

Lung Cancers

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Epidemiology

- Third common ca world wide
- Most common cause of cancer-related deaths in both M & F (30%)
} highly lethal ca
(due to delay presentation)
- kills more people than the next three most common cancers combined (breast, prostate, and colon).
- M:F = 2:1 (♂ male predilection due to smoking more common in male)
- The overall 5-year survival rate for lung cancer is only 18%, primarily because the disease is usually advanced at presentation;
} according to the stage
- diagnosis and treatment at an early stage makes the 5-year survival rate approaches 60%.

Risk factors:

1. Cigarette smoking:

- primary cause of more than 80% of lung cancers.

2. Radon exposure (more common in western countries)

(يوجد بالبيوت والمناطق القريبة من الارض)

- second most common cause of lung cancer

SOURCES

- The main source of indoor radon is radon gas infiltration from soil into buildings. Rock and soil produce radon gas. Building materials, the water supply, and natural gas can all be sources of radon in the home.

3. Passive (secondhand) smoking:

- Third most common cause
- increases the risk of lung cancer by 30%.

3

- Despite the strong association between lung cancer and smoking, lung cancers develop in only 15% of heavy smokers.

4. Urban air pollution:

5. Industrial exposure (asbestos, uranium, arsenic) 6. Family history / somatic denovo mutations

mutations

(- pneumoconiosis may be associated)

(as there's can be targeted treatment against them)

(thing that occur during his life - حتى انولد فيه)

Types of lung cancers:

Benign

Malignant

- Primary (arise from the lung itself)

- Metastatic (secondary) (thyroid, kidney, colorectal)

Primary malignant lung cancers:

- non-small cell lung carcinoma (NSCLC) (non small, non smoker)

- (adenocarcinoma, squamous cell carcinoma, and large cell carcinoma)

- small cell lung carcinoma (SCLC). (small, smoker), more aggressive, rarely diagnosed early

- NSCLC is often managed with surgery when the tumor is localized, whereas SCLC is almost always managed with chemotherapy with or without radiation therapy

slow

Malignant primary LC

1. Non-small cell lung cancer (N.S.C.L).

1. Adenocarcinoma (40-50% of overall lung CA)

- most common lung cancer found in nonsmokers and women.
- Usually peripheral, more likely to develop systemic metastases (الانتواع)

(on imaging and C-x-ray)

2. Bronchioalveolar CA. انواع واحد → new name → lipidic tumor

- tumor cells proliferating along the surface of intact alveolar walls.
- Can be single/multiple nodules, indolent/aggressive course.

Acinar adenocarcinoma.

Papillary adenocarcinoma.

Solid carcinoma with mucus formation.

منه محبات
كثير

central / peripheral → (مع عثانا تعرف بال images وانه العلاج يختلف)

2. Squamous cell carcinoma 25%

- 65% as a central lesions +/- cavitation
- Unlike adenocarcinoma, localized, spread within the pulmonary lobe/ regional lymph nodes
- invasion of the chest wall, mediastinum, or other intrathoracic organs is also known to occur.

3. Undifferentiated large cell carcinoma 7%

- aggressive, with early metastases to the regional nodes in the mediastinum and distant sites such as the brain.

4. Adenosquamous carcinoma 1%

II. Small cell lung carcinoma (S.C.L.C) 20%. (15- 30%).

- ▶ Classified under neuroendocrine tumors because of structural similarities (in immuno-histo-chemical staining) as it can make para-neoplastic synd... (secrete hormones)
- ▶ well-differentiated, benign/typical carcinoid tumor.
- Central, main bronchus, treatment mainly surgery, benign, usually single
- Express (NSE, Chromogranin, Synaptophysin) tumor markers
↳ neuron specific enolase
- ▶ intermediate less differentiated atypical carcinoids or neuroendocrine carcinomas,
- more aggressive than typical carcinoids, surgery mainly but depends on stage
- ▶ undifferentiated malignant small cell carcinomas.

