Work-up of Suspected Lung Cancer

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Lung Cancer Educational Program
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Presenter disclosure

- No conflicts to disclose
Outline

• Scope of the problem
• Lung ca algorithm
• Diagnostic / therapeutic techniques
Lung Carcinoma – a fatal disease

• Most common cancer cause of death in men and women (>breast, colorectal & prostate combined)

• Overall 5-year survival 15%, has not changed significantly over the past 20 years

• 2009: estim. 23,400 Cdns diagnosed with lung ca, 20,500 died*

• Lung cancer curable only if diagnosed and treated at early stage

• Surgery remains best chance for cure for NSCLC (Stage I: 70% 5-year survival)

*Canadian Cancer Statistics 2009
www.cancer.ca
The problem...

- Early stage lung ca: asymptomatic

- Symptoms: Advanced / metastatic ca
Variable symptoms...

- "Classic" presentation: smoker, SOB, cough / hemoptysis: CXR – lung mass...

- Atypical presentation: ex-smoker, back pain, fatigue, weight loss...was told by family MD was "pulled muscle," continued to have worsening pain next 3-4 months...
Critical first step!!

Immediate Referral
- Signs of superior vena cava obstruction (swelling of the face or neck with fixed elevation of jugular venous pressure, prominent veins on chest)
- Stridor
- Massive hemoptysis (more than 1 cup/250cc in 24 hrs)
- New neurological signs suggestive of brain metastases or cord compression

Urgent Referral and CT Scan
- Two or more episodes of hemoptysis (1 tablespoon / 15 ml or more of clotted blood)
- Supraclavicular lymphadenopathy
- Incidental CT Finding: Any solid or ground glass nodule over 1 cm

Immediate Chest X-Ray
- Unexplained single episode of hemoptysis
- Finger clubbing
- Suspicious cervical lymphadenopathy
- Features suggestive of cancer that has metastasized elsewhere (bone, skin, brain, liver)
- Features suggestive of a paraneoplastic syndrome (unexplained hyponatremia, hypercalcemia, etc.)

Chest X-Ray for Persistent Symptoms
- Unexplained new symptoms lasting more than 3 weeks (OR sooner in patients with risk factors)
- Cough
- Chest and/or shoulder pain
- Loss of appetite or weight loss
- Unexplained changes in existing symptoms in patients with chronic lung disease

Non-Urgent Referral
- Interstitial lung disease
- On CT: Any solid or ground glass nodule less than 1 cm

Referral to Emergency Department (Thoracic Surgeon or Respiriologist on Call in Winnipeg (HSC) or Brandon)

Higher Risks for Lung Cancer
- Smokers / former smokers / second hand smoke exposure
- History of COPD
- Asbestos / radon / wood dust / silica exposure
- Previous cancer
- History of TB, silicosis

Referral to Diagnostic Specialist (Thoracic Surgeon or Respiriologist) AND Order infused CT Scan of Thorax +/- Upper Abdomen

Chest X-ray (PA and Lat)
Record the History, Exam, Diff Dx and Risk Factors on Requisition

Normal Findings
- High Clinical Suspicion of Lung cancer
- Monitor & Manage

Abnormal Findings
- Chest X-ray suggestive of lung cancer including:
  - Single or multiple pulmonary nodules
  - Mediastinal or hilar lymphadenopathy
  - Unexplained large unilateral pleural effusion
  - Infiltrate, consolidation or effusion attributed to pneumonia and not resolved in 6 week follow-up X-ray

Chest X-ray and clinical findings suspicious for pneumonia
Treat with Antibiotics. Repeat Chest X-ray in 6 weeks to confirm resolution
Case: 66 yr old female

- Cough x 2 mo, non resolving
- Smoker, 50 pack yr history
CXR normal March 2013
Case: 66 yr old female

• Now what?
Case: 66 yr old female

- Over next 3 months developed worsening chest, back pain, headaches, inability to lie flat
- Presented to ER November 2013
CXR: mediastinal mass
CT: mediastinal adenopathy causing SVC obstruction, liver and bone mets
Case: 66 yr old female

- On exam: swollen neck veins, palpable R supraclavicular adenopathy
- LN bx: small cell lung ca
- Referred to medical and radiation oncology
Diagnostic pitfalls

• “Why didn't CXR pick it up?”

