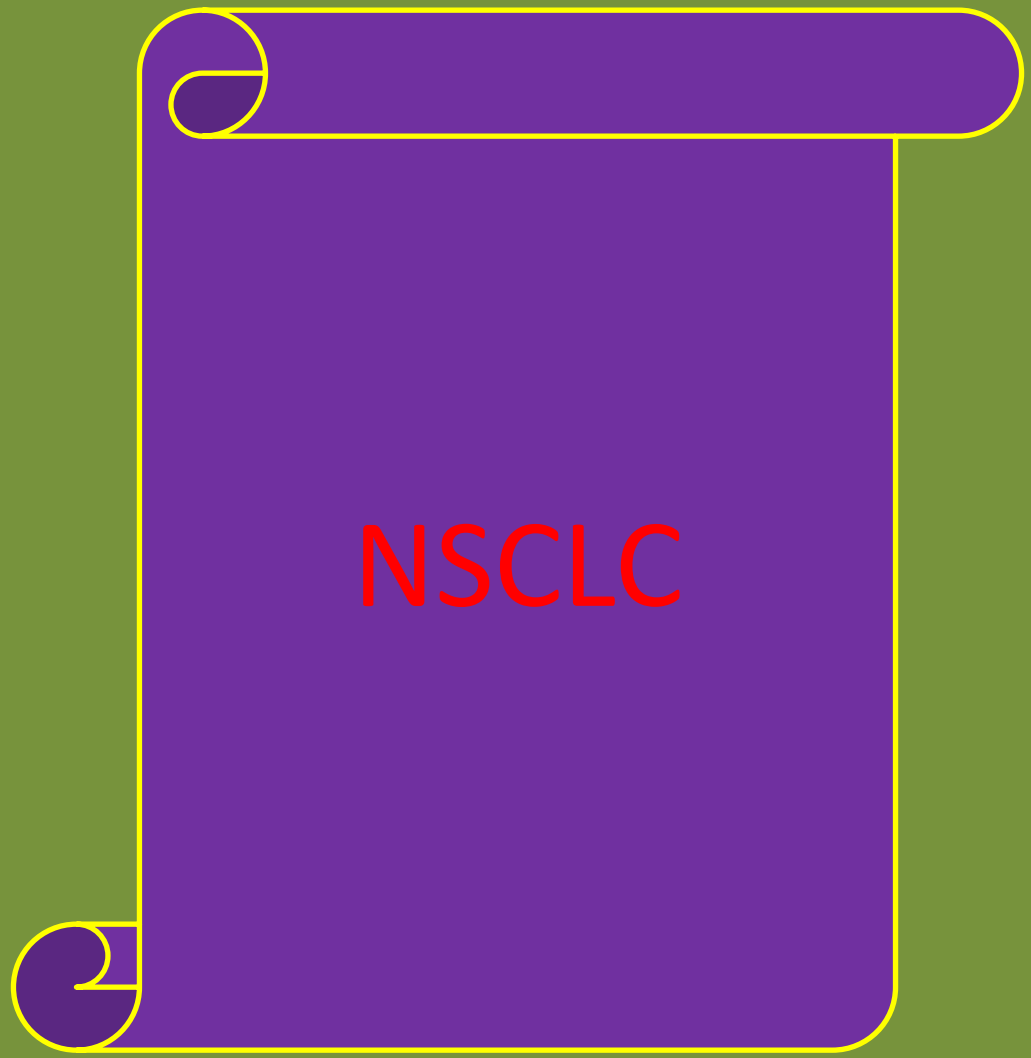

NSCLC

ETIOLOGY

Smoking

❖Approximately 80% of cases of NSCLC in men and 50% of these neoplasms in women are directly attributable to cigarette smoking.

❖Most cigarettes consumed worldwide contain filters

❖This reduce tar within inhaled smoke, resulting in deposition of carcinogens deeper in the lungs

❖The effects of cigarette smoke on respiratory epithelial cells are mediated by carcinogens such as 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)

❖The Carcinogens cause epigenetic alterations coinciding with malignant transformation human respiratory epithelia.

❖ NNK induces expression of type 1 insulin growth factor receptor in respiratory epithelial cells; in addition, NNK activates *k-ras*.

❖Nickel and arsenic induce cancer-associated epigenetic alterations, whereas nicotine activates **raf-1** kinase, promoting cell-cycle progression in respiratory epithelial cells.