II. Small cell lung carcinoma (S.C.L.C) 20%. (15-30%).

▶ most common CA in smoker

- ▶ Highly malignant
 - ▶ Rapid growth
 - ▶ Early mets and invasion
 - ▶ Production of peptides.
- characteristics
1. Dopa decarboxylase.
 2. Adenocorticotrophic hormone ACTH.
 3. Gastrin releasing peptide.
 4. Creatinine kinase.
 5. ADH

TABLE

7.1

Frequency of Histologic Subtypes of Primary Lung Cancer

Cell Type	Estimated Frequency (%)
Non-Small Cell Lung Cancer	
Adenocarcinoma * (most common)	40
Bronchoalveolar	2
Squamous cell carcinoma *	25
Large cell carcinoma	7
Small Cell Lung Cancer	
Small cell carcinoma *	20
Neuroendocrine, well differentiated	1
Carcinoids	5

Clinical Presentation

- Asymptomatic 5%. (discovered incidentally on CXR/CT)

e.g. => pt. with renal colick and make CT for him (lung mass) فوجيا

Bronchopulmonary symptoms: (within the lung Due to tumor it self)

- cough 75%
- hemoptysis 57%
- chest pain
- dyspnea
- febrile respiratory symptoms. (infection in obstructed bronchus)

most alarming sign and sympt } cough, hemoptysis, weight loss

esp. if in long period + smoker + old age

- fever, wheezing, stridor, wt. loss

if present it superimpose infection

Clinical Presentation

II. Extrapulmonary intrathoracic symptoms 15%

- hoarseness of voice. (RLN paralysis) (recurrent laryngeal nerve)
- superior vena cava syndrome. (in apical lung tumor) (thoracic outlet obst)
- Pancoast apical lung tumor :- (in apical lung tumor) ← neuropathic pain, ischemia, DVT, edema
- (pain in the upper extremity, Horner's syndrome).
- chest pain / chest wall invasion
- dysphagia. (esophagus) ← if invasion of
- pleural effusion.
- phrenic / vagus nerve paralysis.

(in apical lung tumor)

But substances secreted by tumor

malignancy الـ سببها الـ malignancy فـassw الـ
it self

10% of lung Ca pt. have it

Clinical Presentation

III. Extrathoracic nonmetastatic symptoms

- Paraneoplastic syndromes. (10%)
- More with SCLC *
- Cushing's syndrome (ACTH production). → Cushing disease (adrenal JB al-1)
- Excessive Anti-diuretic hormone production (SIADH) → water retention, no osmolarity, high urine osmolarity, electrolytes imbalance
- Hypercalcemia of malignancy ↑ Ca^{2+} (يكون الـ كـ الـ) → ↓ Na^+ , ↓ K^+ (dilutional)
- Hypertrophic pulmonary osteoarthropathy.
- Lambert-Eaton myasthenic syndrome (LEMS)
- Clubbing of fingers. ↳ Ab against Ach receptors → weakness
- Thrombophlebitis.
- Dermatomyositis, limbic encephalitis, opsoclonus,etc

aggressive fluid

↑
2:1s

confusion
drowsy

Clinical Presentation

IV. Extrathoracic metastatic symptoms.

- ▶ Neurologic symptoms. (brain)
- ▶ Bone pain, pathological fracture. (Bone)
- ▶ Jaundice, ascites, abdominal mass. (liver)
- ▶ Non-specific symptoms. →
 - Wt loss, weakness, anorexia, malaise.

Metastasis

1. Direct extension. (locally)
2. Lymphatic metastasis. (L.N)
3. Hematogenous spread. (Blood)
 - = brain, liver, lungs, bone, adrenal glands, kidney, pancreas, skin, subcutaneous tissue.
 - = bone: ribs, spine, femur, humerus, pelvis.

Diagnosis

Imaging:

- (A) • CXR (initial test) → not very useful
 - determine location of lesion
 - ~~stippled~~ features ~ ~
 - if single mostly Cg (stellate)
- (B) • Chest CT scan with IV contrast (including liver and adrenals)
 - confirms dx, assess tumor extension, mediastinal LN, help staging)