- High index suspicion: smoking history, persistent symptoms, history ca, radon / asbestos exposure

- CT scan is key initial diagnostic test
Suspected lung cancer

• What is it? - Diagnosis
• How far has it spread? - Staging
• What can be done? – Treatment
Suspected lung cancer

- What is it? - Diagnosis
  - How far has it spread? - Staging
  - What can be done? – Treatment
Lung Cancer - histology

**Non-small cell (NSCLC)**
- Squamous - central, bronchus
- Adenocarcinoma - peripheral - (bronchoalveolar / adenoca in situ)
- Large cell
  ➔ Surgery for early stage NSCLC, chemo and/or radiation for advanced / metastatic disease

**Small cell (SCLC)**
- Lymphadenopathy, hematogenous dissemination
  ➔ Chemotherapy, radiation for SCLC
The Suspicious Pulmonary Nodule

- New
- Increasing size
- Non-calcified
- High risk pt
- Enhancing
- Spiculated
### Fleischner Guidelines: Incidental Pulmonary Nodule Followup

<table>
<thead>
<tr>
<th>Nodule Size (mm)*</th>
<th>Low-Risk Patient†</th>
<th>High-Risk Patient‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤4</td>
<td>No follow-up needed§</td>
<td>Follow-up CT at 12 mo; if unchanged, no further follow-up‖</td>
</tr>
<tr>
<td>&gt;4–6</td>
<td>Follow-up CT at 12 mo; if unchanged, no further follow-up‖</td>
<td>Initial follow-up CT at 6–12 mo then at 18–24 mo if no change‖</td>
</tr>
<tr>
<td>&gt;6–8</td>
<td>Initial follow-up CT at 6–12 mo then at 18–24 mo if no change</td>
<td>Initial follow-up CT at 3–6 mo then at 9–12 and 24 mo if no change</td>
</tr>
<tr>
<td>&gt;8</td>
<td>Follow-up CT at around 3, 9, and 24 mo, dynamic contrast-enhanced CT, PET, and/or biopsy</td>
<td>Same as for low-risk patient</td>
</tr>
</tbody>
</table>
Suspicious Lung Nodule

**Diagnostic Techniques**

- Bronchoscopy
- CT Guided Needle Biopsy
- VATS / open resection

**try to do least invasive procedure, if necessary**
Flexible Bronchoscopy

- Lavage, cytology brush, biopsy
- Best for **central / hilar** tumors, **endobronchial** component
- Resp symptoms: cough, hemoptysis, SOB
- Less helpful for small peripheral nodules
CT-guided Needle Biopsy

- local anesthesia, conscious sedation
- good for larger, more peripheral tumors
- Risk pneumothorax 10-20%
- Accuracy <60% for lesions <15 mm
- reserve for pts who are not surgical candidates (comorbidities, unresectable) or if suspect alternate diagnosis (eg. Lymphoma, TB)
VATS (video assisted thoracic surgery)

- Resect tumor in its entirety
- Can send for frozen section to confirm diagnosis, proceed to more extensive resection (lobectomy) if NSCLC
- Smaller tumors more difficult to localize via VATS

**preferred procedure for solitary resectable tumor in good operative candidate, no metastases on staging CT / PET**
Best diagnostic test?
- bronchoscopy
- CT needle biopsy
- VATS wedge resection
Suspected lung cancer

• **What is it? - Diagnosis**

• **How far has it spread? - Staging**

• **What can be done? - Treatment**
Staging

- Strongly correlated with outcome
- T-tumor
- N- lymph node involvement
- M - metastatic disease
- TNM combined to stage cancer from 1-4
### TNM Staging of Lung Cancer (2009)

<table>
<thead>
<tr>
<th>Stage</th>
<th>T1a</th>
<th>T1b</th>
<th>T2a</th>
<th>T2b</th>
<th>T3</th>
<th>T4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>≤ 2 cm</td>
<td>&gt; 2 cm, ≤ 3 cm</td>
<td>&gt; 3 cm ≤ 5 cm</td>
<td>&gt; 5 cm ≤ 7 cm</td>
<td>Any size ≤ 7 cm if 1 or more of the criteria of extent are present.</td>
<td>Any size if 1 or more of the criteria of extent are present.</td>
</tr>
</tbody>
</table>

