Lung Neoplasms

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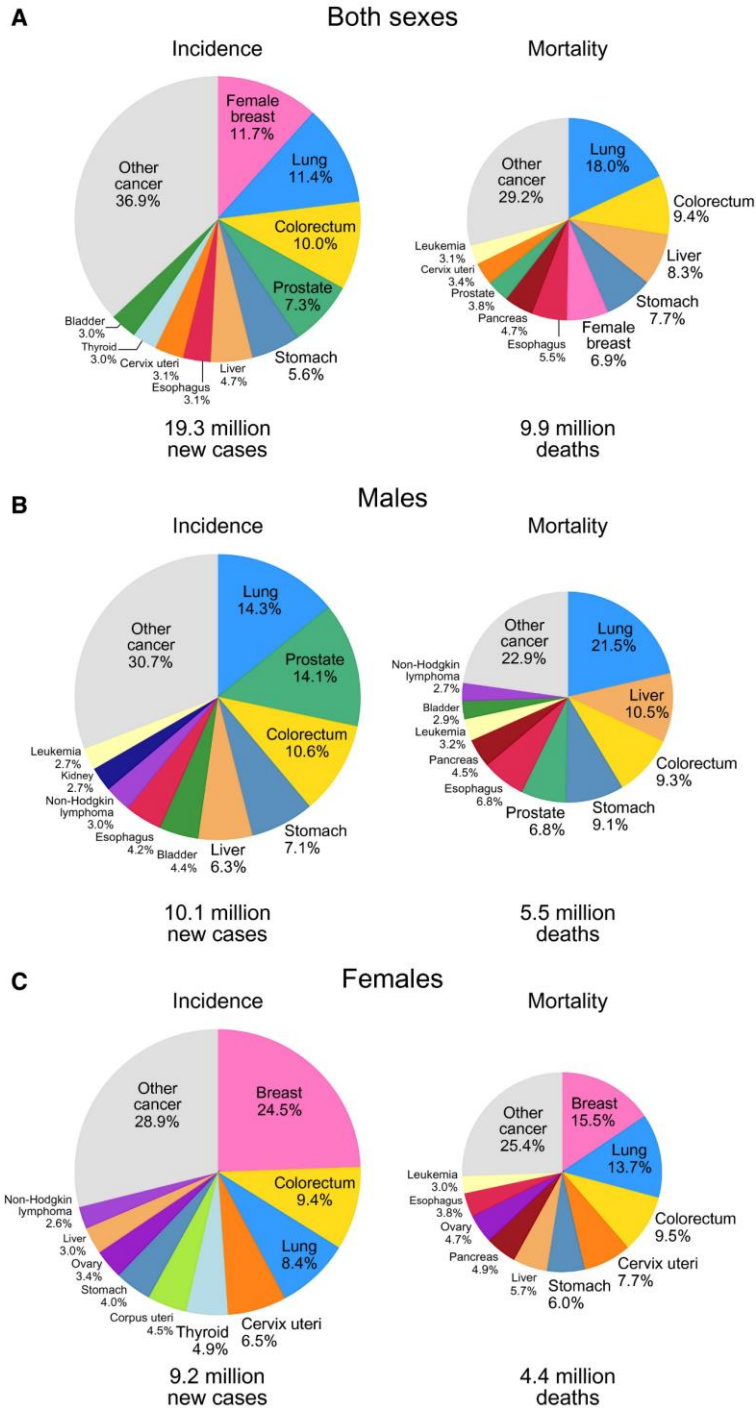
Incidence in 2020

- Lung cancer remains the leading cause of cancer-related deaths.



Risk Factors:

- Tobacco-related
  - The leading risk factor (22-fold in Men, 12% increase in risk in women).
  - 10-20% Never smoke.
  - Smoking linkage: small cell> squamous > adenocarcinoma
- Nontobacco-related
  - Old age (70 yr)
  - Gender (more in males)
  - Race (African American)
  - Low SES.
  - Environmental factors
    - Air pollution
    - 2ndary smoking
    - Occupational exposure
    - Inhalation of smoke from charcoal, heating, or cooking.

Smoking cessation

- In the United States, lower tobacco smoking rates have led to reductions in lung cancer incidence and mortality.
- lung cancer incidence and mortality improved 20 to 30 years after smoking prevalence began to fall.