Genetic Predisposition

❖Several recent genome studies have identified major susceptibility loci at 15q25, 5p15 and 6p21.

❖An gene locus mapping to chromosome 6q confers susceptibility to lung cancer, particularly in never-smokers, and individuals with cumulative tobacco exposures to 20 or less pack-years.

❖Several polymorphisms affecting lung cancer risk. For example, X chromosome inactivation in peripheral blood cells correlates with early development of lung cancer in women

Occupational/Environmental Exposure

❖A variety of occupational and environmental exposures have been implicated in the pathogenesis of lung cancer:

1) Asbestos and silica fibers

2) Organic compounds such as chloral methyl ether

3) Diesel fumes and air pollution

4) Ionizing radiation

Diet

❖ Zinc, copper, and selenium intake appears to be associated with reduced lung cancer risk.

❖The inverse correlation between dietary folate intake and lung cancer risk appeared in patients who drank alcohol, smoked more, did not take supplemental folate,and had a family history of lung CA.

PATHOLOGY

❖Through the 1960s, the predominant type of NSCLC was SCC

❖ Adenocarcinoma has increased in both relative and absolute incidence, a phenomenon that has been associated with changes in tobacco blends and the use of filters on cigarettes.

Adenocarcinoma

❖ Nearly all adenocarcinomas arise in the smaller airways histologically, and can he detected radiographically, especially with **CT scan**, in the **periphery** of the lung.

❖ They are less likely to present with cough and hemoptysis.

❖AdenoCA are less amenable to detection by cytology or bronchoscopy, but more accessible to CT-guided FNA.

❖The histologic precursor to pulmonary adenocarcinoma is atypical adenomatous/alveolar hyperplasia (AAH).

❖ AAH is composed of atypical type II pneumocytes proliferating on an alveolar wall that is either normal in thickness or altered by inactive fibrous scarring.

Bronchioloalveolar Carcinoma

❖The 1999 WHO Classification of Lung Tumors specified BAC as a noninvasive carcinoma spreading on the surface of alveolar walls without invasion.

❖ BAC is an uncommon type of lung CA. it is found in mucinous and nonmucinous variants.

❖ Mucinous BAC is an unusual variant characterized by the presence of malignant mucus-containing goblet cells on the surface of normal alveolar walls and has high mortality rate.

❖It has a tendency to be multifocal or to spread through airways

❖ Nonmucinous BAC is much more commonly found.

❖ That is composed of type II pneumocytes exhibit nuclear anaplasia and pleomorphism greater than AAH, but less than invasive adenocarcinoma.

❖These cancers exhibit unique epidermal growth factor (EGFR) mutations that confer sensitivity to EGFR-tyrosine kinase Inhibitors such as erlotinib and gefitinib.

Large Cell Carcinoma

❖Large cell carcinomas are composed of large cells that their cytoplasm lacks the differentiating of mucin production or dense keratinization and the cells form no glandular structures.

❖They account for approximately 15% of all lung cancers

Squamous Cell Carcinoma

❖Squamous cell carcinoma classically arises in proximal bronchi (segmental or larger) and tends to be slow growing

Adenosquamous Carcinomas

❖Adenosquamous carcinomas have histologic areas differentiated as both SCC and AC, are predominantly found in the periphery of the lung, and have clinical behavior much like that of AC

Pleomorphic Carcinomas

These tumors includes carcinomas with:

1) giant and multinucleated cells or
2) with spindle cell

❖These tumor are aggressive malignancies, and are advanced when diagnosed.

MODES OF METASTASIS

❖left and right lower lobe as well as right middle lobe lymphatics drain to the posterior mediastinum and subcarinal lymph nodes.

❖Right upper lobe lymphatics drain toward the superior mediastin, the left upper lobe lymphatics typically course lateral to the aorta in the anterior mediastinum

❖all of these lymphatic channels drain into the right lymphatic or left thoracic ducts, which empty into the subclavian veins

❖Retrograde lymphatic spread to the pleural surface can occur, particularly with peripheral tumors

❖ Bone, liver, adrenals, and brain are the most frequent sites of distant disease.

CLINICAL MANIFESTATIONS

1) Tumors arising in the larger airways may cause persistent cough, wheezing, or hemoptysis

2) Continued growth of endobronchial tumors frequently results in atelectasis with or without pneumonia and abscess.