**1- Size**

- Stage I
  - T1a: Carcinoma in situ
  - T1b: Endo-bronchial Carcinoma (% 100 T1b)

**2- Criteria of Extent**

- **Local Invasion**
  - None: The tumor is surrounded by lung or visceral pleura
  - Visceral pleura
  - Chest wall, diaphragm, phrenic nerve, mediastinal pleura and/or plexus of pneumothorax
  - Mediastinum, trachea, heart, great vessels, recurrent laryngeal nerve, esophagus, vertebral body

- **Satellite Nodule(s)**
  - None

**3- Staging**

- **Stage IA**
- **Stage IB**
- **Stage IIA**
- **Stage IIB**
- **Stage IIIA**
- **Stage IIIB**
- **Stage IIIC**
- **Stage IV**

**Explanation of lymph node staging:**

- For any category, one or more of the groups marked by ○ must be involved and the involvement of all groups marked by □ should be absent.
- The presence or absence of involvement in groups marked by □ does not alter N staging in the corresponding category.
Staging for dummies

- Stage 1 - early disease, high cure rate
- Stage 4 - advanced disease with metastases, essentially incurable
**Staging for dummies**

- Stage 2 - curable but less favorable than stage 1, early lymph node involvement / larger more aggressive tumor

- Stage 3 – low cure rate but not metastatic
Infused CT chest

• Most important initial diagnostic / staging investigation lung ca
• Location / size of primary tumor
• Mediastinal / hilar LNs
• Distant mets (liver, adrenal), pleural effusion

• Consider CT head for neuro symptoms, extensive disease on CT chst (mediastinal adenopathy, distant mets)
• +/- bone scan, MRI (liver)
Position emission tomography - PET

- Highlight areas increased metabolic activity
- Ca cells hypermetabolic – PET can help with diagnosis, staging
- Cannot visualize brain
- False positive – infectious, inflammatory lesions
- False negative – small tumours (<1cm), BAC/in-situ adenocarcinoma, carcinoid, lymphoma
- Still need tissue for definitive diagnosis
TNM Stage groupings & 5-year survival (%)
Mediastinal LN (N2) staging important in NSCLC

Stage I: Surgery
- Primary tumor
- Affected lymph nodes

Stage II: Chemoradiation
- Primary tumor
- Affected lymph nodes

Stage III Cancer: Chemoradiation
- Mediastinal lymph node metastasis
- Tumor
Mediastinoscopy

- Gold standard mediastinal staging lung ca
- Day surgery
- General anesthesia
- Biopsy mediastinal and hilar LNs under direct vision with mediastinoscope
- Risk bleed, nerve injury
EBUS staging in NSCLC

RADIAL PROBE EBUS

CONVEX-PROBE EBUS
EBUS staging in NSCLC
Yasufuku K, Nakajima T, Motoori K et al. Chest 2006;130;710-718
Comparison of Endobronchial Ultrasound, Positron Emission Tomography, and CT for Lymph Node Staging of Lung Cancer*

Kazuhiro Yasufuku, MD, FCCP; Takahiro Nakafima, MD; Ken Motoori, MD; Yasuo Sekine, MD; Kiyoshi Shibuya, MD; Kenzo Hiroshima, MD; and Takehiko Fujisawa, MD

78 out of 102 study patients underwent surgery

Table 3—Comparison of CT, PET, and EBUS-TBNA to the Final Diagnosis*

<table>
<thead>
<tr>
<th>Tests</th>
<th>True Positive</th>
<th>True Negative</th>
<th>False Positive</th>
<th>False Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>20</td>
<td>42</td>
<td>34</td>
<td>6</td>
</tr>
<tr>
<td>PET</td>
<td>20</td>
<td>54</td>
<td>23</td>
<td>5</td>
</tr>
<tr>
<td>EBUS-TBNA</td>
<td>24</td>
<td>76</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 4—Characteristics of CT, PET, and EBUS-TBNA in the Correct Prediction of Mediastinal Lymph Node Staging*