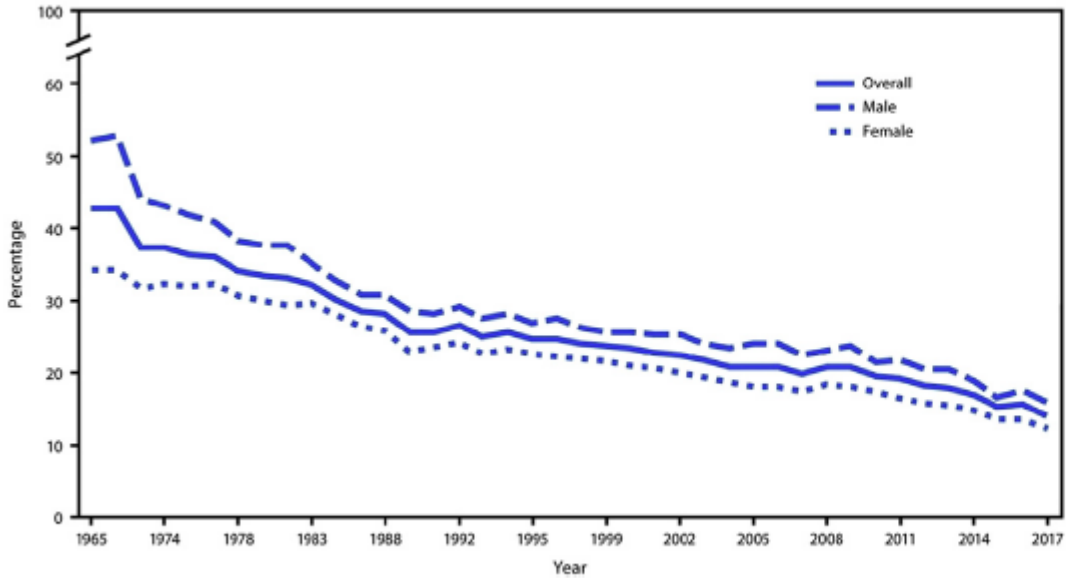


Fig. 5. Percentage
18 years and older w
cigarette smokers, over
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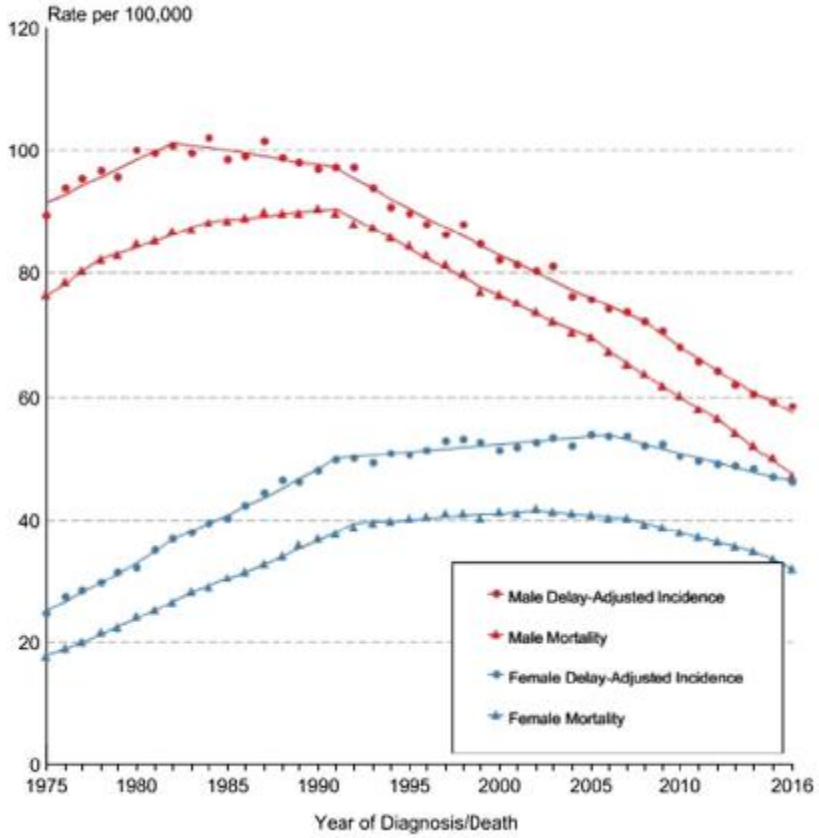
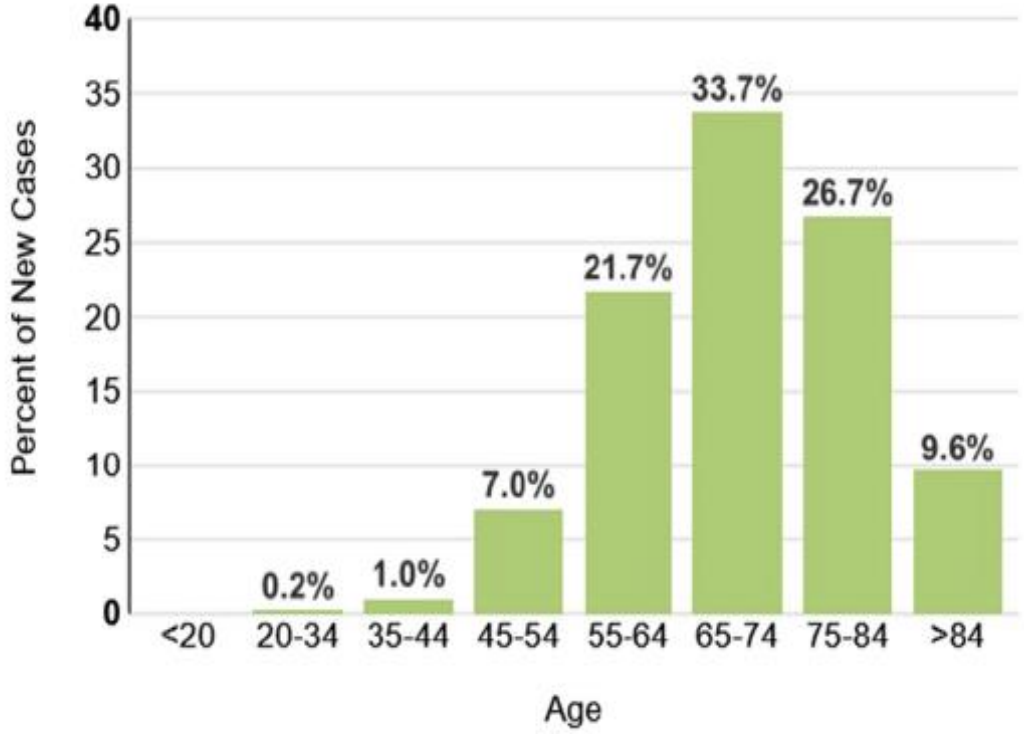
2017. MMWR Morb M
2018;67(44):1225-1232;

