Lung Cancer

Chapter: Epidemiology

Age at diagnosis

The median age for lung cancer diagnosis, is 70.

a) Age of diagnosis in USA
In the US, between 1998 to 2003, the age of diagnosis of lung cancer was:

i) Under 20: 0%
ii) 20 to 34: 0.3%
iii) 35 to 44: 2.1%
iv) 45 to 54: 8.8%
v) 55 to 64: 21.1%
vi) 65 to 74: 32.6%
vii) 75 to 84: 28.2%
viii) 85 + : 6.9%

b) Age of diagnosis in Europe
The European data for 2006 is shown below.

Ethnicity

Ethnicity is an important aspect of any patient history. Within the UK, south Asians have a lower incidence of lung cancer than non-south Asians, but increasing incidence has been reported amongst south Asian men, in contrast to the rest of the
UK male population. South Asian women also have increasing lung cancer trends but this is in line with the rest of the UK female population. In the USA lung cancer rates in the black population are higher for both males and females compared to the white population. Other ethnic groups such as Hispanics and Asians have lower rates than whites. Other cancers are more common in other ethnic groups - Chinese men have a very high incidence of nasopharyngeal carcinoma, for example. To learn more about the incidence, and relative risk factors for lung cancer in the UK visit the Cancer Research UK site.

**Epidemiology**

Here are some key statements about the epidemiology of lung cancer

- Lung cancer is the commonest cause of cancer deaths in men and women in the UK.
- There are 38,000 new cases per annum.
- The ratio of cases male:female is 2:1, but cases are decreasing in men and increasing in women due to increased smoking.
- 90% of cases are smoking related.
- Stopping smoking decreases risk but the risk remains higher than never smokers.
- Risk is further increased by asbestos exposure, arsenic and heavy metal exposure and coexistent lung fibrosis (usual interstitial pneumonitis)

**References:**

1. *Oxford Handbook of Respiratory Medicine* (http://)

**Chapter: Sub-Types**

**Types of lung cancer**

There are several types of lung cancer, but in practical terms, as outlined in the Oxford Handbook of Respiratory Medicine there are two main groups:

1. Non-small cell lung cancer (NSCLC)
2. Small cell lung cancer (SCLC)

**Non-small cell lung cancer**

- 75-80% of all lung cancers are non-small cell lung cancers
- Squamous cell is the commonest - it can present as a mass on CXR but can cavitate.
- Adenocarcinoma - can occur in scar tissue or sites of fibrosis and is not always smoking related. It can be primary or secondary from other sites and can have pleural infiltration with resultant malignant pleural effusion.
- Alveolar cell - this is rare. It can rarely cause copious sputum production (bronchorrhoea). Fluffy air space shadowing on CXR.

**Small cell lung cancer**

- 20-25% of all lung cancers are small cell lung cancer (SCLC).
• Usually disseminated by time of diagnosis (haematogenous spread).
• Metastases to live, bones, bone marrow, brain, adrenals are not uncommon.
• SIADH is common.
• Surgery is usually not appropriate.
• Chemo and radiosensitive.
• Untreated extensive SCLC is rapidly progressive and had a median survival of 6 weeks.

All lung cancer types

Taken from the WHO definition 1999
- Squamous
- Small cell
- Large cell
- Adenocarcinoma
- Adenosquamous
- Pleomorphic/sarcomatoid
- Carcinoid

Chapter: Clinical Features of Cancer

Symptoms and signs

Symptoms and signs of cancer may be due to local tumour effects, metastatic disease or paraneoplastic phenomena. Often asymptomatic until advanced disease.

Local effects

• Persistent cough
• Haemoptysis
• Chest pain (could suggest chest wall invasion or pleural involvement)
• Unresolving pneumonia or lobar collapse
• Unexplained dyspnoea, wheeze or stridor (bronchial narrowing or obstruction)
• Shoulder pain (diaphragmatic involvement)
• Pleural effusion (direct tumour extension or pleural metastases)
• Hoarse voice (tumour invasion left recurrent laryngeal nerve)
• Dysphagia
• Raised hemi-diaphragm (phrenic nerve paralysis)
• Superior vena-cava obstruction (facial & upper limb swelling, facial plethora & cyanotic appearance)
• Horner’s Syndrome (meiosis, ptosis, enophthalmos, anhidrosis) due to apical or Pancoast’s tumour

Metastatic tumour effects

• Cervical, supraclavicular or axillary lymphadenopathy (may be a useful biopsy site to make diagnosis)
• Palpable liver edge (liver metastases)
• Bone metastases (pain or pathological fracture)
• Cerebral metastases: Confusion, focal neurological deficit, seizures, personality changes
• Effects of hypercalcaemia (confusion, constipation, dehydration either from bone metastases or tumour production of PTH related peptide (commonly squamous)
• Dysphagia (compression from large mediastinal nodes)