<table>
<thead>
<tr>
<th>Tests</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>76.9</td>
<td>55.3</td>
<td>37.0</td>
<td>87.5</td>
<td>60.5</td>
</tr>
<tr>
<td>PET</td>
<td>80.0</td>
<td>70.1</td>
<td>46.5</td>
<td>91.5</td>
<td>72.5</td>
</tr>
<tr>
<td>EBUS-TBNA</td>
<td>92.3</td>
<td>100</td>
<td>100</td>
<td>97.4</td>
<td>98.0</td>
</tr>
</tbody>
</table>

p < 0.00001

Chest 2006;130;710-718
Suspected lung cancer

- **What is it? - Diagnosis**
- **How far has it spread? - Staging**
- **What can be done? – Treatment (stage I-II NSCLC)**
Diagnosis of early stage NSCLC

- In majority of patients with sufficient pulmonary reserve:
  - anatomic resection: lobectomy
Open lobectomy for early stage NSCLC

- Posterolateral thoracotomy
- Anatomic resection (individual division pulmonary artery, vein, bronchus), removal involved lobe
- Lymph node sampling / dissection
Thoracotomy

- Division of chest wall muscle, ribs spread / cut / fractured
  - Impairment of respiratory function
  - Immune suppression
  - PAIN!
    - short term narcotic requirements
    - long term – chronic pain
Thoracoscopic lobectomy – technique

- No rib spreading
- Access incision 4-5 cm
- 2-3 additional port sites
- Anatomic dissection, division hilar vessels, bronchus
- Lymph node sampling / dissection
- Local anesthetic, intercostal nerve blocks, NSAIDs, opioids
### Table 4

Perioperative results of current video-assisted thoracic surgery and open lobectomy

<table>
<thead>
<tr>
<th>Study</th>
<th>Operative time (min)</th>
<th>Intraoperative blood loss (mL)</th>
<th>Chest tube drainage (d)</th>
<th>Length of stay (d)</th>
<th>Acute pain&lt;sup&gt;a,b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattaneo et al, [19]</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>5</td>
<td>NR</td>
</tr>
<tr>
<td>Whitson et al, [16]</td>
<td>228</td>
<td>212</td>
<td>251</td>
<td>6.1</td>
<td>6.4</td>
</tr>
<tr>
<td>Muraoka et al, [17]</td>
<td>288</td>
<td>293</td>
<td>151</td>
<td>6</td>
<td>NR</td>
</tr>
<tr>
<td>Shiraiishi et al, [58]</td>
<td>227</td>
<td>225</td>
<td>142</td>
<td>204&lt;sup&gt;b&lt;/sup&gt;</td>
<td>NR</td>
</tr>
<tr>
<td>Watanabe et al, [22]</td>
<td>215</td>
<td>221</td>
<td>236</td>
<td>3.8</td>
<td>7.8&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Demmy et al, [18]</td>
<td>133</td>
<td>312&lt;sup&gt;b&lt;/sup&gt;</td>
<td>NR</td>
<td>3</td>
<td>4.2</td>
</tr>
<tr>
<td>Craig et al, [23]</td>
<td>121</td>
<td>141</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Nagahiro et al, [25]</td>
<td>250&lt;sup&gt;b&lt;/sup&gt;</td>
<td>186</td>
<td>187</td>
<td>3.6</td>
<td>3.8</td>
</tr>
<tr>
<td>Yim et al, [24]</td>
<td>78</td>
<td>82</td>
<td>NR</td>
<td>3.2</td>
<td>4.1</td>
</tr>
<tr>
<td>Mean</td>
<td>192</td>
<td>195</td>
<td>VATS&lt;sup&gt;c&lt;/sup&gt;</td>
<td>36</td>
<td>VATS&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Abbreviations: NR, not recorded; POD, postoperative day; VATS, video-assisted thoracoscopic surgery.

<sup>a</sup> Less pain refers to VATS groups.

<sup>b</sup> $P < .05$ in original study.