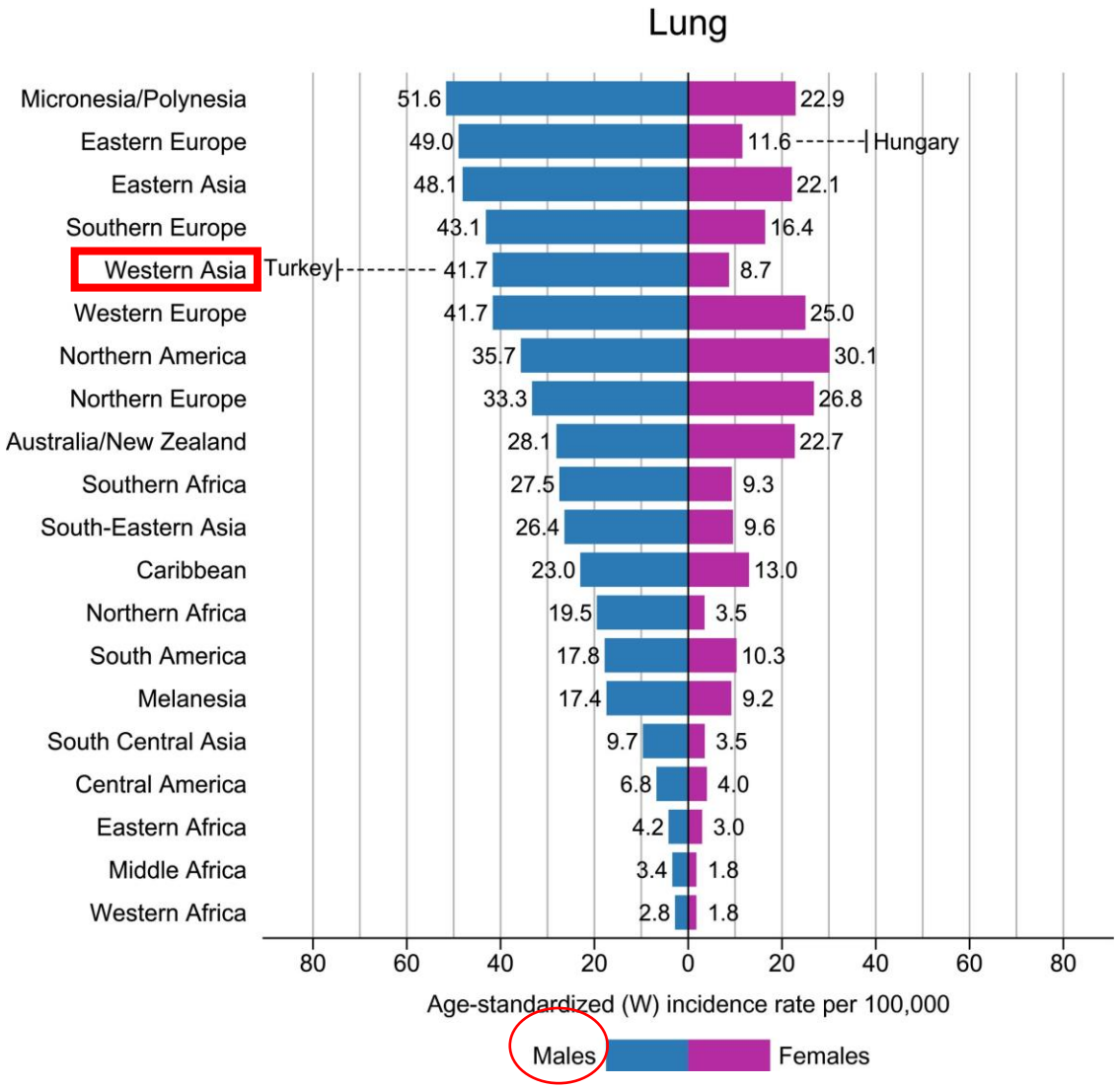


Age

- Median age is 70 yrs.



Gender


Lung
Micronesia/Polynesia 51.6 22.9
Eastern Europe 49.0 11.6 Hungary
Eastern Asia 48.1 22.1
Southern Europe 43.1 16.4
Western Asia Turkey 41.7 8.7
Western Europe 41.7 25.0
Northern America 35.7 30.1
Northern Europe 33.3 26.8
Australia/New Zealand 28.1 22.7
Southern Africa 27.5 9.3
South-Eastern Asia 26.4 9.6
Caribbean 23.0 13.0
Northern Africa 19.5 3.5
South America 17.8 10.3
Melanesia 17.4 9.2
South Central Asia 9.7 3.5
Central America 6.8 4.0
Eastern Africa 4.2 3.0
Middle Africa 3.4 1.8
Western Africa 2.8 1.8
80 60 40 20 0 20 40 60 80
Age-standardized (W) incidence rate per 100,000
Males
Females

- most lung cancers (57%) are diagnosed when the cancer has metastasized outside the lung.

Clinical Presentation

- History
  - Cough
    - Changes in chronic cough (sputum production, frequency)
  - Dyspnea
  - Hemoptysis
    - Present for 6 months or more, more likely CA
    - Small to moderate (less than 500ml/24hr)
  - Chest pain
  - Weight loss
  - Anorexia
  - Fatigue
  - Hoarseness

Paraneoplastic Syndromes

- 2%
- SIADH
- Hypercalcemia
- Cushing syndrome
- Clubbing
- Hypertrophic pulmonary osteoarthropathy
  - Almost always associated with lung cancer.
- Neurologic and myopathic syndromes.
- Anemia and Hematological abnormalities.
- Trousseau’s Syndrome and acute arterial thrombosis.

Paraneoplastic Syndromes

General

- Weight loss/cachexia
- Fatigue
- General malaise

Skeletal

- Clubbing 10%-20%
- Hypertrophic pulmonary osteoarthropathy (HPOA) 5%

Endocrine

- Cushing's syndrome from ACTH
- Inappropriate ADH causing hyponatremia
- Carcinoid syndrome
- Hypercalcemia
- Rarely, hypoglycemia or ectopic gonadotropins.

Paraneoplastic Syndromes

Neuromuscular (15% and most common with SCLC)

- Polymyositis
- Myasthenia-like syndrome (Eaton-Lambert)
- Peripheral neuropathy
- Subacute cerebellar degeneration
- Encephalopathy

Preoperative Assessment

- History
- Physical examination
- Hematological and biochemical investigation
- Lung function assessment.
- Non invasive staging investigation
- Invasive staging investigation

Preoperative Assessment

- History
    - Age: 50-70 yr rarely <30yr
    - Few patients are asymptomatic at the time of diagnosis
    - Cough 75%
    - Dyspnea 60%
    - Chest pain 50%
    - Hemoptysis 30%
    - Anorexia, malaise, fatigue, and weight loss may occur in up to 70%

Preoperative Assessment

- Physical examination
  - Paraneoplastic syndromes
  - Cervical or supraclavicular lymph nodes.
  - General respiratory examination.