micro stellate, calcification
 ~ ~

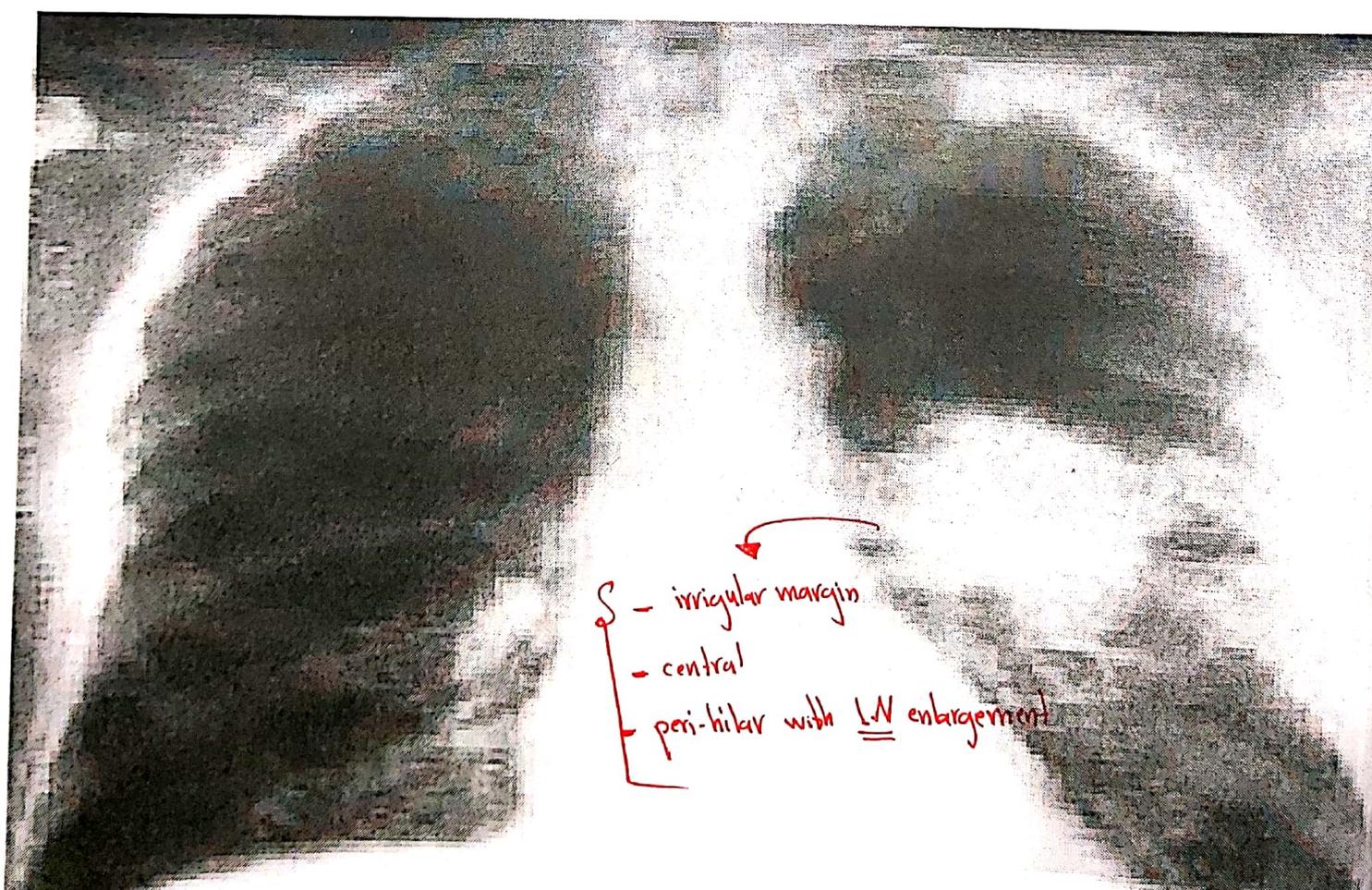
مع ويا
 ما اكتشف
 ال CT

- (C) • MRI (adds little to CT, mainly in superior sulcus tumor with spine / neurovascular involvement)

- (D) • PET/ PET-CT scans: (accuracy 90%) → can detect occult mets
 - Performed routinely for diagnosis and staging.
 - Distinguish Benign vs malignant mass (hyperactive)
 - False -ve in carcinoid and Bronchoalveolar adeno. → they are usually metabolically inactive
 - False +ve like T.B., infectious disease, granulomatous disease

لازم نقله

(اول activity)



S - irregular margin
 - central
 - peri-hilar with LN enlargement

Histological diagnosis:

▶ Always required to confirm dx

لازم توخذ Biopsy قبل ما نبلن
اي علاج

Ⓐ ▶ Sputum cytology +ve 45-90%.

