Role of Surgery in Management of Non Small Cell Lung Cancer

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• Introduction
• Surgical approach
• Principle and type of surgery
• Surgery according to stage of the disease
• Pleural effusion
• Advance stages
• Follow up
Lung cancer

• The second most common cancer among both men and women

• Worldwide, lung cancer occurred in approximately 1.8 million patients in 2012 and caused an estimated 1.6 million deaths.¹

• In the United States, there will be an estimated 224,000 new cases of lung cancer and 159,000 deaths in 2014.²

• Nearly 60% of people diagnosed with lung cancer die within 2 years. This had not improved in 10 years.

2009 Estimated US Cancer Deaths*

Men 292,540
Women 269,800

Lung & bronchus 30%
Prostate 9%
Colon & rectum 9%
Pancreas 6%
Leukemia 4%
Liver & intrahepatic bile duct 4%
Esophagus 4%
Urinary bladder 3%
Non-Hodgkin lymphoma 3%
Kidney & renal pelvis 3%
All other sites 25%

Lung & bronchus 26%
Breast 15%
Colon & rectum 9%
Pancreas 6%
Ovary 5%
Non-Hodgkin lymphoma 4%
Leukemia 3%
Uterine corpus 3%
Liver & intrahepatic bile duct 2%
Brain/ONS 2%
All other sites 25%

ONS=Other nervous system.
Source: American Cancer Society, 2009.
INTRODUCTION

• Surgical resection for lung cancer is still regarded as the most effective method of controlling the primary tumor

• The median survival is stage dependent
  - Stage IA; 95 months
  - Stage IIIA; 19 month
**TABLE 32-1** 5-Year Survival Rates by Stage Following Complete Resection for Lung Cancer at Memorial Sloan-Kettering Cancer Center

<table>
<thead>
<tr>
<th>Stage</th>
<th>Survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I (n = 539)</td>
<td>76</td>
</tr>
<tr>
<td>T1N0</td>
<td>84</td>
</tr>
<tr>
<td>T2N0</td>
<td>68</td>
</tr>
<tr>
<td>Stage II (n = 214)</td>
<td>47</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td></td>
</tr>
<tr>
<td>T3N0 (chest wall)</td>
<td>56</td>
</tr>
<tr>
<td>T3N0 (carina)</td>
<td>36</td>
</tr>
<tr>
<td>T3N0 (mediastinum)</td>
<td>29</td>
</tr>
<tr>
<td>N2 (surgery) (n = 151)</td>
<td>30</td>
</tr>
<tr>
<td>N2 (chemotherapy + surgery) (n = 89)</td>
<td>26</td>
</tr>
</tbody>
</table>

Surgical Approach

• Diagnosis: Is this cancer?
• STAGE: Is there spread?
• What is the best treatment option?
• Suitability: can the patient receive such therapy?
Diagnosis

- History and physical
- Chest X-ray
- CT scan
- Percutaneous biopsy
- Bronchoscopy
- Bone scan and CT head
- PET scan
- Mediastinoscopy
Figure 3

Stage Groupings for Lung Cancer

Stage I
- Rx: Surgery

Stage II
- Rx: Chemotherapy/Radiation
- 4-8 weeks recovery
- Surgery

Stage IIIA

Stage IIIB
- Rx: Chemotherapy +/- Radiation

Stage IV
- Or
- Chemotherapy/Radiation
- and no Surgery

Fitness for Surgery

- Age
- Pulmonary function
- Cardiovascular function
- Medical conditions
- Nutritional Status
- Performance status
ROLE OF SURGERY

• DIAGNOSTIC

• THERAPUTIC
  - CURABLE
  - PALLATIVE
CERVICAL MEDIASTOTOSCOPY
Surgical Principles and Management

• The tumor and all intrapulmonary lymphatic drainage should be removed completely.
• En bloc resection of closely adjacent or invaded structures.
• Avoid tumor spillage during surgery.
• Assesses the resection margins by frozen-section analysis. Positive resection margins should be Re-resected whenever is possible.
• Complete the staging by removing All accessible Mediastinal lymph node stations for accurate staging.
Standard of Care For Peripheral Nodules

1940’s  Pneumonectomy
1960’s  Lobectomy
1990’s  ?Segmentectomy/Wedge (and adjuvant local/systemic Rx)
2005    VATS LOBECTOMY
Thoracotomy - Posterolateral
Video Assisted Thoracic Surgery
1.6 × 1.5 cm adenocarcinoma

