PULMONARY NODULES DETECTED INCIDENTALLY OR BY SCREENING: LOTS OF GUIDELINES BUT WHERE IS THE EVIDENCE?

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PASADENA, CA

Michael K. Gould, MD, MS, is a pulmonologist and health services researcher with longstanding interest in the care of patients with respiratory disease, venous thromboembolism and lung cancer. He currently serves as Director for Health Services Research and Implementation Science and leader of the Care Improvement Research Team (CIRT) in the Department of Research and Evaluation at Kaiser Permanente Southern California (KPSC), where he conducts both externally-funded and operationally-focused research. The CIRT is deeply embedded in the delivery system at KPSC, and is actively engaged in both observational and interventional studies of care delivery. Now a full-time researcher, Dr. Gould was a practicing pulmonologist specializing in the evaluation of patients with suspected lung cancer and respiratory complications of cancer while on faculty at Stanford University Medical Center and the VA Palo Alto Health Care System (1998-2009), and the Keck School of Medicine of USC (2009-2011). Dr. Gould has published over 150 original research articles, book chapters and reports, and his research has been supported by the Department of Veterans Affairs, the National Cancer Institute and the Patient-Centered Outcomes Research Institute. He is principal investigator of the Watch the Spot trial, a large, pragmatic, multi-center, cluster randomized trial of more versus less intensive strategies for CT surveillance in patients with small pulmonary nodules. Dr. Gould completed undergraduate studies in biology at Cornell University, earned his medical degree from the SUNY Upstate Medical University, and obtained a Master’s degree in health services and health policy from Stanford University.

OBJECTIVES:
Participants should be better able to:

1. Compare and contrast existing guidelines for pulmonary nodule evaluation
   - Fleischner Society
   - Lung-RADS/ACR
   - ACCP, NCCN, BTS
2. Discuss limitations of existing guidelines
3. Describe trial of nodule evaluation strategies

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Pulmonary Nodule Evaluation: Lots of Guidelines, but Where’s the Evidence?

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Disclosures

- Grant support from PCORI to conduct a pragmatic trial of more versus less intensive CT surveillance in patients with small pulmonary nodules
- Research support from Medial EarlySign, Inc. to help develop computer models of lung cancer risk
- Editor, ACCP guidelines for lung nodule evaluation, 2nd and 3rd editions
Learning Objectives

1. Compare and contrast existing guidelines for pulmonary nodule evaluation
   - Fleischner Society
   - Lung-RADS/ACR
   - ACCP, NCCN, BTS
2. Discuss limitations of existing guidelines
3. Describe trial of nodule evaluation strategies

Preview

- Best options for nodule evaluation remain uncertain
- Default option for patients with small nodules is CT surveillance
  - Multiple guidelines exist, but optimal frequency and duration have not been determined
  - 2017 guidelines from Fleischner Society are less intensive than original guidelines from 2005
- Decision-making for patients with large nodules should be individualized, depending on:
  - Risk of cancer (pCA)
  - Risk of active infection or inflammation, e.g. endemic mycosis
  - Risk of procedure-related complications
  - Patient preferences and anticipated adherence
  - Center-specific expertise
Definitions

- Nodule: rounded or irregular opacity, well or poorly defined, measuring up to 3 cm in diameter
- Solid nodule: homogeneous soft-tissue attenuation
- Sub-solid nodule: ill-defined border
  - Non-solid (GGN): hazy increased attenuation; does not obliterate bronchial and vascular structures
  - Part-solid: contains both ground glass and solid attenuation components

Good Old Days and the New Normal

- Detected by routine CXR
- Solitary
- Larger
- Clues: size, edge, calcification
- Few or no associated findings
- Sole priority

- Detected by diagnostic or screening CT
- Often multiple
- Smaller
- Clues: size, edge, calcification, attenuation, location
- Associated findings common
- Competing priorities

Mr. T is a 62 year old male, a former smoker with a 20 pack year smoking history. He quit 25 years ago. He reported exposure to Agent Orange. He was found to have a 9 mm, ground glass nodule in the right lower lobe on chest CT.