Hematological and functional investigation

- CBC
- KFT, LFT, Electrolytes
- PFT (FEV1, VC)
- Diffusion DLCO
- Cardio-pulmonary exercise test.
- Perfusion ventilation scan

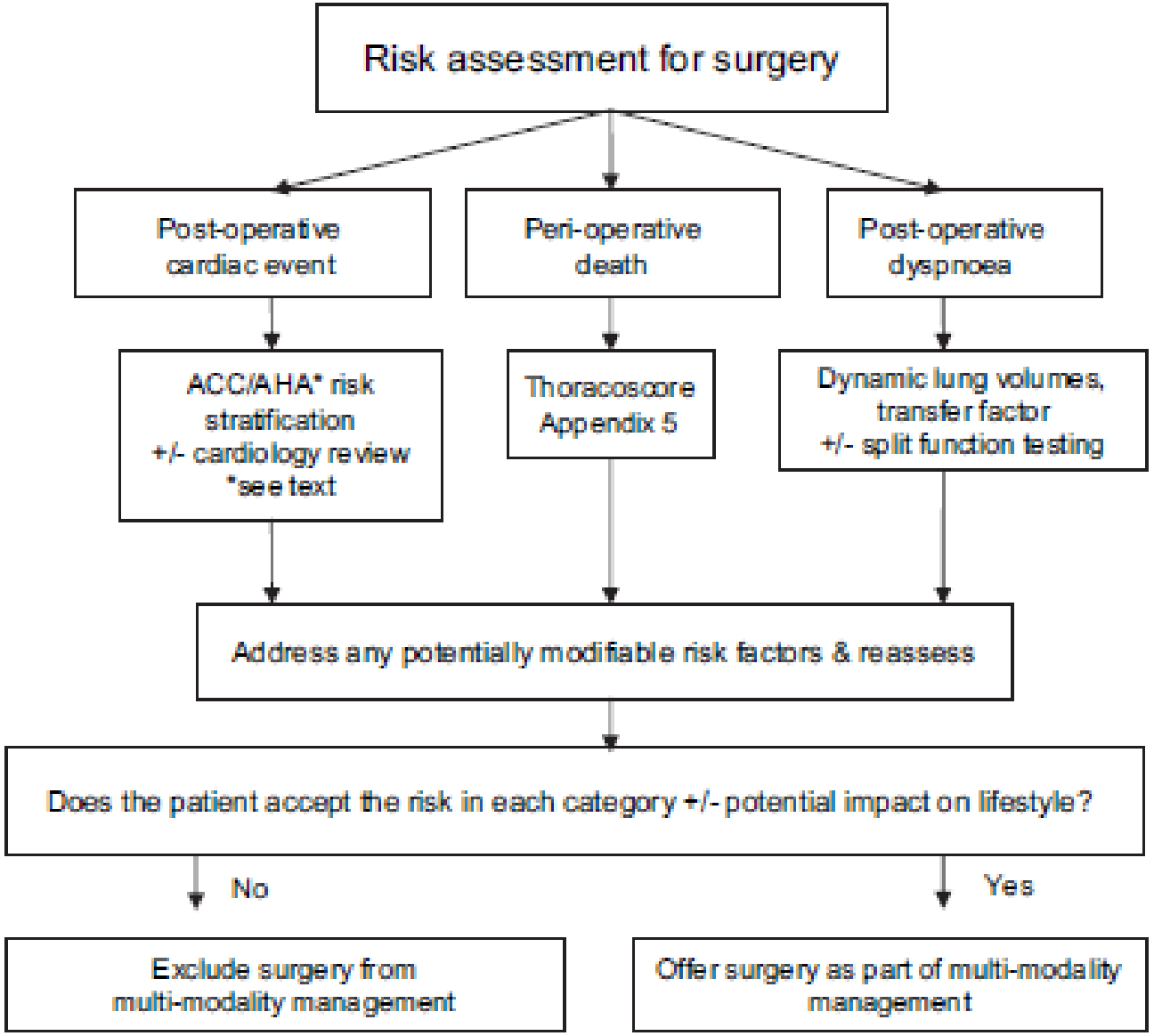