3) Pleural involvement by tumor or associated infection may cause pleuritic pain with or without effusion.

4) Diminished lung function may result in dyspnea

5) Fatigue and decreased activity are reported by more than 80% of patients with advanced NCSLC

❖ Tumors arising within the superior sulcus may cause a classic Pancoast syndrome from invasion of T1 and C8 nerve roots, satellate ganglion, and chest wall or vertebra.

❖Invasion or encasement of structures within the mediastinum may cause superior vena cava (SVC) syndrome.

Diagnosis

❖Evaluation of any patient suspected of having lung cancer include:

1) A detailed history

2) physical examination

3) Posteroanterior and lateral chest radiograph

4) CT scans of the chest and upper abdomen

5) Any patient with a newly diagnosed lesion suspicious for lung cancer should undergo whole-body (FDG-PET) imaging.

Integrated PET-CT scans are superior to either of these modalities for staging lung cancer

6) EUS is helpful for evaluating mediastinal lymph nodes in lung CA

❖ EUS can detect lesions 3 mm or more in the paratracheal, aortopulmonary window , subcarinal and paraesophageal regions

TISSUE DIAGNOSIS ESTABLISHMENT

1) Sputum Cytology

❖Cytologic analysis of exfoliated cells in sputum is a rapid, relatively inexpensive means to establish a tissue diagnosis

❖molecular techniques such as analysis of *k-ras and p53 mutations* increase the diagnostic yield of sputum cytology.

2) Bronchoscopy

- brushing
- Bronchial needle aspiration
- biopsy

❖The diagnostic yield of Fiberoptic bronchoscopy (FOB) is 90%.

❖The bronchus draining the area of suspicion can be lavaged, and effluent obtained for cytologic analysis.

❖Transbronchoscopic needle aspiration through the airway wall, can confirm the presence of malignancy in enlarged hilar or mediastinal LN without the need for mediastinoscopy, thoracoscopy

3) Percutaneous fine-needle aspiration

❖This can be performed using fluoroscopic or CT-guided techniques, even if lesions are less than 1 cm in diameter.

❖ FNA cannot rule out malignancy unless a positive benign diagnosis (i.e hematoma or infectious process) definitively establish.

4) Endoscopic Ultrasound-FNA

❖EUS-FNA is a minimal invasive and safe means to assess subcarinal and lower mediastinal LN that are not accessible via standard CME.

❖EUS-FNA can reduce the number of patients requiring CME and unwarranted thoracotomy

5) Mediastinoscopy/Mediastinotomy

❖ CME (cervical mediastinoscopy) remains the most accurate technique to assess paratracheal , proximal peribronchial , and subcarinal lymph nodes in lung cancer patients.