<sup>c</sup> $P < .05$ by Wilcoxon rank sum test.
### VATS vs. open: morbidity

#### Table 3
Summary of complications comparing video-assisted thoracic surgery and open lobectomy

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Type of study</th>
<th>VATS</th>
<th>Open</th>
<th>Total complications&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattaneo et al, [19]</td>
<td>2008</td>
<td>Case-control</td>
<td>82</td>
<td>82</td>
<td>91</td>
</tr>
<tr>
<td>Whitson et al, [16]</td>
<td>2007</td>
<td>Case-control</td>
<td>59</td>
<td>88</td>
<td>20</td>
</tr>
<tr>
<td>Muraoka et al, [17]</td>
<td>2006</td>
<td>Case-control</td>
<td>43</td>
<td>42</td>
<td>11</td>
</tr>
<tr>
<td>Shiraishi et al, [58]</td>
<td>2006</td>
<td>Case-control</td>
<td>81</td>
<td>79</td>
<td>NR</td>
</tr>
<tr>
<td>Watanabe et al, [22]</td>
<td>2005</td>
<td>Case-control</td>
<td>221</td>
<td>190</td>
<td>11</td>
</tr>
<tr>
<td>Demmy et al, [18]</td>
<td>2004</td>
<td>Case-control</td>
<td>20</td>
<td>38</td>
<td>5</td>
</tr>
<tr>
<td>Craig et al, [23]</td>
<td>2001</td>
<td>Randomized</td>
<td>22</td>
<td>19</td>
<td>NR</td>
</tr>
<tr>
<td>Nagahiro et al, [25]</td>
<td>2001</td>
<td>Case-control</td>
<td>13</td>
<td>9</td>
<td>NR</td>
</tr>
<tr>
<td>Yim et al, [24]</td>
<td>2000</td>
<td>Case-control</td>
<td>18</td>
<td>18</td>
<td>NR</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td>559</td>
<td>565</td>
<td>130</td>
</tr>
</tbody>
</table>

P<0.01 by Chi squared test

Decreased post-op pain with VATS

- Pain reduction with VATS lobectomy over open: preserved even at 12 months
  
  Nagahiro *Ann Thor Surg* 2001

- 3 weeks

  Demmy *Ann Thor Surg* 2008
VATS lobectomy associated with lower need for home health services after discharge

Survival for resected Stage I NSCLC

- Open thoracotomy: 5-year survival 64.6%

Mountain Ann Thor Surg 2000

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Recent series of thoracoscopic lobectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Series</td>
<td>N</td>
</tr>
<tr>
<td>Kaseda [14]</td>
<td>128</td>
</tr>
<tr>
<td>Sugi [15]</td>
<td>50</td>
</tr>
<tr>
<td>Solaini [16]</td>
<td>125</td>
</tr>
<tr>
<td>Walker [17]</td>
<td>158</td>
</tr>
<tr>
<td>Roviaro [18]</td>
<td>193</td>
</tr>
<tr>
<td>McKenna [6]</td>
<td>1,100</td>
</tr>
<tr>
<td>Onaitis [7]</td>
<td>500</td>
</tr>
</tbody>
</table>

VATS lobectomy patients tolerate adjuvant therapy better

<table>
<thead>
<tr>
<th>Compliance</th>
<th>Thorascopy n = 57 (%)</th>
<th>Thoracotomy n = 43 (%)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to initiation of chemo (days)</td>
<td>58 ± 31</td>
<td>54 ± 35</td>
<td>0.277</td>
</tr>
<tr>
<td>Percentage of planned regimen received</td>
<td>88% ± 24%</td>
<td>89% ± 19%</td>
<td>0.835</td>
</tr>
<tr>
<td>Pts with delayed chemotherapy doses</td>
<td>10 (18)</td>
<td>25 (58)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pts with reduced chemotherapy doses</td>
<td>15 (26)</td>
<td>21 (49)</td>
<td>0.020</td>
</tr>
<tr>
<td>&gt;75% of total planned regimen</td>
<td>35 (61)</td>
<td>17 (40)</td>
<td>0.030</td>
</tr>
<tr>
<td>Toxicity grade ≥2</td>
<td>29 (51)</td>
<td>24 (56)</td>
<td>0.624</td>
</tr>
<tr>
<td>Toxicity grade ≥3</td>
<td>7 (12)</td>
<td>9 (21)</td>
<td>0.243</td>
</tr>
</tbody>
</table>

Peterson Ann Thor Surg 2007
Thoracoscopic lobectomy – proposed advantages

- Less pain
- Shorter chest tube duration
- Shorter hospital stay
- Faster return to full function
- Better tolerance for adjuvant therapy
Summary

• Lung cancer remains most common cause cancer related death – only curable if diagnosed early

• Patients may not have “classical” presentation

• Lung ca algorithm → high index suspicion, timely referral keys to expeditious workup

• Multidisciplinary thoracic oncology team, variety newer diagnostic / therapeutic techniques – available to assist in care of lung cancer pts