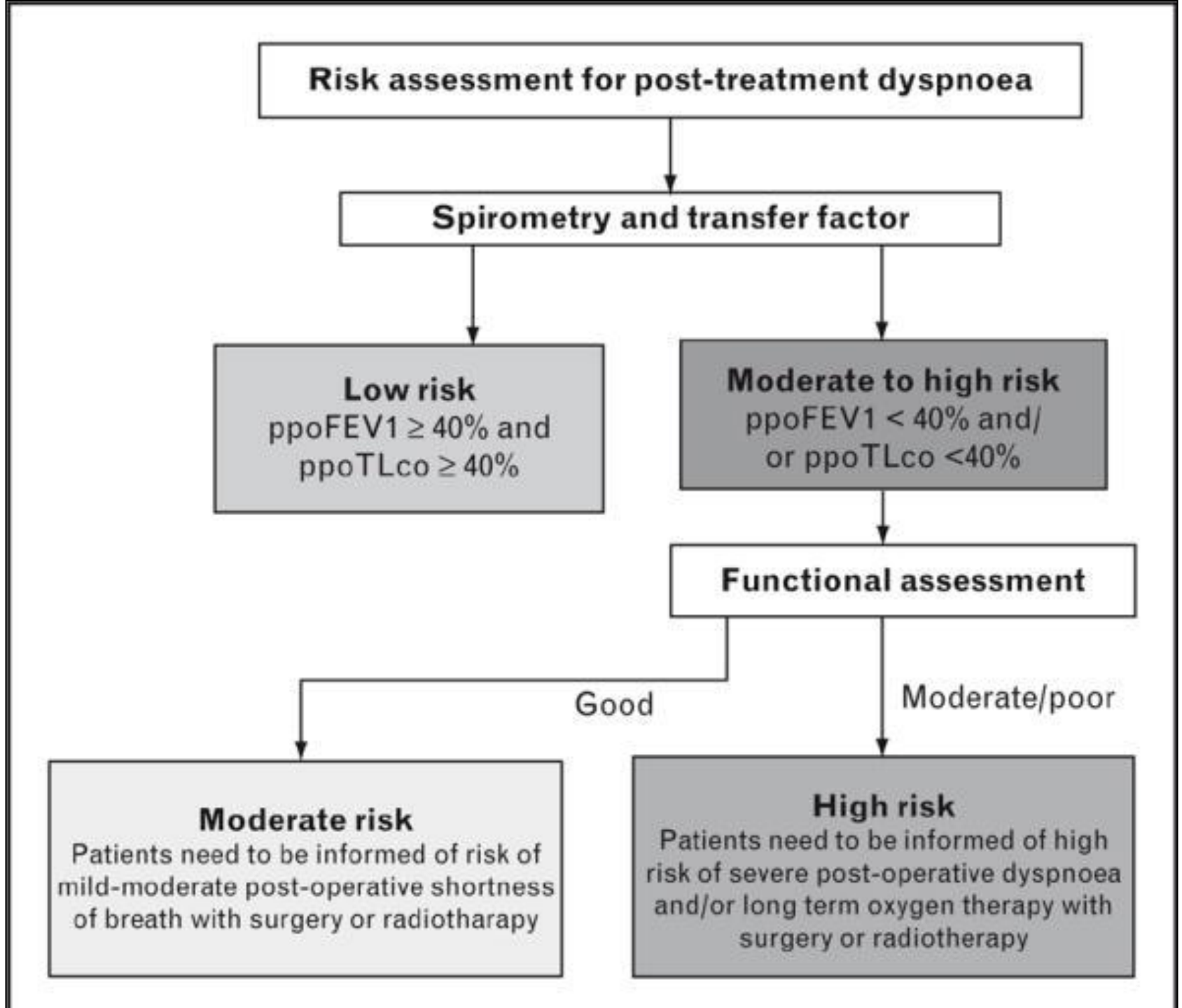
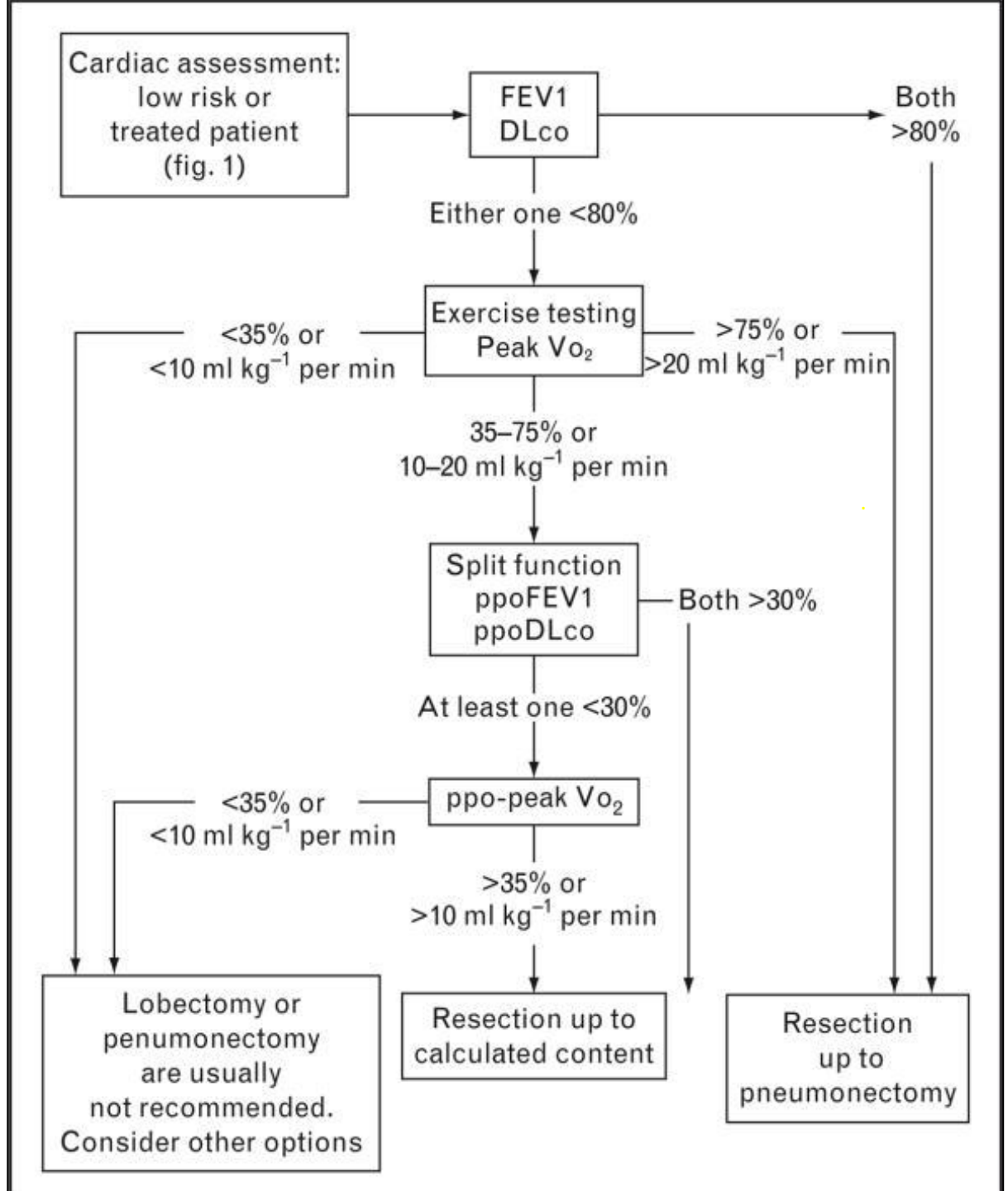


Figure 2 Tripartite risk assessment. ACC, American College of Cardiology; AHA, American Heart Association.