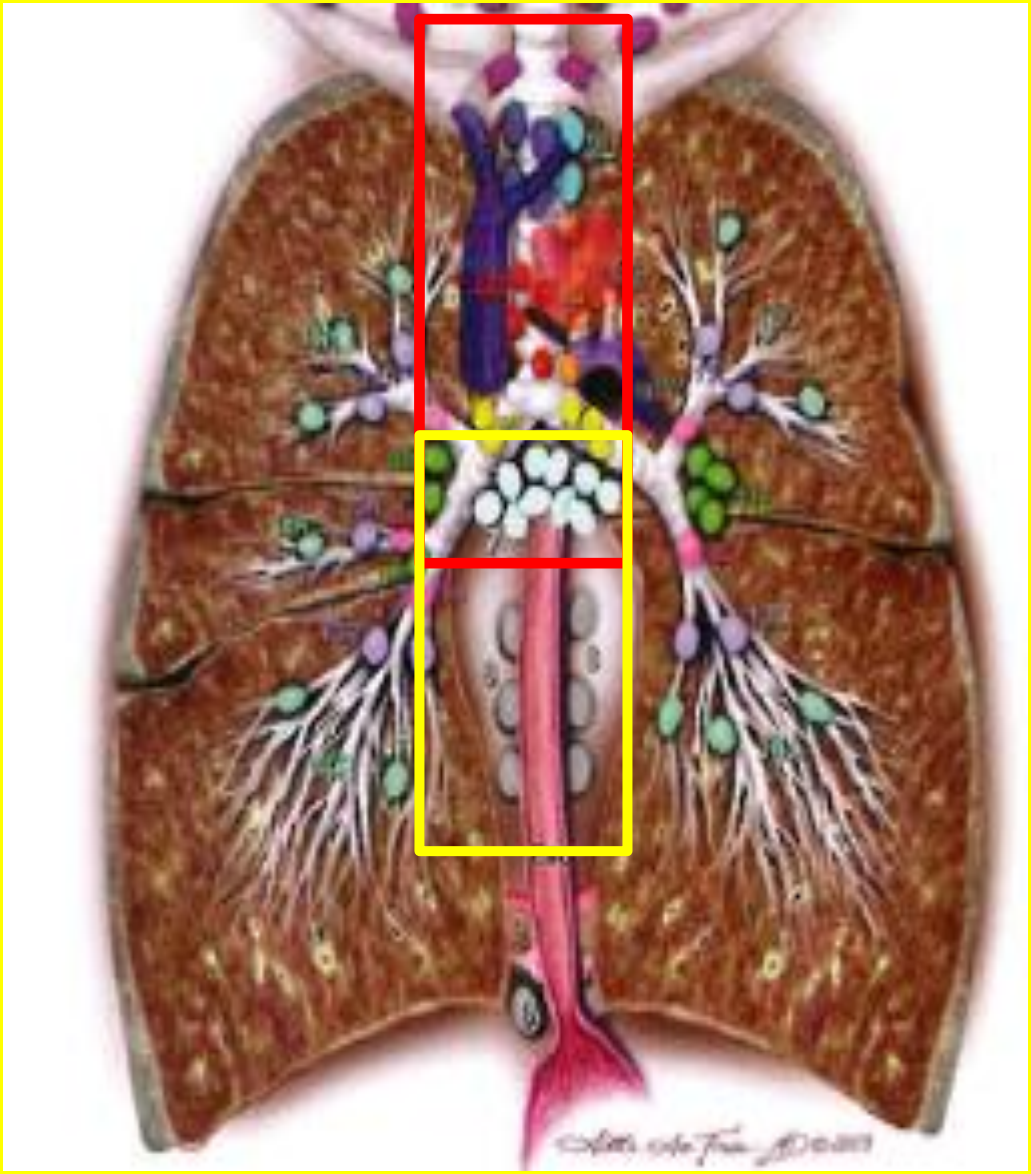
Mediastinoscopy is indicated in any patient :

1- suspected of having locally advanced disease

2- enlarged lymph nodes on CTscan

3- mediastinal uptake on PET scan.

4- In patients with clinical stage I disease for pertaining to chemoT



SUPERIOR MEDIASTINAL NODES

Upper zone

- 2R Upper Paratracheal (right)
- 2L Upper Paratracheal (left)
- 3a Prevascular
- 3p Retrotracheal
- 4R Lower Paratracheal (right)
- 4L Lower Paratracheal (left)

AORTIC NODES

AP zone

- 5 Subaortic
- 6 Para-aortic (ascending aorta or phrenic)

INFERIOR MEDIASTINAL NODES

Subcarinal zone

- 7 Subcarinal

Lower zone

- 8 Paraesophageal (below carina)
- 9 Pulmonary ligament

N1 NODES

Hilar/Interlobar zone

- 10 Hilar
- 11 Interlobar

Peripheral zone

- 12 Lobar
- 13 Segmental
- 14 Subsegmental

❖Lymph nodes within the aortopulmonary window and along the ascending aorta can be evaluated by extended mediastinoscopy or anterior mediastinotomy.

6) Thoracentesis

❖Typically, a bloody pleural effusion is malignant

❖Needle drainage of a pleural effusion associated with a presumed lung cancer can identify inoperable, pleural disease (MIa).

❖In general, a diagnosis of cancer can be established in 70% of malignant effusions by thoracentesis.

7) Thoracoscopy

❖Thoracoscopy is ideal for assessment of mediastinal nodes that:

1- Not accessible by mediastinoscopy or EUS-FNA Techniques
2- Evaluation of suspected T4 lesions.

❖Video-assisted thoracoscopic surgery (VATS) is frequently used for the diagnosis, staging, and resection of lung cancer.

❖Peripheral nodules can be identified and excised using VATS.

8) Thoracotomy

❖more than 95% of tumors can be accurately diagnosed and staged prior to thoracotomy.

❖in a small minority of cases, the diagnosis of lung cancer is made only at thoracotomy.

❖In general, these are cases in which there is a large, inflammatory component associated with a small focus of cancer

The TNM system includes clinical as well as pathologic criteria, with clinical parameters alone, many patients are understaged .