Paraneoplastic syndromes

• Cachexia & wasting
• Clubbing (commoner in squamous & adenocarcinoma)
• SIADH (mainly small cell lung cancer/SCLC)
• Ectopic ACTH (mainly SCLC)
• Hypertrophic pulmonary osteoarthropathy (HPOA, commonly SCC or adenocarcinoma)
• Eaton-Lambert myasthenic syndrome (SCLC) - may pre-date lung cancer by up to 4 years
• Cerebellar Syndrome (usually SCLC)
• Limbic Encephalitis (usually SCLC)

Chapter: Staging of Lung Cancer

Staging

• All suspected lung cancers should be staged with a CT chest and abdomen.
• Staging helps to determine the appropriate course of treatment be that surgical intervention, chemotherapy or radiotherapy. In advanced disease a palliative approach is adopted.
  • If clinical suspicion staging may include CT head to exclude cerebral metastases
  • Most lung cancer patients now receive a CT-PET scan. This may upgrade/downgrade the staging of a cancer (e.g. unexpected distant metastases not visible on standard CT).

TNM (Staging for NSCLC)

TNM Staging System for Non-small Cell Lung Cancer (NSCLC)

The TNM staging system is constructed to reflect the poorer prognosis and limited treatment options associated with increasingly advanced disease. Therefore, proper staging of a patient’s disease is required in order to make an informed decision regarding treatment. This can only be accomplished after utilizing all of the appropriate clinical, radiological and surgical methods of diagnosis during the patient’s workup.

(T) Primay Tumour

The classification of the primary tumour is broken up into four types:

A T1 lesion is less than 3cm in diameter and is considered to be easily resectable, being located in the periphery of the lung.

A T2 lesion is either greater than 3cm in diameter or invades the visceral pleura, or is more centrally located so as to cause obstruction. Because of its size or involvement of the pleura or bronchi, this tumour is associated with a more involved resection and increased risk of recurrence.

A T3 lesion invades the chest wall, pericardium or diaphragm, or is centrally located so as to cause complete lung collapse. Although an involved surgery can produce agreeable results, these tumours may be treated with preoperative radiation or chemotherapy.

A T4 lesion involves major structures in the chest, including vertebral bodies, the heart, major vessels, trachea and oesophagus. A tumour with the presence of any satellite nodules is also classified as a T4 lesion. Because of the obvious complications related to resection, surgery is not typically an option for these lesions.

Click through this Flash object for a further overview of staging for NSCLC.
TNM

(N) Nodal Involvement

The classification of any nodes found to contain metastatic disease is broken up into four types:

The N0 designation is reserved for patients with no signs of nodal involvement.

Involvement of N1 nodes indicates metastatic foci in ipsilateral hilar or intrapulmonary nodes.

Involvement of N2 nodes indicates more centrally located metastatic foci in ipsilateral mediastinal or subcarinal nodes.

Involvement of N3 nodes indicates progression to contralateral mediastinal or hilar nodes. Involvement of any scalene or supraclavicular nodes is also classified as N3.

(M) Metastases

The classification of any distant metastases is broken up into two types:

The M0 designation is reserved for patients with no signs of distant metastatic foci.

The M1 designation is used to classify patients with any distant spread of their disease, both to other lobes of the lungs, as well as distant organs or other sites in the body.

References:

1. Harvard Medical School: Daniel D. Karp, MD, Justin P. Lafreniere, Robert L. Thurer, MD (http://)
Limited: confined to ipsilateral hemithorax and supraclavicular nodes.

Extensive: everything else

Introduction to bronchoscopy: Its role in lung cancer

A safe endoscopic examination of the airways

Bronchoscopy is a form of endoscopy that serves to visualise the tracheo-bronchial tree. It is performed with small flexible instruments that are passed through the nose or mouth, through the vocal cords, into the airways. The airways are then closely inspected. This examination is frequently performed on an outpatient basis with conscious sedation, but can also be performed under general anaesthesia through an endo-tracheal tube.

A special form of bronchoscopy, known as rigid bronchoscopy, is performed under general anaesthesia mainly for therapeutic purposes, but will not be addressed in this tutorial.

Image caption: Here the long, black, flexible bronchoscope is connected to a processor and viewing monitor in preparation for use in a procedure.

Direct Visualisation
On the left, a bronchoscopic examination under normal white light shows abnormal appearing mucosal tissue in the lower right hand corner of the viewing field. On the right, a close up examination of the abnormal area using autofluorescence technology confirms the presence of a malignant lesion. The image shows how malignant tissue has a much lower fluorescence intensity compared to the surrounding normal mucosa.