Risk assessment for post-treatment dyspnoea
Spirometry and transfer factor
Low risk
ppoFEV1 ≥ 40% and
ppoTLco ≥ 40%
Moderate to high risk
ppoFEV1 < 40% and/
or ppoTLco <40%
Functional assessment
Good
Moderate/poor
Moderate risk
Patients need to be informed of risk of mild-moderate post-operative shortness of breath with surgery or radiotharapy
High risk
Patients need to be informed of high risk of severe post-operative dyspnoea and/or long term oxygen therapy with surgery or radiotherapy


Cardiac assessment: low risk or treated patient (fig. 1)
FEV1
DLco
Both >80%
Either one <80%
Exercise testing Peak Vo2
<35% or <10 ml kg−1 per min
>75% or >20 ml kg−1 per min
35–75% or 10–20 ml kg−1 per min
Split function ppoFEV1 ppoDLco
Both >30%
At least one <30%
ppo-peak Vo2
<35% or <10 ml kg−1 per min
>35% or >10 ml kg−1 per min
Lobectomy or penumonectomy are usually not recommended. Consider other options
Resection up to calculated content
Resection up to pneumonectomy

Radiological Evaluation

- CXR
- CT
- PET-CT
- PET

8th TNM staging system

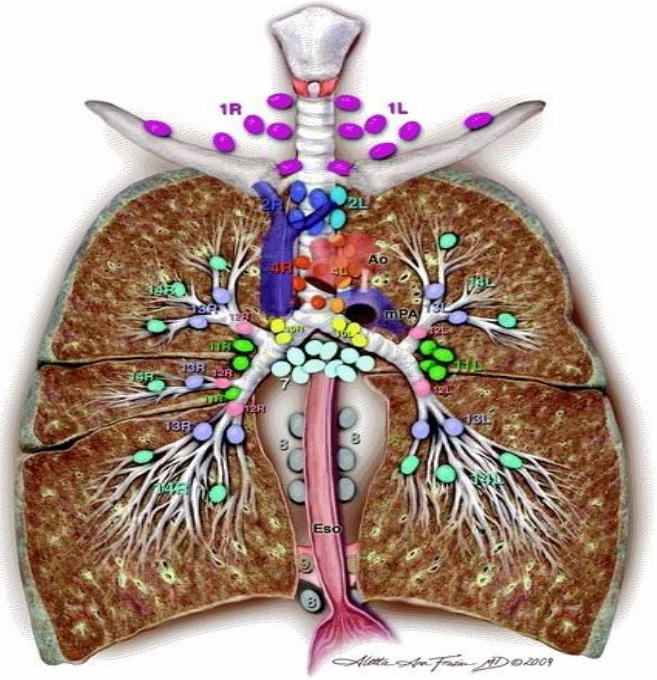
- Invasive vs non-invasive
- Invasive
  - Bronchoscopy and Biopsy
  - Video-Mediastinoscopy
  - Endobronchial US and Biopsy (EBUS)
  - Endo-esophageal US and Biopsy (EUS)
  - Anterior mediastinoscopy
  - Video-assisted thoracoscopy
  - Transthoracic CT-guided biopsy

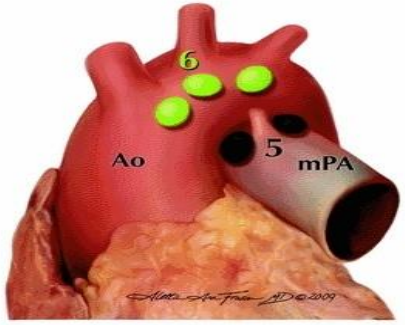
Primary Tumor (T)

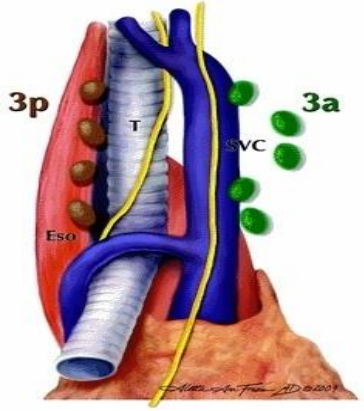
T classification		T components on CT	
Tis (AIS)		Pure GGN ≤ 3 cm	
T1	T1mi	≤ 0.5 cm solid part within part-solid tumor total size ≤3 cm	
	T1a	0.6–1.0 cm solid part within part-solid tumor total size ≤3 cm	
		Pure GGN >3 cm	
		≤ 1 cm solid tumor	
	T1b	1.1–2.0 cm solid part within part-solid tumor total size ≤3 cm	
		>1–2 cm solid tumor	
	T1c	2.1–3 cm solid part within part-solid tumor total size ≤3 cm	
		>2–3 cm solid tumor	
T2	T2a	3.1–4 cm	Involves main bronchus without involvement of carina
	T2b	4.1–5 cm	Total/partial atelectasis
			Total/partial pneumonitis
			Involves hilar fat
			Involves visceral pleura (PL1 or PL2)
T3		5.1–7 cm	Separate tumor nodules in the same lobe as the primary
			Involves parietal pleura (PL3)
			Parietal pericardium
			Chest wall
			Phrenic nerve
T4		>7 cm	Involves diaphragm
			Mediastinal fat or other mediastinal structures (trachea, great vessels, heart, recurrent laryngeal nerve, esophagus)
			Carina
			Vertebral body
			Visceral pericardium
			Separate tumor nodules in the same lung but different lobes as the primary

Nodal Status (N)