There are no previous x-rays or CT scans to review and the patient is asymptomatic.
Mr. B is a 77 year old, Pacific Islander male who has never smoked. He was found to have a 16 mm non-calcified nodule with a prominent cystic component in the left lower lobe on chest CT.

Mr. G is a 63 year old white male, former smoker with a 25 pack-year smoking history, who quit 19 years ago. He was incidentally noted to have a 15 mm, non-calcified, spiculated nodule in the left upper lobe on chest CT, which was performed during hospitalization for a RUL pneumonia.

There are no previous x-rays or CT scans to review and the patient is asymptomatic.
Question 1

- Compared with pulmonary nodules detected in early studies of chest radiography, CT-detected nodules are different in what respect?
  a. More often solitary
  b. More difficult to determine attenuation
  c. More likely to be calcified
  d. More often accompanied by associated findings
Question 1

- Compared with pulmonary nodules detected in early studies of chest radiography, CT-detected nodules are different in what respect?
  - a. More often solitary
  - b. More difficult to determine attenuation
  - c. More likely to be calcified
  - d. More often accompanied by associated findings

Answer: d

Guidelines for Evaluation of Small (≤10 mm) Pulmonary Nodules

- Default option is CT surveillance
- For incidental nodules, frequency and duration guided by recommendations from the Fleischner Society (2017)
  - ACCP guidelines are aligned with prior FS guidelines (2005)
  - BTS guidelines published in 2015 rely on volumetric measurement
- For nodules detected by screening, recommendations have been developed by ACR (Lung-RADS) and NCCN

Gould et al. Chest 2013;143(suppl):e93S-e120S.
Callister et al. Thorax 2015;70:ii1-ii54.
https://www.acr.org/Clinical-Resources/Reporting-and-Data-Systems/Lung-Rads
Rationale for Recommendations

- Frequency of follow-up increases as risk of cancer increases
  - Patients with risk factors (smoking) more likely to have cancer
  - Larger nodules more likely to be cancerous
  - Minimum size threshold for follow-up based on pCA ≥1%
- Frequency of follow-up increases as expected aggressiveness of cancer increases
  - Pure GGNs and part-solid nodules are more likely to be cancerous, but such cancers are typically more indolent
- Frequency of follow-up decreases as difficulty of measurement increases
  - Smaller nodules more difficult to measure and detect growth

Size and Attenuation Matter

<table>
<thead>
<tr>
<th>Sample</th>
<th>Size (mm)</th>
<th>Risk of Cancer (%)</th>
<th>Percent of Nodules</th>
</tr>
</thead>
<tbody>
<tr>
<td>NLST prevalence</td>
<td>4 to 6</td>
<td>0.5</td>
<td>51</td>
</tr>
<tr>
<td></td>
<td>7 to 10</td>
<td>1.7</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>11 to 20</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>NLST incidence</td>
<td>4 to 6</td>
<td>0.3</td>
<td>55</td>
</tr>
<tr>
<td></td>
<td>7 to 10</td>
<td>2.4</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>11 to 20</td>
<td>9.1</td>
<td>12</td>
</tr>
<tr>
<td>ELCAP/Japan</td>
<td>Solid</td>
<td>7 to 9</td>
<td>81</td>
</tr>
<tr>
<td></td>
<td>Pure GGN</td>
<td>18 to 59</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Part-solid</td>
<td>63 to 49</td>
<td>7</td>
</tr>
</tbody>
</table>