Ⓑ ▶ Bronchial Lavage cytology.

non-invasive confirm Cg but not exclude it)

Ⓒ ▶ Invasive Diagnostic Procedures.

• Bronchoscopy - endobronchial US (EBUS). } for central tumor

• Percutaneous transthoracic needle BX (CT guided FNA/CNB).

• VAT (video assisted thoracoscopy).

• Supraclavicular lymph node biopsy. under US guided

• mediastinoscopy.

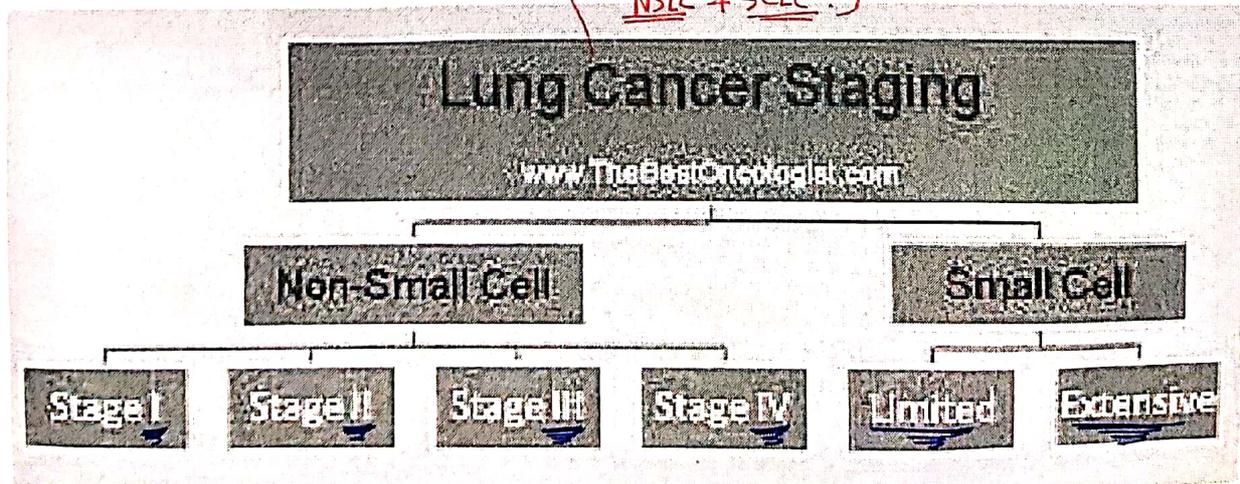
usually for peripheral tumor
لانه صعب اوصلح بال Bronchoscope
لكن صيغته كالتالي chest tumor

↳ During surgery ⇒ make an opening in supra sternal notch ⇒ واي فتحة فوق القصبة بتوخذ منه Biopsy

Staging of primary lung cancers:

▶ Essential to determine extent of disease, formulate proper treatment plan and predict prognosis / survival.

Different staging of NSCLC + SCLC ?? } due to Differ behaviour



Staging of SCLC:

thus, the surgery has no role in them
make simple staging system (مبسط)

- ▶ In SCLC, most patients present with metastatic or advanced locoregional disease.
- ▶ A simple two-stage system classifies the SCLC as **limited** or **extensive** disease.
- ▶ **Limited disease** is confined to one hemithorax, ipsilateral or contralateral hilar or mediastinal nodes, and ipsilateral supraclavicular lymph nodes.
- ▶ **Extensive disease** has spread to the contralateral supraclavicular nodes or distant sites such as the contralateral lung, OR liver, brain, bone marrow.
- ▶ Staging for SCLC requires CT scan / PET-CT and brain MRI ✗
- ▶ May need mediastinoscopy / EBUS for LN staging

Staging of NSCLC:

- ▶ According to the 8th AJCC (TNM) – released in 2016
- ▶ CXR
- ▶ CT scan of the chest and upper abdomen (liver/adrenals)
- ▶ PET-CT (detect occult mets)
- ▶ Brain MRI (for stage II and more) → (لانه stage I الالعاب ما يكون في mets)
- ▶ May need EBUS, mediastinoscopy to confirm mediastinal LN mets (not indicated in early tumors T1N0)

بتعلمه لاي شيء اكثر من stage Ia

TNM 8th - Primary tumor characteristics

زایما محفوظ

- T_x** Tumor in sputum/bronchial washings but not be assessed in imaging or bronchoscopy
T₀ No evidence of tumor
T_{is} Carcinoma in situ