Assessment of Radiological Abnormalities

Generally speaking, in patients with a peripheral nodule or mass, the likelihood of reaching the lesion by bronchoscopy is directly dependant on its size and location.

When deciding whether a bronchoscopy should be performed on a patient, it is important to remember that only the central airways down to the level of the sub-segments can be directly visualized.

A bronchoscopy can provide direct visualization of centrally located abnormalities seen on CXR or CT scan, as well as obtain tissue samples for a biopsy. Besides forceps biopsies, one can also obtain cytology samples by brushing, washing or needle techniques. Many times, all of these biopsy techniques are employed together to maximize the yield.

References:

1. Virtual Bronchoscopy (http://www.thoracic-anesthesia.com/?page_id=2)

EBUS - Role in staging of disease

A useful alternative to mediastinoscopy

Many times during the staging and clinical workup of a lung cancer patient, a chest CT may indicate enlargement of a mediastinal lymph node, necessitating some type of pathologic confirmation of regional node involvement. Frequently, this is accomplished via a mediastinoscopy.

However, in many patients there is an alternative, and less invasive, bronchoscopic technique called Trans-Bronchial Needle Aspiration (TBNA). With the help of the bronchoscope, and sometimes fluoroscopy or ultrasound, a needle is passed through the bronchial wall and into the lymph node in question. The diagnostic yield of the sampled material depends both on the lymph node size and location, and varies from 50-90%. This biopsy technique has been found to be increasingly useful, and allows many patients to forgo a painful mediastinoscopy.
Image caption:

This picture shows the tip of a bronchoscope used in EBUS (or endobronchial ultrasound). EBUS is gaining recognition as an additional way to obtain tissue from paratracheal, subcarinal & some lymph nodal ‘stations’ within the mediastinum.

Mediastinoscopy

- Biopsy of enlarged mediastinal lymph nodes to determine whether they are inflammatory or have malignant invasion.
- Suprasternal notch incision under G.A., blunt dissection, palpation, and endoscopic visualisation and biopsy of nodes (93% sensitivity & 96% specificity)

CT-PET

Positron Emission Tomography (PET) or FDG-PET (Fluorodeoxyglucose-Positron Emission Tomography)

- A highly sensitive imaging technique used to diagnose both primary neoplasms and extrathoracic metastases, as well as obtain information used for the staging of lymph nodes.
- Instead of relying on the anatomic differences between malignant and benign nodules used in standard CT, PET imaging capitalizes on the increased glucose metabolism seen in neoplastic lesions. A radioactive form of glucose (FDG) is given intravenously
- Combining this ‘metabolic’ scan with standard CT enables accurate anatomical location of any PET abnormalities.
Specificity

It is important to remember that all "hot spots" identified on a PET scan need to be interpreted with a clinical correlate in mind. Positive scans can indicate both malignant and benign processes.

Cancers vary with regard to their FDG avidity. For example, prostate cancer has only modestly increased FDG uptake, while both small cell and non-small cell lung cancer have very high FDG uptake in primary and metastatic lesions. However, other lung cancers such as bronchioalveolar and carcinoid have variable or low avidity for FDG, leading to false negative results.

On the other hand, granulomatous lesions may also be FDG avid, and present with false positive results. Cocidiomycosis and histoplasmosis are well known causes for false positive findings in the evaluation of single pulmonary nodules. These infectious lesions can be a frequent problem in endemic regions or in patients with an appropriate travel history. Other inflammatory lesions may also show increased uptake of FDG, although the uptake is often only mildly increased.

CT-PET continued

Sensitivity

This FDG-PET scan was obtained after the patient’s chest CT identified a 2.5 cm spiculated mass in the left lower lobe of the lung, as well as some mediastinal lymphadenopathy. These results show focal uptake in the left lower lobe mass (large arrow), as well as in numerous mediastinal lymph nodes (small arrows). A mediastinoscopy later showed poorly differentiated NSCLC in the contralateral mediastinum (right lower paratracheal region, arrow head).
The sensitivity of FDG-PET for detection of lung cancer in a single pulmonary nodule depends upon a number of factors: the avidity of the cancer for FDG, the size of the lesion, the location of the lesion, and the type of PET camera. As a general rule, a modern dedicated PET scanner will have a sensitivity of 95% for a single pulmonary nodule greater than 8 mm.

As stated, the anatomic location of some lesions can also affect the sensitivity of the scan. Lesions near the diaphragm may be somewhat more difficult to detect due to respiratory motion, and high myocardial uptake may make lesions adjacent to the heart more difficult to detect.

Chapter: Performance status

ECOG Performance Status

These scales and criteria are used by doctors and researchers to assess how a patient’s disease is progressing, assess how the disease affects the daily living abilities of the patient, and determine appropriate treatment and prognosis.