Aberle et al. NEJM 2013;369:920-931.
**Nodule Size and Cancer Prevalence**

Never-smokers vs. Current smokers

**Nodule Size and Cancer Risk (%)**

<table>
<thead>
<tr>
<th>Nodule Size (mm)</th>
<th>NLST (all rounds)</th>
<th>I-ELCAP (baseline)</th>
<th>KPSC ever smokers</th>
<th>KPSC never smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>0.2</td>
<td>-</td>
<td>1.4</td>
<td>0.4</td>
</tr>
<tr>
<td>5</td>
<td>0.3</td>
<td>0.3</td>
<td>1.8</td>
<td>1.0</td>
</tr>
<tr>
<td>6</td>
<td>0.6</td>
<td></td>
<td>1.9</td>
<td>0.6</td>
</tr>
<tr>
<td>7</td>
<td>1.3</td>
<td></td>
<td>2.5</td>
<td>1.0</td>
</tr>
<tr>
<td>8</td>
<td>2.1</td>
<td></td>
<td>3.1</td>
<td>0.8</td>
</tr>
<tr>
<td>9</td>
<td>2.2</td>
<td>4.7</td>
<td>5.4</td>
<td>2.4</td>
</tr>
<tr>
<td>10-14</td>
<td>6.7</td>
<td></td>
<td>8.1</td>
<td>2.6</td>
</tr>
<tr>
<td>15-19</td>
<td>16.1</td>
<td>29.8</td>
<td>14.9</td>
<td>6.3</td>
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<tr>
<td>20-29</td>
<td>21.5</td>
<td></td>
<td>28.0</td>
<td>9.4</td>
</tr>
</tbody>
</table>
New Fleischner Society Recommendations

- Recommendations apply to:
  - Patients with incidental nodules detected by CT
  - Age ≥35 years

- Not intended for use in:
  - Patients with known primary cancers at risk for metastasis
  - Immunocompromised patients at risk for infection

- Goals
  - Reduce number of unnecessary follow-up CT exams
  - Provide greater discretion to clinicians and patients regarding management

- “ACCP grading system” for quality of evidence/strength of recommendations

Fleischner Society Recommendations:
Solid Nodules

<table>
<thead>
<tr>
<th>Size, mm (mm³)</th>
<th>Number</th>
<th>Without Risk Factors Follow-up (months)</th>
<th>With Risk Factors Follow-up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6 (&lt;100)</td>
<td>Single</td>
<td>None (1C)</td>
<td>Optional at 12 (2A)</td>
</tr>
<tr>
<td></td>
<td>Multiple</td>
<td>None (2B)</td>
<td>Optional at 12 (?)</td>
</tr>
<tr>
<td>6 to 8 (100 to 250)</td>
<td>Single</td>
<td>6 to 12, consider 18 to 24 (1C)</td>
<td>6 to 12, 18 to 24 (1B)</td>
</tr>
<tr>
<td></td>
<td>Multiple</td>
<td>3 to 6, consider 18 to 24 (1B)</td>
<td>3 to 6, 18 to 24 (1B)</td>
</tr>
<tr>
<td>&gt;8 (&gt;250)</td>
<td>Single</td>
<td>PET, biopsy or CT at 3 months (1A)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Multiple</td>
<td>3 to 6, consider 18 to 24 (1B)</td>
<td>3 to 6, 18 to 24 (1B)</td>
</tr>
</tbody>
</table>

Fleischner Society Recommendations: Sub-Solid Nodules

<table>
<thead>
<tr>
<th>Size, mm (mm³)</th>
<th>Number and Attenuation</th>
<th>Follow-up, months</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6 (&lt;100)</td>
<td>Single</td>
<td>None (1B)</td>
</tr>
<tr>
<td></td>
<td>Multiple</td>
<td>3 to 6 months; if stable consider CT at 24 and 48 months (1C)</td>
</tr>
<tr>
<td>≥6 (&gt;100)</td>
<td>Single Ground Glass</td>
<td>6 to 12 months; if stable repeat every 2 years until 5 years (1B)</td>
</tr>
<tr>
<td></td>
<td>Single Part-Solid</td>
<td>6 to 12 months; if stable and solid component &lt;6, annual CT x 5 years; if solid ≥6, consider highly suspicious (1B)</td>
</tr>
<tr>
<td></td>
<td>Multiple</td>
<td>3 to 6 months; subsequent management based on most suspicious nodule (1C)</td>
</tr>
</tbody>
</table>