≤ 2 cm

T1a

2.2 × 1.5 cm adenocarcinoma

> 2 cm to 3

T1b
Stage I Disease

- IA (T1a (≤2cm), T1b(>2-3cm), N0,M0
- IB T2a(≤5cm),N0,M0

• Surgery is the treatment of choice, usually in form of lobectomy & systematic lymph node dissection or sampling.
• Lesser resection therapy should be used only for patient with limited lung reserve.
• Curative radiotherapy:
  - surgical resection is not possible
  - patient with positive surgical margins in whom surgical re-resection can not be performed.
Randomized Trial of Lobectomy Versus Limited Resection for T1 N0 Non-Small Cell Lung Cancer (125 Lobectomy, 122 Limited Resection)

RJ Ginsberg, LV Rubinstein and Lung Cancer Study Group
Ann Thorac Surg 1995;60:615-23
Lobectomy vs Limited Resection

Time to death (from any cause) by treatment

logrank p=0.088 (one-tailed)

Ginsberg and Rubinstein
Ann Thorac Surg
T2a

- Tumour: >3 cm, ≤5 cm
- Tumour ≤5 cm, Invasion of the visceral pleura
- Tumour involves main bronchus, 2 cm or more distal to carina

T2b

- Tumour: >5 cm, ≤7 cm (with or without other T2 descriptors)
- Associated atelectasis or obstructive pneumonitis that extends to the hilar region but does not involve the entire lung
Stage IIA Disease

- T1a,b or T2a, N1 M0
  - T2b (>5-7cm) N0 M0

• Accounts <5% of lung cancer and < 10% for all resected lung cancer.
• Lobectomy is the procedure of choice in most patients. Complete lymph node sampling or dissection should be added for better control.
• Pneumonectomy or even Sleeve resection can be used if needed to achieve complete resection (R0).

• Postoperative radiation therapy (no impact on survival).
The survival rate following resection depends upon:

- **Size of Tumor**

- **Number of Lymph Nodes Involved**
  With 5 year survival is 45% for single lymph node compared with 31% in-patient with multiple lymph nodes.

- **Histological Type**
  Local or regional recurrences are more prevalent in patients with **Squamous carcinoma** &
  Distant meta occurred more with **Adenocarcinoma**.
Role of adjuvant Chemotherapy in early stage lung cancer

• No adjuvant treatment is recommended for patients with stage I disease following resection. Except for lesions $\geq 4$ cm with high-risk features (poorly differentiated, wedge resection, minimal margins, and vascular invasions).

• With new introduction of the 7th TNM staging system recently the size of tumor had major role in chemotherapy for even early stage.
Impact of 7th TNM

- TUMOR SIZE
  
  Tumors < 3 no chemotherapy

  3-5 the chemotherapy is optional

  5-7 chemotherapy is preferred,

  >7cm they consider as T3 and chemotherapy is indicated.
• **NODAL STATUS**

  - They found that multiple involvement N1 disease needs chemotherapy while single station of N1 disease doesn't.

  - Patient with N2 disease that present as single disease has better survival than multiple LN although this did not reach statistically significant and wasn't included in 7th TNM staging.
T 3
Stage IIB Disease

- T2b (>5-7 cm) N1 M0
- T3 (>7 cm or invasion or two nodules on same lobe)

N0 m0

**Tumors Invading Chest wall T3**:  
- Factors that appear to influence survival in this group of patients include
  1. Completeness of resection of the tumor
  2. The extent of invasion of the chest wall
  3. The presence or absence of regional lymph node metastases.

The 5 years survival rate for T3N0 up to 40-50%. In patient with macroscopic or microscopic incomplete resection is zero.
Option for Chest wall reconstruction

- *Nothing* for one or two small rib segment especially if located posteriorly beneath large muscle or scapula

- *Taut Marlex mesh or Gore-tex patch* for bigger defect to achieve acceptable cosmetic results and chest wall instability if 2 – 3 rib removal or to prevent trapping of tip of scapula.

- *Marlex mesh methyl methacnylaste sandwich* technique for big defect in sternum or when chest wall instability is anticipated.
Superior Sulcus Tumors T3

- Majority are squamous cell or adeno carcinomas, but 3% to 5% are small cell carcinomas.