<table>
<thead>
<tr>
<th>Grade</th>
<th>ECOG</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>Fully active, able to carry on all pre-disease performance without restriction</td>
</tr>
<tr>
<td>1</td>
<td>Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work</td>
</tr>
<tr>
<td>2</td>
<td>Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours</td>
</tr>
<tr>
<td>3</td>
<td>Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours</td>
</tr>
<tr>
<td>4</td>
<td>Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair</td>
</tr>
<tr>
<td>5</td>
<td>Dead</td>
</tr>
</tbody>
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References:

Chapter: Treatment

Treatment of lung cancer

- Chemotherapy
- Radiotherapy
- Surgery
- Combined approaches
- Can be with curative intent or palliative (i.e to reduce symptoms and prolong life)
- The specifics of chemotherapy & radiotherapy are not covered in this tutorial

Surgical treatment (NSCLC)

Surgical approaches
Only after the patient’s disease has been appropriately staged can a surgical option be considered as a first line treatment modality. Obviously, more advanced disease requires increasingly invasive surgical approaches, until finally surgery is no longer an option.

A segmental or wedge resection can be used for local control of a small, peripherally located lesion, or in patients who cannot tolerate a more substantial resection. These two resections vary in that a segmental resection follows anatomic divisions in the lung, while a wedge resection is more of a “scoop” procedure. These can be done both using an open approach or a less invasive, video assisted (VATs) method.

A lobectomy, or removal of a single lobe of a lung, is considered to be the standard procedure for best local control of peripheral lesions, although it may not be feasible in patients with decreased pulmonary reserves. It should be done concurrently with sampling of hilar and mediastinal nodes for the most accurate staging of the disease.

A pneumonectomy, or removal of an entire lung, is performed for control of large centrally located tumors, or advanced peripheral lesions with hilar node involvement. All potential candidates should have a complete pulmonary workup, including PFT’s prior to this procedure. It carries with it many potential complications, including later dependence on supplemental oxygen.

Stage 1A/1B
Patients with these stages of disease generally have a good prognosis with surgical intervention.

Stage IA (T1N0M0) disease can almost always be controlled with either a segmental/wedge resection or a standard lobectomy, and inoperable patients can achieve acceptable results with radiotherapy.

Stage IB (T2N0M0) disease should be treated with a lobectomy, as the tumors are larger and more invasive than T1 lesions. There may also be a role for postoperative chemotherapy in this group of patients.

All Stage I patients should especially be targeted for smoking cessation programs as well as chemoprevention trials.

Surgical treatment options

Stage II A/II B
This group of patients can also benefit from an aggressive surgical approach, although the invasiveness of their disease
Stage IIA (T1N1M0) disease can be controlled with a lobectomy or pneumonectomy depending on the extent of hilar lymph node involvement. It is also reasonable to consider postoperative radiotherapy and/or chemotherapy in patients with this stage of disease.

Stage IIB (T2N1M0, T3N0M0) patients will almost always require a complete pneumonectomy for best control of their disease, should their pulmonary reserve allow it, although lobectomy may still be possible in some cases. Patients with T3 lesions will usually also require combination treatment with chemo or radiotherapy to shrink these invasive tumours.

Stage III/IV
Unfortunately, due to the advanced nature of the disease, the majority of these patients do not have viable surgical options.

Stage IIIA (T3N1M0, T1-3N2M0) patients have a low chance for resection alone to control their disease. Most surgical approaches to stage utilize preoperative chemo and radiotherapy to shrink the tumour and control potential distant micrometastasis prior to resection.

Stage IIIB (T1-4N3M0, T4N0-3M0) disease is incredibly invasive and therefore does not have any surgical options beyond palliation using minimally invasive techniques.

Stage IV (T1-4N0-3M1) patients have distant metastases, a contraindication for surgical intervention.

References:
1. Harvard Medical School: Daniel D. Karp, MD, Justin P. Lafreniere, Robert L. Thurer, MD (http://)

Summary of stage-based treatment options for NSCLC

Click through the Flash object below for a summary overview of stage-based treatment options in NSCLC.

Stage Based Treatment Modalities for Non-Small Cell Lung Cancer

- Stage IA (T1N0M0)
- Stage IB (T2N0M0)
- Stage IIA (T1N1M0)
- Stage IIIB (T2N1M0, T3N0M0)
- Stage IIIA (T3N1M0, T1-3N2M0)
- Stage IIIB (T1-4N3M0, T4N0-3M0)
- Stage IV (T1-4N0-3M1)

Treatments for NSCLC patients include surgery, chemotherapy, radiation therapy, and combinations thereof. The particular treatment approach is dictated by both the individual patient's stage of disease and performance status. Click on a stage of disease for more information regarding typical treatment approaches.

Designed by Justin P. Lafreniere 2002