The Fine Print…

- Prior imaging studies should always be reviewed
- Use low-dose technique with thin-section (≤1.5 mm) reconstruction
- Record size to nearest mm by calculating average of widest cross-sectional diameter
- Measure attenuation on thinnest available non-sharpened image (typically soft tissue window)
- Consider more intensive follow-up for suspicious morphology or upper lobe location
- For multiple nodules, use most suspicious nodule as guide to management
- Morphology: large size or large solid component, spiculation, upper lobe location, multiplicity (up to 4) all increase pCA
- Risk factors not specifically defined, but include older age, family history, cigarette smoking, asbestos/radon/uranium exposure, and associated radiographic findings (e.g. emphysema, fibrosis)
### ACCP (GRADE) System for Quality of Evidence

#### Table 2—Grading Recommendations

<table>
<thead>
<tr>
<th>Grade of Recommendation/ Description</th>
<th>Benefit vs Risk and Burden</th>
<th>Methodological Quality of Supporting Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1A (strong recommendation, high-quality evidence)</td>
<td>Benefits clearly outweigh risk and burden, or vice versa</td>
<td>RCTs without important limitations or overwhelming evidence from observational studies</td>
</tr>
<tr>
<td>1B (strong recommendation, moderate-quality evidence)</td>
<td>Benefits clearly outweigh risk and burden, or vice versa</td>
<td>RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies</td>
</tr>
<tr>
<td>1C (strong recommendation, low-quality or very low-quality evidence)</td>
<td>Benefits clearly outweigh risk and burden, or vice versa</td>
<td>Observational studies or case series</td>
</tr>
</tbody>
</table>

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### Lung-RADS Categories and Recommendations
**LungRads Category 1: normal**
- No nodules
- Nodules with benign calcification: complete, central, popcorn, concentric rings
- Nodules containing fat
  
  **Management: continue annual screening**

**LungRads Category 2: benign**
- Solid or part-solid nodule <6mm
- New nodule <4mm
- Ground glass nodule <20mm
- Ground glass nodule ≥20mm, unchanged or slowly growing
- Cat 3 or 4 nodule unchanged for ≥3 months
  
  **Management: continue annual screening**

**LungRads Category 3: probably benign**
- Solid nodule ≥6 to <8mm or new nodule ≥4 to <6mm
- Part solid nodule ≥6mm with solid component <6mm or new <6mm
- Nonsolid nodule ≥20mm
  
  **Management: 6 month f/u CT, if no change, return to annual screening**

**LungRads Category 4A:**
- Solid nodule: ≥8 to <15mm or growing <8mm or new nodule ≥6 to <8mm
- Part solid nodule: ≥6mm with solid component ≥6 to <8mm or any new/growing <4mm solid component
- Endobronchial nodule
  
  **Management: 3 month f/u CT, if no change, return to annual screening; PET/CT may be used when there is a ≥8 mm solid component**

**LungRads Category 4B:**
- Solid nodule ≥15mm or new/growing ≥8mm
- Part solid nodule with ≥8mm solid component or new/growing ≥4mm component
  
  **Management: perform f/u CT at 3 months, PET/CT and/or tissue sampling depending on the probability of malignancy and comorbidities; PET/CT may be used when there is a ≥8 mm solid component**

**LungRads Category 4X:**
- Category 3 or 4 nodules with additional features or imaging findings that increases the suspicion of malignancy
  