- Mediastinoscopy is important
- N2 disease patient have poor survivals not longer than 1 year if they are treated with combined chemotherapy treatment or radiation therapy
- Unresectability
- The involvement of subclavian artery or vertebral body with or without cord compression, and wide spread involvement of major division of brachial plexus.
Superior Sulcus Tumors T3

• The current standard therapy pre-operative induction chemo-radiotherapy, followed-up with surgery then post-op chemotherapy with 3-year survival up to 44% for all patients and 54% after complete resection.
Superior Sulcus Tumors T3

- Surgery involves En bloc removal of the affected lobe and chest wall, including the entire first rib and the posterior segments of ribs two, three, and often four; the transverse processes of the contiguous thoracic vertebrae; the nerve roots C8 and T1 to T3; the lower trunk of the brachial plexus; and the dorsal sympathetic chain with mediastinal node dissection.
Tumor into main stem bronchus < 2cm from carina but does not involve carina that associated with complete collapse of lung.
Stage IIB Disease (cont)

- **Tumors in Proximity to Carina T3:**
  - Central tumors that extend within 2 cm of the carina without carinal involvement.
  - The nodal involvement severely affect prognosis.
  - The 5 year survival rate can reach up to 30% to 40%
  - Pneumonectomy is most common resection but sleeve lobectomy can be used as this will provide lower morbidity, mortality and preserve pulmonary function.
Stage IIB Disease (cont)

- Tumors presented with two lung nodules in same lung lobe T3:
  - Patient usually will be treated with adjuvant chemotherapy followed by surgery.
Pancoast tumours with invasion of one or more of the following structures:
- vertebral body or spinal canal
- brachial plexus (C8 or above)
- subclavian vessels

Tumour invades trachea and/or SVC or other great vessel

Tumour involves carina

Tumour invades adjacent vertebral body

Tumour invades aorta and/or recurrent laryngeal nerve

Tumour invades esophagus, mediastinum and/or heart

Tumour accompanied by ipsilateral nodules, different lobe
Stage IIIA Disease

Tumors that present with lymphatic metastasis to the mediastinum as N2 disease, or tumors that invade adjacent organ (T4) or tumors presented with two nodule in ipsilateral lung.

Distant metastases should be ruled out by CT scan or whole body PET scan/CT scan.

Preoperative mediastinoscopy
• The survival rate following complete resection in the presence of nodal disease is less than 20% at 5 years.

• pre operative adjuvant chemotherapy with re-evaluation for response.
• There is no evidence that preoperative radiation therapy alone for clinical N1 or N2 disease benefits patients with tumors invading the chest wall.
• Postoperative radiation therapy in patients who have evidence of mediastinal lymph node metastases or residual disease is usually advised in an attempt to decrease the incidence of local recurrence but does not impact overall survival.
The role of primary surgery in N2

• Unsuspected N2 disease at thoracotomy, surgery should be continued unless pneumonectomy is needed.

• Mediastinal lymph node dissection is strongly advisable and postoperative adjuvant chemotherapy is indicated.

• Preoperative radiotherapy alone for clinically N2 disease will not improve survival because most of patients die of distant metastasis.
N2 disease at Mediastinoscopy

* Neoadjuvant concurrent chemoradiotherapy or induction chemotherapy followed by assessment of response.
  * For responders, surgery can be offered with mediastinal lymph node dissection.

* Non-responder should be treated with chemotherapy or concurrent chemoradiotherapy if not given before as sole treatment.
• **T4 (two lesion in ipsilateral lung lobes).**
  * Neo adjuvant chemotherapy.
  * Curative Pneumonectomy can be offered.
  * Adjuvant preoperative radiotherapy should be **avoided** as it carries high risk morbidity, and mortality in post Pneumonectomy patients epically in the right side.

* Patient with tumors invading mediastinal structures or main airway involvement surgery should be consider only if curative attention is approach. (R0).
Stage IIIB Disease

- T4  N2  MO - Any T  N3M0

• These patients present with
  - Invasion of the spine, trachea, carina, esophagus, aorta or heart (T4) with N2 Disease
  - Supraclavicular or contralateral mediastinal lymph node metastases (N3);

* These patients are considered inoperable. Most of these patients are treated by combined concurrent chemoradiation.
T4 Disease, Carinal Involvement

• Pneumonectomy with tracheal sleeve resection and direct re-anastomosis of the trachea to the contralateral mainstem bronchus has been offered to patients with good surgical risks with up to 20-40% 5-year survival rare, often in the face of 13% to 30% operative mortality rates.