T₁ ≤ 3 cm surrounded by lung/visceral pleura, not involving main bronchus

- T_{1a(mi)}** Minimally invasive carcinoma
T_{1a} ≤ 1 cm
T_{1b} > 1 to ≤ 2 cm
T_{1c} > 2 to ≤ 3 cm

T₂ > 3 to ≤ 5 cm or involvement of main bronchus without carina, regardless of distance from carina or invasion visceral pleura or atelectasis or post obstructive pneumonitis extending to hilum

- T_{2a}** >3 to ≤4cm
T_{2b} >4 to ≤5cm

T₃ >5 to ≤7cm in greatest dimension or tumor of any size that involves chest wall, pericardium, phrenic nerve or satellite nodules in the same lobe

T₄ > 7cm in greatest dimension or any tumor with invasion of mediastinum, diaphragm, heart, great vessels, recurrent laryngeal nerve, carina, trachea, oesophagus, spine or separate tumor in different lobe of ipsilateral lung

N₁ Ipsilateral peribronchial and/or hilar nodes and intrapulmonary nodes

2 Ipsilateral mediastinal and/or subcarinal nodes

3 Contralateral mediastinal or hilar; ipsilateral/contralateral scalene/supraclavicular

M₁ Distant metastasis

M_{1a} Tumor in contralateral lung or pleural/pericardial nodule/malignant effusion

M_{1b} Single extrathoracic metastasis, including single non-regional lymphnode

M_{1c} Multiple extrathoracic metastases in one or more organs

رضو صفا رضو

T/M	Subcategory	N0	N1	N2	N3
T1	T1a	IA1	IIB	IIIA	IIIE
	T1b	IA2	IIB	IIIA	IIIE
	T1c	IA3	IIB	IIIA	IIIB
T2	T2a	IIE	IIB	IIIA	IIIE
	T2b	IIA	IIB	IIIA	IIIE
T3	T3	IIB	IIIA	IIIE	IIIC
T4	T4	IIIA	IIIA	IIIE	IIIC
M1	M1a	IVA	IVA	IVA	IVA
	M1b	IVA	IVA	IVA	IVA
	M1c	IVB	IVB	IVB	IVB

Pre-treatment assessment :

العنف ↓

- to determine the patient's ability to tolerate various therapeutic modalities

Includes :

general

CVS

- overall medical status (comorbidities, drugs, nutritional status)
- Full cardiovascular assessment (hx, PEx, CXR, ECG, ECHO,
- +/- exercise testing, nuclear cardiac perfusion, cardiac cath)

when you make resection you remove entire lobe or segment not only tumor
 tumor ↓ lung capacity as it occupies a portion of lung

ما في دايي تغلغ كلغ

if young age
 if old

لازم تغلغ كلغ

RS

- Full pulmonary evaluation

ماقتة بخسر capacity ← فلانزا تعرف
 اريفين بيشتغل ولا لا

- Especially when going for pulmonary resection as the lung reserve is usually less in those patients due to smoking/COPD and the cancer itself.

- spirometry, PFT, VQ scan

- Majorly impaired pulmonary reserve might be a contraindication to lung resection

⇒ وهو اريفين وضعه ما
 بمقتل عليه، ما يعالجها
 (single, simple but slightly large tumor not mets)
 يعني ممكن يكون

Pre-treatment assessment :

- Preoperative incentive spirometer training (to ↓ complication after surgery)
- initiation of bronchodilators
- weight reduction — if obese
- good nutrition
- cessation of smoking for at least 2 weeks before surgery (2 اسبوع)

All can help minimize complications and improve performance on spirometry for patients with marginal pulmonary reserve

حسته مطلوبه محفوظه الارقام

TABLE
7.2

Pulmonary Assessment and Risk for Thoracic Resection

Average Risk (العادي)	High Risk (بعد العملية بنوعه ICU)	Prohibitive Risk (ممنوع نعمل عليه)
ppoFEV1% > 40	ppoFEV1% 20-40	ppoFEV1% < 20
ppoDLCO% > 40	ppoDLCO% 20-40	ppoDLCO% < 20
pO ₂ > 60	pO ₂ 45-60	pO ₂ < 45
pCO ₂ < 45	pCO ₂ 45-60	pCO ₂ > 60
VO ₂ max > 15 (consumption of O ₂)	VO ₂ max 10-15	VO ₂ max < 10

