 HU
  - air trapping = expiratory to inspiratory ratio of mean lung density

Identification of COPD at lung cancer screening (NELSON)

- 437 (38%) had PFT dx of COPD
- Logistic regression used to develop a multivariable model with FEV1/FVC ratio of < 70% as the outcome
- 5 factors independently associated with COPD
  - CT emphysema, CT air trapping, BMI, pack-years, and smoking status
  - Automated dx with low dose CT
    - PPV 76%, NPV 79%

Significant causes of mortality in the lung cancer screening population

- Cardiovascular disease
- COPD
- Other cancers

<table>
<thead>
<tr>
<th>Author</th>
<th>LDCT Study</th>
<th>Subjects with extrapulmonary malignancy</th>
<th>Details of extrapulmonary malignancies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mets et al 2011</td>
<td>1140</td>
<td>17 (1.6%)</td>
<td>Renal cell (4), Breast (3), Lymphoma (2), Bronchial carcinoma (2), Gastric (2), Ovarian (1), Spinal metastases, Melanoma, Pancreatic, Glioblastoma</td>
</tr>
<tr>
<td>Swensen et al 2003</td>
<td>1,520</td>
<td>17 (1.1%)</td>
<td>Renal cell (4), Breast (3), Lymphoma (2), Bronchial carcinoma (2), Gastric (2), Ovarian, Spinal metastases, Melanoma, Pancreatic, Glioblastoma</td>
</tr>
<tr>
<td>van de Wiel et al 2007</td>
<td>1,929</td>
<td>10 (0.5%)</td>
<td>Liver metastases, Colon, Lung, Adrenal, Gastric</td>
</tr>
<tr>
<td>Kucharzyk et al 2011</td>
<td>4,073</td>
<td>10 (0.8%)</td>
<td>RB Plasmocytoma (2), Thyroid (1), Breast (4), Ovary (1)</td>
</tr>
<tr>
<td>Rampinelli et al 2011</td>
<td>5,201</td>
<td>27 (0.5%)</td>
<td>Renal Cell (5), Renal Clear Cell (2), Lymphoma (5), Thyroid (3), Phaeochromocytoma (2), Parathyroid (2), Breast (2), Prostate (2), Pancreas (2), Lung (2), Ovary (2)</td>
</tr>
<tr>
<td>Nath et al 2011</td>
<td>1,724</td>
<td>416 (2.4%)</td>
<td>Renal cell (3), Thyroid (2), Liver metastases, Adrenal, Prostate, Pancreas, Melanoma, Cervix, Ovary, Colon, Lung, Stomach, Stomach, Mesothelioma, Other, Rectum, Cholangiocarcinoma, Others, Renal cell (2), Ovary (2)</td>
</tr>
<tr>
<td>Priola et al 2011</td>
<td>516</td>
<td>6 (1.2%)</td>
<td>Hepatocellular, GI Stromal, Prostate, Adrenal, Thymoma, Breast, Cholangiocarcinoma, Others, Pancreas, Renal cell</td>
</tr>
</tbody>
</table>
Extrapulmonary malignancies detected at lung screening CT

- Continuous Observation of Smoking Subjects [COSMOS]
- 5,201 heavy smokers aged 50+
- screened for lung cancer for 5 consecutive years
- 27 asymptomatic extrapulmonary malignancies
- frequency of one case per 200 individuals (0.5%)


Clinical Implications and Added Costs of Incidental Findings

- Clinically relevant = findings that required further dx investigation or med/surg intervention
- Found in 63/519 (12%) subjects at baseline
- Found in 10 subjects in 4 years of follow-up

Clinically relevant incidental findings

- Thyroid lesions (23)
  - 16 multinodular goiter
  - 3 nodular goiter
  - 2 benign nodule
- Renal lesions (10)
  - 7 Cyst > 20 HU
  - 2 Renal cell carcinoma
  - 1 Oncocytoma
- Adrenal glands (7)
  - 4 Adenoma < 10 HU
  - 2 Adenoma > 10 HU
  - 1 Metastasis (lung cancer)


Neglectable benefit of searching for incidental findings in the NELSON trial using low-dose multidetector CT

- Baseline scans of 1,929 participants
- Liver lesions (76)
  - Multiple cysts (53), single cyst (10), hemangioma (6), FNH (1), hepatic steatosis (1), metastasis (1)
- Renal lesions (53)
  - Solitary cyst (40), multiple cysts (7), hydronephrosis (2), angiomyolipoma (1)
- Thyroid gland (9)
  - Multinodular goiter (5), cyst/nodular goiter/benign nodule (1 each)


Neglectable benefit of searching for incidental findings in the NELSON trial using low-dose multidetector CT

- “The one malignant lesion we found had no clinical benefit for this participant, because it was a metastasis from pancreatic cancer”

Summary

Cardiovascular disease, COPD, and other cancers are significant causes of mortality in the lung cancer screening population.

2. Report the presence, severity of emphysema.
3. Limited opportunity to detect extrapulmonary malignancy. Insufficient evidence to recommend follow-up of low attenuation lesions in thyroid, kidneys, liver.