  **Management: Same as 4B**
### Lung-RADS Summary

<table>
<thead>
<tr>
<th>Category</th>
<th>Descriptor</th>
<th>Management</th>
<th>pCA</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Incomplete</td>
<td>Repeat/compare</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Negative</td>
<td>Return to annual screening</td>
<td>&lt;1%</td>
<td>90%</td>
</tr>
<tr>
<td>2</td>
<td>Benign</td>
<td>6 month</td>
<td>&lt;1%</td>
<td>5%</td>
</tr>
<tr>
<td>3</td>
<td>Probably benign</td>
<td>3 month LDCT or PET/CT</td>
<td>5-15%</td>
<td>2%</td>
</tr>
<tr>
<td>4A</td>
<td>Suspicious</td>
<td>PET/CT or tissue sampling</td>
<td>&gt;15%</td>
<td>2%</td>
</tr>
<tr>
<td>4B</td>
<td></td>
<td>As appropriate</td>
<td>10%</td>
<td></td>
</tr>
<tr>
<td>4X</td>
<td></td>
<td>As appropriate</td>
<td>10%</td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>Incidental finding</td>
<td>As appropriate</td>
<td>10%</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>Prior lung cancer</td>
<td>As appropriate</td>
<td>10%</td>
<td></td>
</tr>
</tbody>
</table>

### The Fine Print…

- Negative screen does not rule out lung cancer
- Size measured on lung windows and reported as average diameter rounded to nearest whole number
- Growth= increase in size of >1.5 mm
- Exam category should be coded based on nodule with highest degree of suspicion
- Category 4B options predicated on pCA
- Category 4X factors include spiculation, enlarged lymph nodes, rapid growth
- Category 3 and 4A nodules that are stable should be recoded as Category 2
British Thoracic Society guidelines for the investigation and management of pulmonary nodules


Callister et al. Thorax 2015:70;ii1-ii54.
**NCCN Guidelines Version 3.2018**

**Lung Cancer Screening**

**Evaluation of Screening Findings**

- **Solid nodule on initial screening LDCT**
  - ≤5 mm: Annual screening LDCT until patient is no longer a candidate for definitive treatment
  - 6–7 mm: LDCT in 6 mo
  - 8–14 mm: Consider PET/CT
  - ≥15 mm: LDCT in 1 mo (immediately after vigorous coughing) → if no resolution, Bronchoscopy

- **Low suspicion of lung cancer**
  - LDCT in 3 mo

- **High suspicion of lung cancer**
  - Biopsy or Surgical excision

**Follow-up of Screening Findings**

- **Annual screening LDCT until patient is no longer a candidate for definitive treatment**

See Evaluation (LCB-7)

See appropriate NCCN Guidelines
Limitations of Recommendations

- Recommendations from existing guidelines based on expert clinical judgment and have never been validated empirically
- Providing ranges, while well-intentioned, complicates implementation and measurement of adherence
- For individuals with benign nodules, surveillance provides no benefit, is inconvenient and costly, entails unnecessary exposure to ionizing radiation, and may lead to unnecessary and risky downstream testing.
- Just because cancer is less likely, it does not necessarily follow that it is safe to wait longer to detect it.

Question 2

- Which one of the following is true about the recommendations in the 2017 Fleischner Society Guidelines for pulmonary nodule evaluation?
  a. They pertain to patients with both incidental and screening-detected nodules
  b. For solid nodules, recommended follow-up is earlier or more frequent with increasing nodule size
  c. Nodule size should be reported using the largest diameter to the nearest tenth of a millimeter
  d. All of the recommendations are supported by high-quality evidence from randomized, controlled trials
Question 2

Which one of the following is true about the recommendations in the 2017 Fleischner Society Guidelines for pulmonary nodule evaluation?

a. They pertain to patients with both incidental and screening-detected nodules
b. For solid nodules, recommended follow-up is earlier or more frequent for larger nodules than for smaller ones
c. Nodule size should be reported using the largest diameter to the nearest tenth of a millimeter
d. All of the recommendations are supported by high-quality evidence from randomized, controlled trials

Answer: b
Unresolved Questions: Small Nodules

- How do we avoid harms from unnecessary radiation exposure and downstream invasive testing?
- What is the optimal frequency and duration of follow-up for nodules of varying size and attenuation characteristics?
- What are the best methods and thresholds to reliably detect growth? Is volumetric measurement better?
- Do all small, malignant nodules need to be treated?
  – Can some be treated more conservatively?