Available Treatment modalities:

- ▶ Surgery.
- ▶ Chemotherapy.
- ▶ Radiotherapy.
- ▶ immunotherapy → only in metastatic disease

Treatment of NSCLC

(مابده تحفظ به افه)

- ▶ Stage I, II (mainly surgery) if they can tolerate.
- ▶ Stage III not fit for surgery ² (less resection or radiation-SBRT)
- ▶ Stage I (60-70% 5-year survival), Stage II 40%
- ▶ Stage III (chest wall invasion with N0) surgery + chemo or definitive radiation + chemo if they can't tolerate
- ▶ Stage IIIA - induction chemoradiation +/- surgery }
 ▶ Stage IIIB - definitive chemoradiation }
- ▶ Stage IV - induction chemo + palliative radiotherapy
- ▶ Surgery for stage IV only in patients with resected primary and less than 3 mets to lung/brain

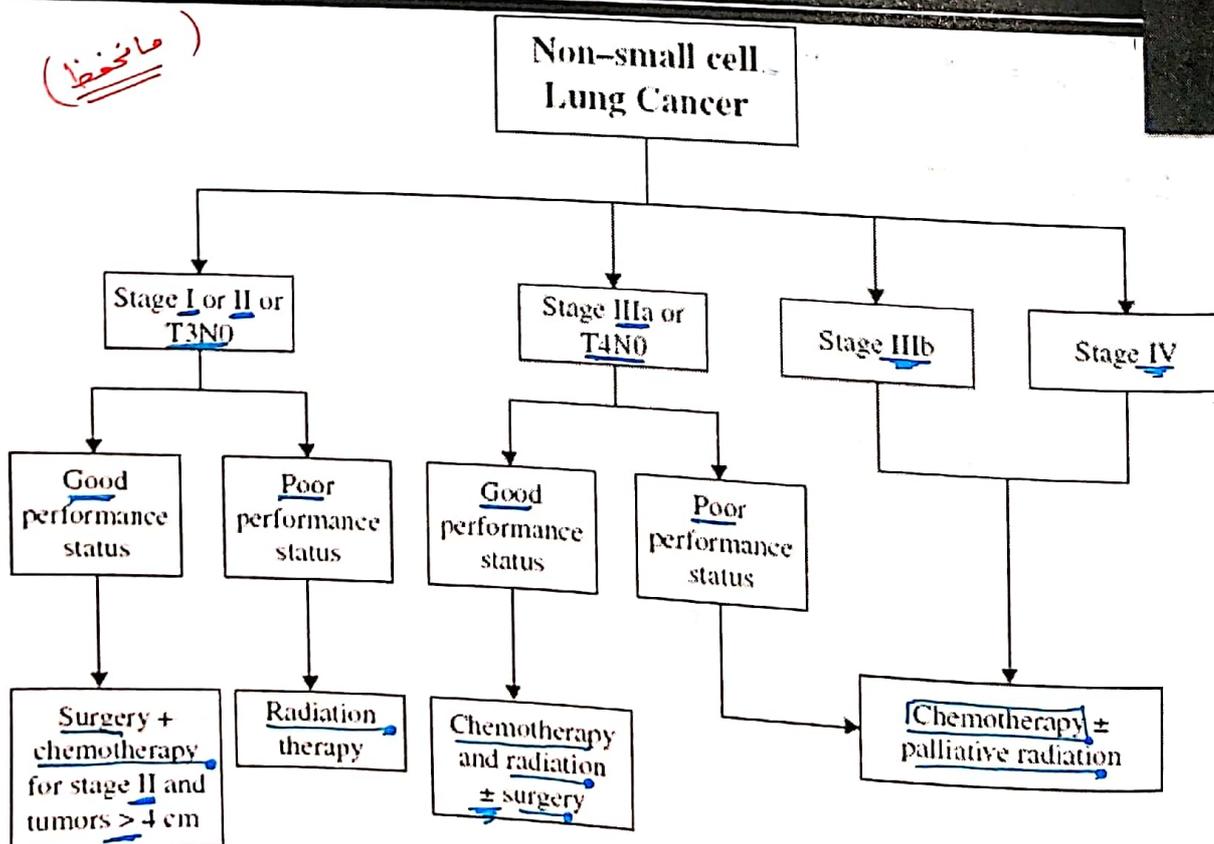


Figure 7.3 Algorithm for treatment of non-small cell lung cancer

Surgical treatment includes :