T	
T1	Tumor ≤3 cm, surrounded by lung or visceral pleura, not more proximal than the lobar bronchus
T1a	Tumor ≤2 cm
T1b	Tumor >2 but ≤3 cm
T2	Tumor> 3 but ≤7 cm" or tumor with any of the following: 1) invades visceral pleura 2) involves main bronchus ≥2 cm distal to carina 3) atelectasis/obstructive pneumonia extending to hilum but not involving the entire lung
T2a	Tumor > 3 but ≤5 cm
T2b	Tumor > 5 but ≤7 cm

T	
T3 >7	Tumor >7cm
T3 Inv	Directly invading :1) chest wall 2) diaphragm 3) phrenic nerve 4) mediastinal pleura 5) parietal pericardium
T3 cent	1) Tumor in the main bronchus <2 cm distal to the carina 2)atelectasis/obstructive pneumonitis of entire lung
T3 satel	Separate tumor nodule(s) in the same lobe
T4 Inv	Tumor of any size with invasion of: 1) heart 2) great vessels 3) trachea 4)Rec laryngeal nerve 5) esophagus 6) vertebral body 7) carina
T4 Ipsi	Separate tumor nodule(s) in a different ipsilateral lobe

N	
N1	Metastasis in ipsilateral peribronchial or perihilar LN and intrapulmonary nodes, including involvement by direct extension
N2	Metastasis in ipsilateral mediastinal or subcarinal LN
N3	Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular LN

M	
M1a cont Nod	Separate tumor nodule(s) in a contralateral lobe
M1a pl Disse	1)Tumor with pleural nodule 2) malignant pleural dissemination
M1b	Distant metastasis

T/M	Subgroups	N0	N1	N2	N3
T1	T1a	IA	IIA	IIIA	IIIB
	T1b	IA	IIA	IIIA	IIIB
T2	T2a	IB	IIB	IIIA	IIIB
	T2b	IIA	IIB	IIIA	IIIB
T3	T3 >7	IIB	IIIA	IIIA	IIIB
	T3 *Inv*	IIB	IIIA	IIIA	IIIB
	T3 *Satell*	IIB	IIIA	IIIA	IIIB
T4	T4 *Inv*	IIIA	IIIA	IIIB	IIIB
	T4 *Ispi Nod*	IIIA	IIIA	IIIB	IIIB
M1	M1a *Contr Nod*	IV	IV	IV	IV
	M1a *Pl Dissem*	IV	IV	IV	IV
	M1b	IV	IV	IV	IV

Lung Cancer Screening

❖Considerable efforts have focused on the evaluation of sputum cytology, chest radiographs, and screening CT scans for early detection of lung cancer.

❖ Serial CT scans have the potential of reducing lung cancer-specific mortality in highrisk Individuals.

Chemoprevention

❖ Trials have failed to demonstrate efficacy of retinoids including : retinal palmitate, isotretinoin, or ß-carotene,for prevention of lung cancer.

TREATMENT MODALITIES

❖Historically, surgery has provided the best chance of cure for patients with resectable NSCLC.

❖Whenever surgery has not been an option for resectable cancers, RT used for control of the primary tumor and regional lymphatics.

❖chemotherapy is rarely curative in lung cancer patients; however, complete responses and prolonged survivals have been seen in patients with advanced locoregional and metastatic disease.

Surgery

❖In stage I & II disease,when the tumor has not extended beyond the bronchopulmonary lymph nodes (N1), complete (R0) resections are almost always feasible.

❖Ipsilateral mediastinal LN involvement (N2), despite being resectable, portends limited survival following surgery alone

❖Stage IIIB lung cancers [contralateral LN (N3) metastases or invasion of carina, heart or great vessels (T4)] are inoperable.

❖lung cancers that are associated with metastasis are generally incurable by surgery

❖ Oligometastases in brain or adrenal Gland may experience long-term survival after resection of the primary and metastatic lesions

❖ Lobectomy is currently the standard of care.

❖If the tumor extends across a fissure, lobectomy with *en bloc segmentectomy,* bilobectomy or pneumonectomy should be performed if the patient can tolerate a larger resection.