N classification	N component on CT
N0	No lymph node metastasis
N1	Ipsilateral peripheral, intrapulmonary or hilar nodes metastasis
N2	Ipsilateral mediastinal (upper, aortico-pulmonary, lower), subcarinal nodes metastasis
N3	Ipsilateral or contralateral supraclavicular/scalene lymph node or contralateral mediastinal, hilar/interlobar, or peripheral nodes metastasis







Supraclavicular zone

1 Low cervical, supraclavicular, and sternal notch nodes

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

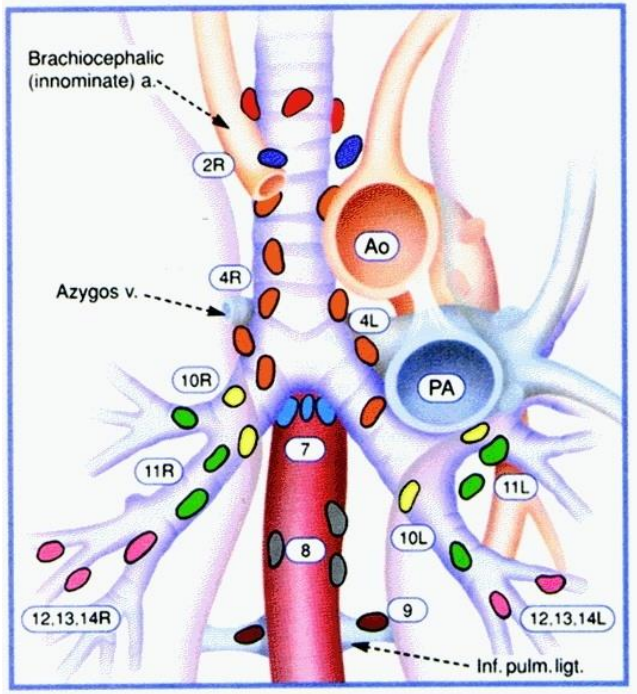
N1 NODES

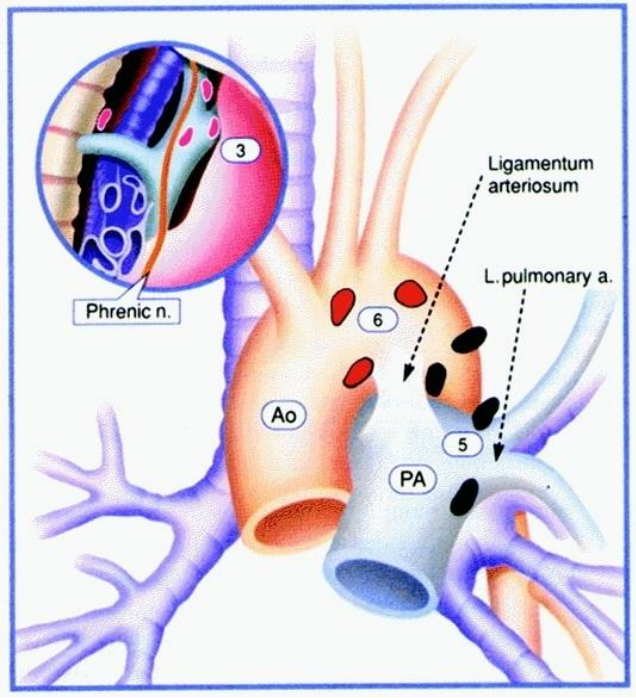
Hilar/Interlobar zone

- 10 Hilar
- 11 Interlobar

Peripheral zone

- 12 Lobar
- 13 Segmental
- 14 Subsegmental





Superior Mediastinal Nodes

- **1** Highest Mediastinal
- **2** Upper Paratracheal
- **3** Pre-vascular and Retrotracheal
- **4** Lower Paratracheal (including Azygos Nodes)

N_2 = single digit, ipsilateral
N_3 = single digit, contralateral or supraclavicular

Aortic Nodes

- **5** Subaortic (A-P window)
- **6** Para-aortic (ascending aorta or phrenic)