Pneumonectomy (the whole lung) :

- Was very commonly performed, now only 20% of surgeries
- Higher mortality 4-10% and morbidity \ominus ← السبب
- Advances in surgical techniques reduced the need for pneumonectomy

Lobectomy: (tumor + lobe + lymphatic pathway) + Blood supply

- The standard and most common surgery performed
- Mortality <2% \oplus

Segmentectomy and non-anatomical wedge resections:

- Higher recurrence rate \ominus
- Only in patients who can't tolerate lobectomy ← لملائمة
- Still under investigation for early small lung cancers (no evidence on their efficacy for early lung cancer) \ominus
- The procedure of choice for metastatic lung cancer from another primary cancer but not for primary lung cancers \oplus

بتشمل ال tumor وكم
نسخة حوالية
وما يتبع ال
I.V + B.V

Video Assisted Thoracoscopic Surgery (VATS):

- Ports inserted and resection under camera visualization ← mechanism
- similar outcome to open thoracotomy surgery (tumor resection) but less morbidity and pain \oplus

Robotic VATS

Mediastinal Lymph Node Dissection

- Decrease recurrence \oplus
- Improve survival ???? (not conclusive)
- More staging accuracy

((ablative radiotherapy))

- Stereotactic body radiation (SBRT) can be an alternative for resectable tumors not fit for surgery with inferior results ((مريض ما يتقبل, small tumor))

مثال 90 years, HTN, ...

Treatment of NSCLC

- ▶ **Chemotherapy**
- ▶ **Radiotherapy**
- Those can be Neoadjuvant / adjuvant or palliative **according to stage**
- Can be definitive in some patients without need for surgery



- ▶ **Immunotherapy / targeted therapy:**
 - Usually in metastatic NSCLC #
 - Anti PD-1 (Nivolumab), Anti PD-L1 (pembrolizumab) (program Death gene)
 - anti-CTLA4 (Ipilimumab)
 - EGFR antagonist (erlotinib)
 - Anti- ALK (anaplastic lymphoma kinase – crizotinib)

Biologic or Genetic Markers and Their Prognostic Value

Biologic Variable	Prognostic Factor
<u>bcl-2</u> مش حفظ	<u>Favorable</u>
TTF1	Adverse
Cox2	Adverse
EGFR overexpression	Adverse
Ras	Adverse
Ki67	Adverse
HER2	Adverse
VEGF	Adverse
Microvascular density	Adverse
p53	Adverse
Aneuploidy	Adverse

Treatment of Small cell lung carcinoma SCLC

- ▶ Most of SCLC are disseminated at presentation.
- ▶ SCLC is very sensitive to chemotherapy.
- ▶ Mainstay of treatment is chemotherapy } #
- ▶ 2/3 of patient get partial response to chemo
- ▶ 20-50% have complete response but still 5 year survival is 10% only due to recurrence
- ▶ RT radiotherapy to chest sometimes } #
- ▶ 80% will develop brain mets, so it is standard now that ALL patients with SCLC should receive prophylactic brain irradiation } #
- ▶ Surgery very rarely in early tumor with no mets (T1,T2) limited disease (only few patients) with brain radiation too