Patient Selection

❖The most common complications after lung cancer surgery are cardiopulmonary (supraventricular arrhythmia &respiratory failure)

❖Assessment of cardiopulmonary reserve for acceptable peri-operative risk include:

1) spirometry with diffusion capacity
2) ABG
3) Echocardiography
4) cardiac MRI
5) cardiac radionuclide scan

❖Individuals in whom preoperative FEV1 and DLCO values exceed 60% predicted are at low risk for pulmonary resection

❖patients with preoperative FEV1 and DLCO values less than 60% should undergo quantitative ventilationperfusion scans and exercise testing (oxygen-consumption studies) to predict pulmonary reserve.

❖Patients with predicted postoperative FEV1/DLCO values less than 40% predicted and a VO2 max less than 15 mL/kg have increased risk of peri-op pulmonary complications and death

❖They should be considered for nonsurgical therapy.

Adjuvant or neoadjuvant Treatment

Adjuvant chemotherapy

❖ Adjuvant chemotherapy is accepted as standard of care for patients with node-positive (stages IIA, IIB, and IIIA) NSCLC.

Induction Chemotherapy

individuals with stage III disease that receiving neoadjuvant CT might have longer survival.

Sequential Chemotherapy and RT

In patients with medically inoperable or unresectable tumors. demonstrated a modest improvement in survival with sequential chemotherapy and radiation (stage III)

Induction and Consolidation Chemotherapy

❖ This approach of systemic CT has the potential to improve outcomes by early treatment of distant micrometastases and downstaging the primary tumor prior to chemoRT in stageIII.

❖But this approach is not standard therapy for unresectable stage III NSCLC yet.

Chemotherapy regimen

(neo)adjuvant setting

❖Generally cisplatin-based chemotherapy suggest for NSCLC chemotherapy

❖ cisplatin and vinorelbine combination appears preferable to other agents.

❖ Expression of ERCC1 has been associated with cisplatin resistance.

❖ Carboplatin and paclitaxel, are advised in patient that can not tolerate cisplatin-based chemotherapy

Chemotherapy in Advanced Disease

❖Optimal chemotherapy regimens for advanced NSCLC include a platinum drug (cisplatin or carboplatin) and a second drug, such as:

1) Vinorelbine
2) Gemcitabine
3) Paclitaxel
4) docetaxel
5) pemetrexed

❖Performance status is the single best factor for identifying those individuals who can tolerate and benefit from chemotherapy.

❖ Patients with (ECOG) performance status of 0 or 1 are the best candidates for chemotherapy

❖they can achieve both prolongation of survival and improvement in quality of life

❖Patients with an ECOG performance status of 2 are at a substantial higher risk chemotherapy complications and have a poor prognosis

❖ Single-agent CT or regimens with a good tolerance (carboplatin and paclitaxcel), are advised in performance status 2 patients .

❖Individuals with an ECOG performance status of 3 or 4 do not benefit from chemotherapy

❖ Thus, BSC is the preferred means of palliation in this groups.

❖ carboplarin-paclitaxel or cisplatin-gemcitabine as the standard chemotherapy backbones commonly used in the United States and Europe in advanced NSCLC.

❖ patients with adenocarcinoma and large cell carcinoma had a significantly better survival with cisplatin-pemetrexed than with cisplatin-gemcitabine

❖ SCC histology have significantly worse with cisplatin-pemetrexed than cisplatin-gemcitabine

❖ bevacizumab has been approved by the FDA for the treatment of first-line advanced NSCLC in combination with carboplatin and paclitaxel, in patients:

1) with nonsquamous histology
2) without brain metastases
3) without serious bleeding

❖ Erlotinib and gefitinib (EGFR-TKI) can use in patients with powerful positive selection criteria :

1) never-smoker status
2) Female Gender
3) adenocarcinoma
4) BAC carcinoma histologies
5) East Asian ethnicity

❖Mutations sensitizings the tyrosine kinase domain of EGFR are the most powerful predictor for dramatic Responses and overall survival in patients receiving EGFR-TKIs.

Optimal Duration of Chemotherapy

❖ There is no evidence that continuing the same regimen prolongs survival of patients exhibiting response or stabilization of disease after 4 to 6 cycles of chemotherapy.

❖it is recommended that chemotherapy be given for 2 cycles, then response should be assessed with imaging.

❖Patients who show a clear response and those who have stable disease should receive additional cycles to maximum of 6 cycles

Maintenance Therapy

❖A significant improvement in survival has been documented with Maintenance pemetrexed, erlotinib, and marginally with docetaxel for advanced NSCLC

❖ Pemetrexed and erlotinib have approved by the FDA for patients who did not progress after induction chemotherapy for advanced NSCLC.