Adherence with Recommendations

- Relatively few studies
- Adherence ranges from 34% to 55%
- Barriers to adherence
  – Complexity of recommendations
  – Competing priorities for evaluation and management
  – Cold handoffs
  – Lack of systems

Wiener et al. JAMA IM 2014;174:871-880
Clinical Sites
N = 24 hospitals

Patients with small (≤ 15 mm) pulmonary nodules N=40,000

More intensive CT surveillance (original Fleischner)

Less intensive CT surveillance (revised Fleischner)

Assessments

Lung cancer-specific outcomes: tumor stage>T1a, time to treatment, survival

PROs: Emotional distress, anxiety, general health status, satisfaction with evaluation

Resource utilization during evaluation: CT scans, other imaging tests, invasive biopsy, surgery, outpatient visits, ED visits and hospitalizations

Adherence: use of low-dose technique; surveillance protocol recommended by radiologist, ordered by provider, completed by patient
## Description of Study Sites and Enrollment Targets

<table>
<thead>
<tr>
<th>Health Care Organization</th>
<th>Type of Setting</th>
<th>Unique patients with chest CT during 20 months of enrollment</th>
<th>Estimated patients with nodules ≤15 mm</th>
<th>Estimated patients with lung cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boston Medical Center</td>
<td>Safety Net</td>
<td>7,840</td>
<td>1,250</td>
<td>37</td>
</tr>
<tr>
<td>Cleveland Clinic</td>
<td>Referral</td>
<td>26,670</td>
<td>5,330</td>
<td>160</td>
</tr>
<tr>
<td>Health Partners, MN</td>
<td>Integrated</td>
<td>4,920</td>
<td>780</td>
<td>23</td>
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<tr>
<td>Kaiser Colorado</td>
<td>Integrated</td>
<td>23,320</td>
<td>3,720</td>
<td>111</td>
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<td>Kaiser Northwest</td>
<td>Integrated</td>
<td>12,680</td>
<td>2,020</td>
<td>61</td>
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<td>Kaiser Southern California</td>
<td>Integrated</td>
<td>90,000</td>
<td>14,330</td>
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<td>Marshfield Clinic</td>
<td>Integrated</td>
<td>6,160</td>
<td>980</td>
<td>29</td>
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<td>University</td>
<td>12,500</td>
<td>1,460</td>
<td>29</td>
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<td>10,540</td>
<td>1,680</td>
<td>50</td>
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<td>Portland VAMC</td>
<td>Veterans</td>
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<td>1,120</td>
<td>34</td>
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<td>University</td>
<td>11,640</td>
<td>780</td>
<td>16</td>
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<tr>
<td>UCLA</td>
<td>University</td>
<td>20,000</td>
<td>2,100</td>
<td>63</td>
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<tr>
<td>UC San Francisco</td>
<td>University</td>
<td>13,990</td>
<td>960</td>
<td>29</td>
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<tr>
<td>University of Pennsylvania</td>
<td>University</td>
<td>30,520</td>
<td>3,470</td>
<td>104</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>279,550</td>
<td>39,980</td>
<td>1,177</td>
</tr>
</tbody>
</table>

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### Evaluation of Large (>8 mm) Nodules

- Review old imaging studies
- Estimate probability of cancer (pCA)
- Assess risk of complications
- Consider PET scan, especially when pCA is low
- Discuss alternatives in context of pCA: CT surveillance, non-surgical biopsy, surgical diagnosis
- Elicit patient preferences

Estimating the Clinical Probability that a Nodule is Cancerous

- Intuition
  - Intuition
  - Incidental nodules (high prevalence)
    - Mayo Clinic model
    - VA model
  - Screening-detected nodules (lower prevalence)
    - McWilliams model (Brock)
  - Mayo and McWilliams had similar accuracy in post-hoc analysis of NLST data (AUC 0.82 versus 0.84 for nodules >8 mm)

Nair et al. AJRCCM 2018 (in press).