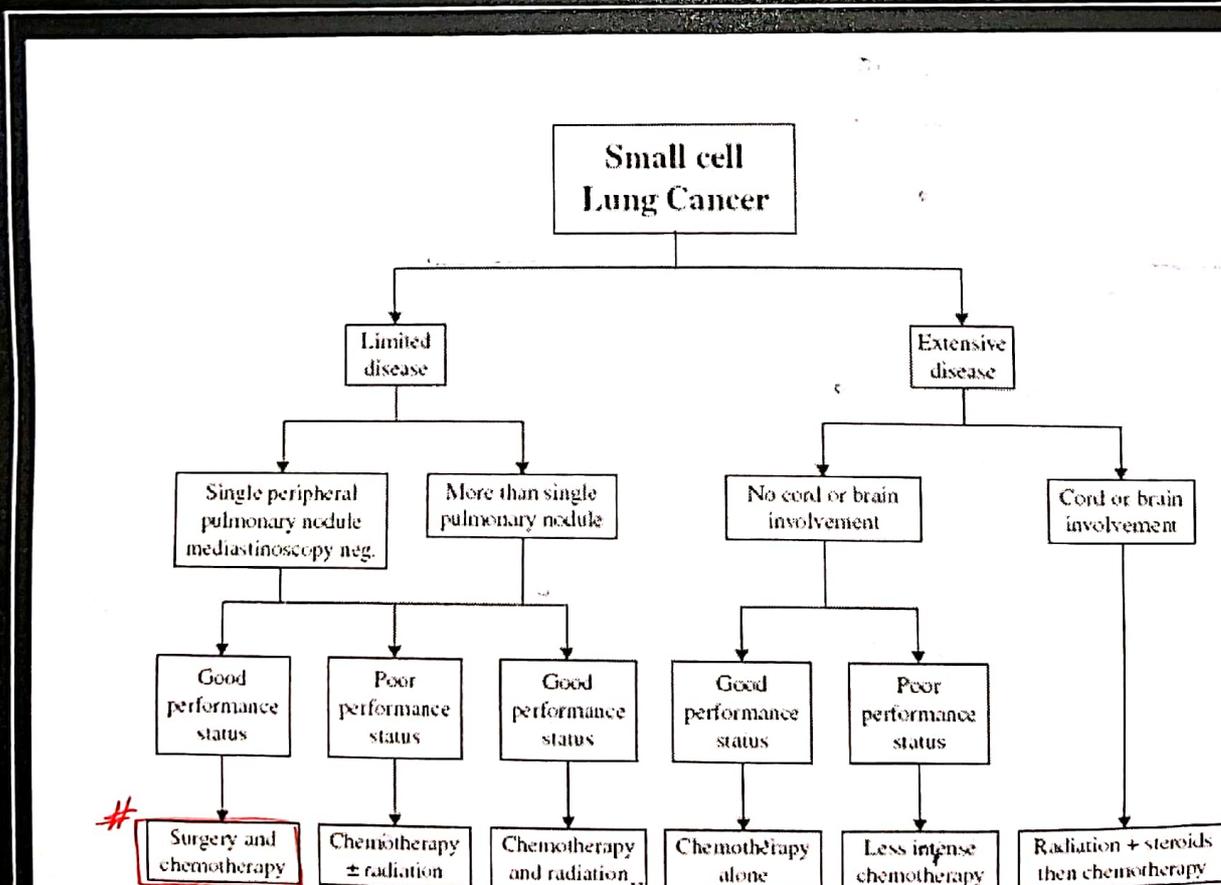


Figure 7.4 Algorithm for treatment of small cell lung cancer.

Metastatic Secondary Neoplasms To The Lung

- most common tumor in lung → primary
 - " " " " " liver → secondary

(- multiple , peripheral , Bilateral)

- ▶ Any malignant tumor can have mets to lungs
- ▶ Mostly from colorectal, breast, thyroid etc
- ▶ Secondary lung mets are Less common than primary lung cancer (unlike liver)
- ▶ Usually multiple , peripheral
- ▶ 95% asymptomatic (discovered during follow up of the primary cancer)
- ▶ (New multiple pulmonary nodules in a patient with known other cancers) is highly suggestive (100%)
- ▶ New single nodule is more likely to be a new primary lung cancer (not secondary mets)
- ▶ Prognosis depend on resectability, disease free interval and number of mets , and biology of main tumor

(العدد / المكان)

lung mets قد يكون تعدد المرفيع كونه كدوما صار
 (كلما طولته الفترة كلما كان احسن)

Treatment

علاج بالعادة يتبع الـ
guidelines of main tumor
(biology of primary tumor)

▶ Surgery (metastatectomy / wedge resection)

▶ Can improve survival in some cancers

مفيدة، ليس من كل المرضى يفيدوا بوجهاً
الجراحة

▶ require

- Ability to remove all mets

- control of the primary tumor

- adequate predicted postoperative pulmonary reserve

- no other organ metastases

▶ Follow the treatment guidelines for the primary tumor (some benefit resection e.g. colorectal, some not – e.g. gastric)

▶ Chemotherapy, radiotherapy (palliative)

- free margins only 2cm

شروط