Second-Line Chemotherapy

❖ second line chemotherapy with docetaxel can improve outcome in patients with reccurence who received prior cisplatin therapy

❖ Pemetrexed has therefore been approved for the second-line treatment of advanced NSCLC.

❖ Patients with recurrence disease that received bevacizumab plus chemotherapy had longer progression-free survivals than the chemotherapy alone

❖ combination chemotherapy showed significantly improved progression-free survival than single-agent chemotherapy, but no better survival

SPECIFICS OF LUNG CANCER MANAGEMENT

Stage I

- T1a → segmentectomy
- T1b → lobectomy
- T2a
  - If ≤ 4cm → lobectomy
  - If > 4cm → lobectomy + CT
- IN large cell tumors all Stage I receive adjuvant Chemotherapy

Stage II

→ lobectomy + CT

Stage IIIA

- T3N1 → lobectomy + CT
- T4 N0/N1 → Surgery + Chemoradiation

  or

  → Neoadjuvant CT+surgery + radiation
- T1-3/N2 → Chemoradiation
- If unsuspected N2 → Surgery + Chemoradiation

Stage IIIB → Chemoradiation

❖ If radiation field is large → Induction CT+ Radiation

Inoperable

Stage I → Definite Radiation (SBRT)

Stage II
- if N0 → Definite Radiation (SBRT)
- if N+ → Definite ChemoRadiation

Stage III → Definite ChemoRadiation

superior sulcus tumor → Neoadjuvant Chemoradiation+ surgery

Post op RT indication:

1) Positive margin 2) close margin <1mm 3) ECE

Stage IV → 1) Chemotherapy

Stage IV → 2) Chemotherapy + palliation RT in specific site

Summary of curative radiotherapy indications

Adjuvant RT

Because of the high incidence of loco-regional failure, RT has been recommended as adjuvant treatment after complete resection in patients with T4 or N2-3 disease.

Concurrent Chemotherapy and Radiation

There was a significant benefit of concomitant chemo-radiotherapy on overall survival in some trial (stage III)

Palliation In Metastatic Disease

Intrathorasic Disease

Surgery

1) Bronchoscopic ablation of tumor with or without stent placement to relieve endobronchial obstruction or hemoptysis.

2) pleurodesis to relieve symptomatic malignant pleural effusions

3) Resection of primary tumors and lung parenchyma are required to control septic complications or massive hemoptysis

Radiation Therapy

❖Common EBRT include 10 Gy in a single fraction or 30 Gy in 10 fractions.

❖Endobronchial brachytherapy is often used to palliate endo-bronchial tumors especially in patients who previously received external beam radiotherapy (EBRT)

Brain Metastases

❖The development of brain metastases in patients with NSCLC Exceeding 25% in autopsy

❖A metachronous presentation typically has a better prognosis than synchronous.

❖long-term survivals reported with resection as well as stereotactic radiosurgery (SRS) of a metachronous solitary brain metastasis, usually followed by whole-brain radiation therapy (WBRT).

❖Many patients present with multiple lesions or extensive extra-cranial disease and corticosteroids and WBRT are standard care.

Bone Metastasis

❖RT is especially effective in palliating pain from bone metastases. Single 8-Gy fractions are often sufficient and well tolerated

❖More protracted regimens (30 Gy in 3-Gy fractions) are used for large fields or when there is interest in minimizing long-term toxicity.

Metastasis to the Adrenal Gland

❖Adrenal metastases are found in one-third of patients at autopsy

❖Excision of the primary tumor and of an isolated adrenal metastasis improve survival.

Radiation Therapy

Techniques

❖External-beam radiation therapy consists of:

1) high-energy photon beams (mega) 2) proton beams

❖This process typically requires a planning CT scan with the patient in the treatment position

❖ PET scan is helpful in discriminating between tumor and atelectasis, and involved versus uninvolved lymph nodes.

❖Photon energies between 4 - 10 MV are preferred for patients with peripheral tumors surrounded by low-density lung parenchyma

❖Higher-energy photons (15-18 MV) may be necessary for in larger patients or when oblique fields are utilized.

Respiratory Motion

❖Lung tumors, especially peripheral tumors in the lower lobes, move during the respiratory cycle.