Clinical probability of malignancy?

- Low (<5%)
  - CT surveillance vs. Non-surgical biopsy
    - Provider concern re: loss to follow-up?
      - Yes
        - Functional imaging vs. Non-surgical biopsy
          - Suspicion of infectious or inflammatory nodule?
            - Yes
              - High risk for biopsy complications?
                - Yes
                  - Wants to avoid physical complications
                - No
                  - Wants to avoid prolonged uncertainty
            - No
              - Patient values and preferences
                - Yes
                  - Wants to avoid physical complications
                - No
                  - Wants to avoid prolonged uncertainty
        - No
          - Patient values and preferences
            - Yes
              - Wants to avoid physical complications
            - No
              - Wants to avoid prolonged uncertainty
  - No
    - Non-surgical biopsy
      - Wants to avoid physical complications
- Intermediate (5-60%)
  - Functional imaging vs. Non-surgical biopsy
    - Suspicion of infectious or inflammatory nodule?
      - Yes
        - High risk for biopsy complications?
          - Yes
            - Wants to avoid physical complications
          - No
            - Wants to avoid prolonged uncertainty
      - No
        - Patient values and preferences
          - Yes
            - Wants to avoid physical complications
          - No
            - Wants to avoid prolonged uncertainty
- High (>60%)
  - Non-surgical biopsy vs. Surgical resection
    - High surgical risk (e.g., severe comorbidities)?
      - Yes
        - Wants definitive diagnosis prior to treatment
      - No
        - Patient values and preferences
          - Yes
            - Wants definitive diagnosis prior to treatment
          - No
            - Wants definitive diagnosis and treatment ASAP

CT surveillance
Non-surgical biopsy
Bronchoscopic biopsy (under guidance if available)
Transathoracic needle lung biopsy
Surgical resection

Wants to avoid physical complications
Wants to avoid prolonged uncertainty
Wants certainty
Wants definitive diagnosis prior to treatment
Wants definitive diagnosis and treatment ASAP

Suspicion of Infectious or inflammatory nodule?
High risk for biopsy complications?
Patient values and preferences

Wants to avoid physical complications
Wants to avoid prolonged uncertainty

Provider concern re: loss to follow-up?

Wants to avoid physical complications
Wants to avoid prolonged uncertainty

Wants definitive diagnosis prior to treatment
Wants definitive diagnosis and treatment ASAP

Surgical resection

Courtesy of Renda Wiener, MD, MPH
Question 3

Which of the following is true regarding pulmonary nodules >8 mm in average diameter?

- The risk of cancer is 1-2%
- They should all be resected promptly, as long as the patient is fit for surgery
- Management decisions should incorporate geographic considerations, the risk of cancer, the risk of procedure-related complications, patient preferences, and local availability of technology and expertise
- They usually represent a benign harmartoma
Conclusions

- Best options for nodule evaluation remain uncertain
- Default option for patients with small nodules is CT surveillance
  - Multiple guidelines exist, but optimal frequency and duration have not been determined
  - 2017 guidelines from Fleischner Society are less intensive than original guidelines from 2005
- Decision-making for patients with large nodules should be individualized, depending on:
  - Risk of cancer (pCA)
  - Risk of active infection or inflammation, e.g. endemic mycosis
  - Risk of procedure-related complications
  - Patient preferences and anticipated adherence
  - Center-specific expertise

Thank You!

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