• This should be reserved for young healthy patient with clinically no disease determined by mediastinoscopy.
T4 Disease, Carinal Involvement

- All other patients should be treated primarily with chemoradiation without resection.
- Local therapy in form of
  - Transbronchoscopic brachytherapy
  - Photodynamic therapy.
• **N3 Disease** Absolute contraindication to surgery

• **M1 Distant metastasis**
  * **M1a** Separate tumor nodule(s) in a contralateral lobe; tumor with pleural nodules or malignant pleural (or pericardial) effusion
  * **M1b** Distant metastasis
Surgical management of pleural effusion M1a

- Palliative
- Aggressive Chemotherapy.
- Pleural drainage & pleurodesis.
- Trap Lung treated with ambulatory pleural tap or insertion of pleural catheter as part of home care support.
- Diagnostic Thoracoscopic surgery with talc insertion.
- Radiotherapy or surgery in rare cases for Painful recurrence in chest wall
Advanced Lung Cancer M1b Brain

- Brain metastasis M1b
- Surgery versus radiation
- Synchronized or metastatic
- Solitary
- Primary lung is resectable
Advanced Lung Cancer M1b Adrenal

- Adrenal metastasis M1b
- Best if ipsilateral with lower lobe
- Enblock resection trans diaphragmatic
- Resectable lung
- Curative resection
Advanced Lung Cancer M1b Bone

- Bone metastasis M1b
- Post operative finding
- Resection and radiotherapy
- Relatively poor results
- Same for liver or multiple sites
surgery in Advanced NSCLC

- Never as routine
- A tumor board decision
- Specialized centers
- Part of the guidelines
- Supported with adjuvant therapy
- Patient counseling
## Role of surgery in current stages

<table>
<thead>
<tr>
<th>Stage</th>
<th>Tis/T1a,b,T2a,T3</th>
<th>N0/N1/N0,N1,N2</th>
<th>M0/M0/M0</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
<td>Surgery</td>
</tr>
<tr>
<td>Stage IA</td>
<td>T1a,b</td>
<td>N0</td>
<td>M0</td>
<td>Surgery</td>
</tr>
<tr>
<td>Stage IB</td>
<td>T2a</td>
<td>N0</td>
<td>M0</td>
<td>Surgery</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T1a,b,T2a,T2b</td>
<td>N1,N0</td>
<td>M0</td>
<td>Surgery</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T2b,T3</td>
<td>N1,N0</td>
<td>M0</td>
<td>Surgery</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T1,T2,T3</td>
<td>N2,N1,N2,N0,N1</td>
<td>M0</td>
<td>Chemo/Radio +/-Surgery</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T4</td>
<td>N2</td>
<td>M0</td>
<td>???Surgery</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1a,b</td>
<td>???Surgery</td>
</tr>
</tbody>
</table>
Table 5: Surveillance for nonsmall cell lung cancer after resection

<table>
<thead>
<tr>
<th>Stage I, II and III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postoperative visits every 3 months for 2 years, then every 6 months for 3 years and then annually CXR</td>
</tr>
<tr>
<td>History and physical examination, CXR, and laboratory tests</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stage IV (not on treatment or in-home hospice)</th>
</tr>
</thead>
<tbody>
<tr>
<td>History and physical examinations, CXR, CBC and other tests as clinically indicated every 2–3 months</td>
</tr>
</tbody>
</table>

*The postresection follow-up guidelines modified from the protocol suggested by The University of Texas M.D. Anderson Cancer Center (Houston) for nonsmall cell lung cancer, CBC, complete blood count; CXR, chest radiograph*
Post-resection Follow-up for Non-Small Cell Lung Cancer

<table>
<thead>
<tr>
<th>Table 2: Signs and symptoms of local recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest pain – localized or pleuritic</td>
</tr>
<tr>
<td>Cough</td>
</tr>
<tr>
<td>Decreased performance status</td>
</tr>
<tr>
<td>Weight loss, fatigue</td>
</tr>
<tr>
<td>Pleural effusion</td>
</tr>
<tr>
<td>Superior vena caval obstruction</td>
</tr>
<tr>
<td>Phrenic nerve paralysis</td>
</tr>
<tr>
<td>Thoracic rib or vertebral/back pain</td>
</tr>
<tr>
<td>Dysphagia</td>
</tr>
<tr>
<td>Anorexia</td>
</tr>
<tr>
<td>Horner's syndrome</td>
</tr>
<tr>
<td>Hoarseness</td>
</tr>
</tbody>
</table>
• Thank you