❖This motion must be taken into account during the planning process by some approaches :

1) Determination the motion of the tumor during the respiratory cycle:

- obtaining a breath-hold CT in inspiration and expiration and combining these volumes, obtaining a (4 dimensional) CT.

2) Treatment the tumor when it is in a certain phase of the respiratory cycle. (Respiratory gating)

3) Treatment planning and delivery are performed with the patient holding his or her breath in deep inspiration.

This reduces tumor motion from respiration and can decrease the volume of normal lung in the field.

IMRT

- IMRT increases the volume of lung receiving a low dose of RT, and may actually increase the rate of injury.

- Because the possible confounding impact of respiratory motion on IMRT dose delivery

SBRT

- SBRT refers to the delivery of large doses of radiation to a small treatment volume. usually employing multiple beams. using a small number of fractions .

- It´s dose range is from 12 to 22Gy in 3 to 5 fraction.

CTV

For the primary tumor a 6-9mm margin would encompass all microscopic disease in approximately 95% of lung cancers.

PTV

calculated uncertainty setup margins is from 9 to 13 mm for patients

Dose

1) Dose in pre op RT: 45GY

2) Dose in post op RT: 50-60 GY

3) Dose in definite RT: 60GY≤ (to 74 Gy)

4) Dose in SBRT : 3 X 20GY

Elective Nodal Irradiation

❖The conventional approach for locally advanced NSCLC include lymph node regions in the mediastinum and ipsilateral hilum at risk of harboring microscopic disease (ENI).

➢ Opponents of ENI have argued that:

1) Larger fields are likely associated with more acute (esophageal) and late (lung)toxicity.

2) may hinder the ability to escalate dose to gross disease.

3) PET is used increasingly in NSCLC staging and is more sensitive

4) The reported rates of isolated nodal failure in patients who did not receive ENI are modest (5% to 10%).

➢ Proponents of ENI assert that :

1) PET ability is limited to identify all sites of microscopic tumor extension within the chest

2) An isolated mediastinal recurrence (10%) is high relatively.

❖ It is reasonable to suppose that ENI does not need to be an all-or-nothing phenomenon. The use of ENI based on the involved lobe seems reasonable.

Radiation Therapy Toxicity

Pulmonary Toxicity

❖Radiation-induced lung injury is relatively common, and divided into early (acute) and late (chronic) toxicity.

❖ Early toxicity (radiation pneumonitis) is a clinical diagnosis.

❖This manifested as shortness of breath, dry cough, and fever, occurring 1 to 6 months after treatment.

❖ Radiographic abnormalities without symptoms do not warrant intervention

❖Pneumonitis typically responds well to oral prednisone. (typically 40 to 60 mg daily for to 2 weeks), followed by a slow taper.

❖The differential diagnosis of radiation pneumonitis includes : tumor progression, infection, drug toxicity, cardiac disease, anemia.

❖Because steroids Can exacerbate an infection, an initial short course of antibiotics be considered.

❖ Late toxicity (fibrosis) is often detected on radiographic studies, but is usually asymptomatic.

❖Dyspnea can be progressive , often requiring long-term steroids.

❖Pulmonary function tests typically show a decline in FEV1 by 3 to 6 months post-RT.

❖In high doses of RT (70 Gy or more), unusual pulmonary complications have been reported, such as:

1) bronchial stenosis

2) bronchopleural fistula

3) fatal hemoptysis

❖ TGF-ß has been shown to predict for RT-induced lung injury.

Esophageal Toxicity

❖ Odynophagia secondary to esophagitis occurs in most patients receiving mediastinal RT

❖Esophagitis is managed with narcotic analgesics, topical agents such as viscous lidocaine, and occasionally antifungal agents (if a candidal infection is suspected).

❖Late esophageal injury (stricture or dysmotility) is uncommon with conventional doses of RT (> 66 Gy).

Cardiac Toxicity

❖Radiation can cause pericardial and myocardial injury.

❖Cardiac Toxicity increase in doses more than 30 Gy.

Radiation Protectors

❖A variety of agents have been used to mitigate the effects of RT on normal tissue. The most widely tested agent is amifostine

❖ IT is believed to scavenge free radicals produced by the interaction of ionizing radiation and water molecules.

❖Some study demonstrated that addition of pentoxifylline reduce the incidence of lung injury

❖Because results been conflicting these agents is not widely used for patients receiving thoracic RT.

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