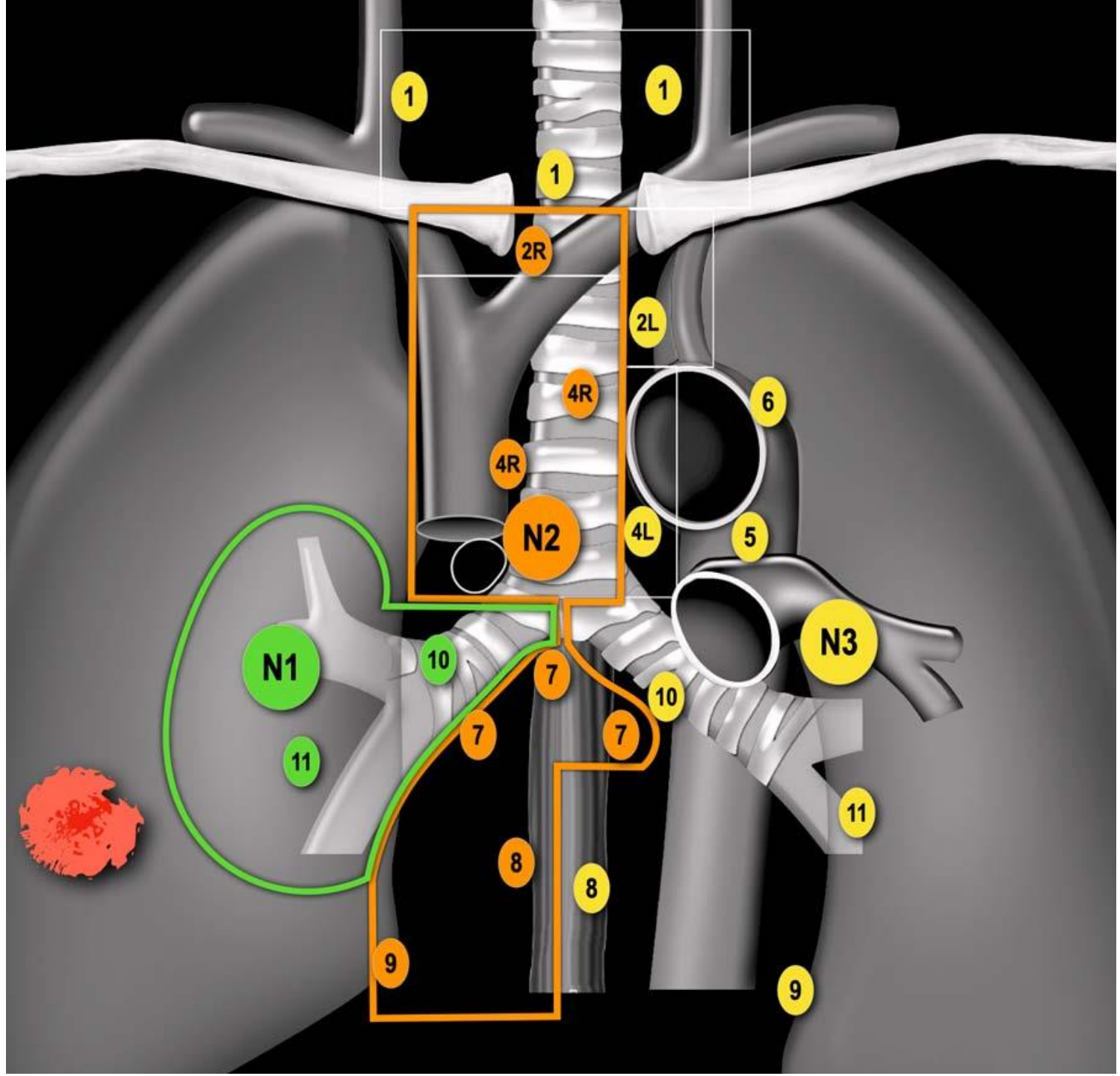
Inferior Mediastinal Nodes

- **7** Subcarinal
- **8** Paraesophageal (below carina)
- **9** Pulmonary Ligament

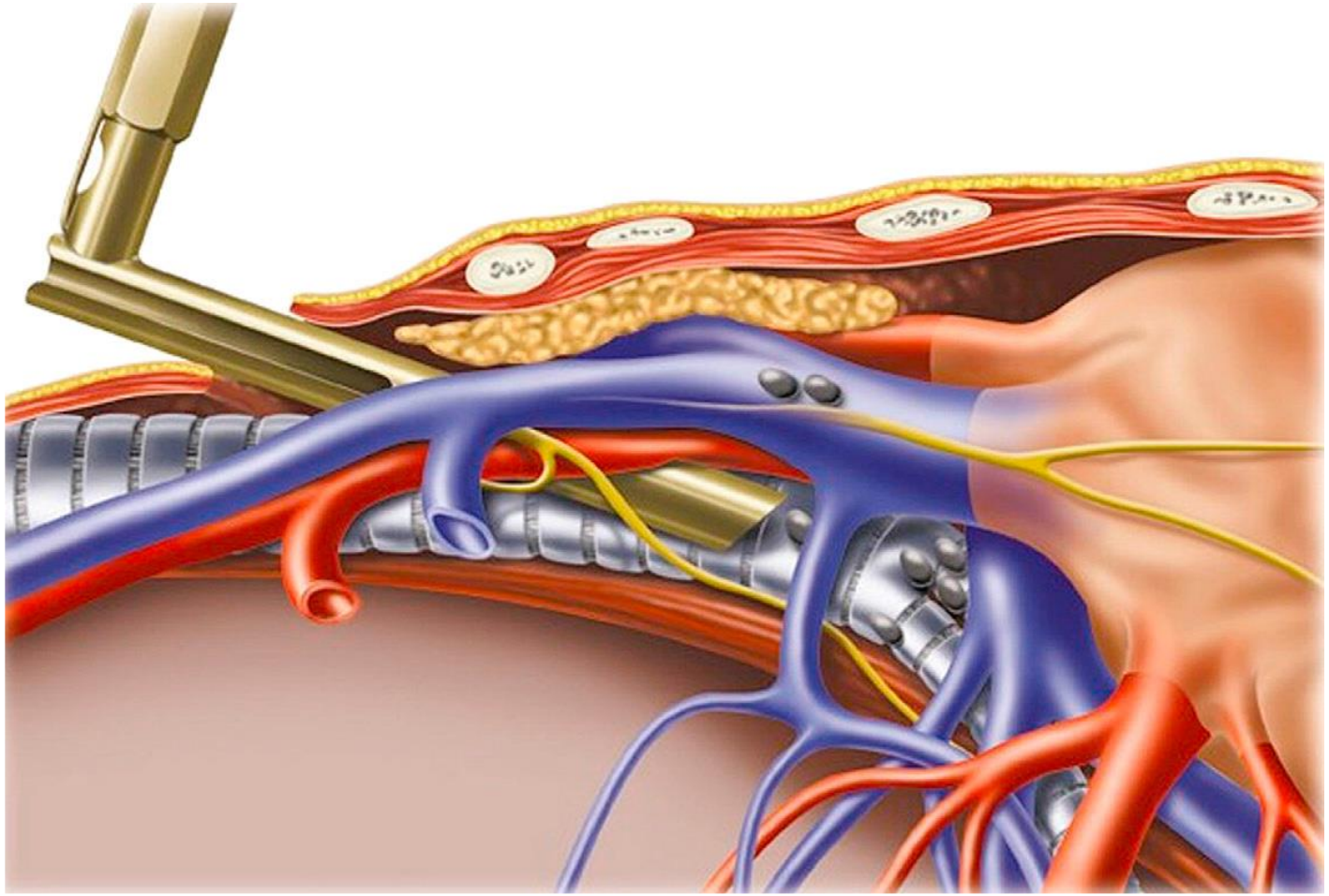
N_1 Nodes

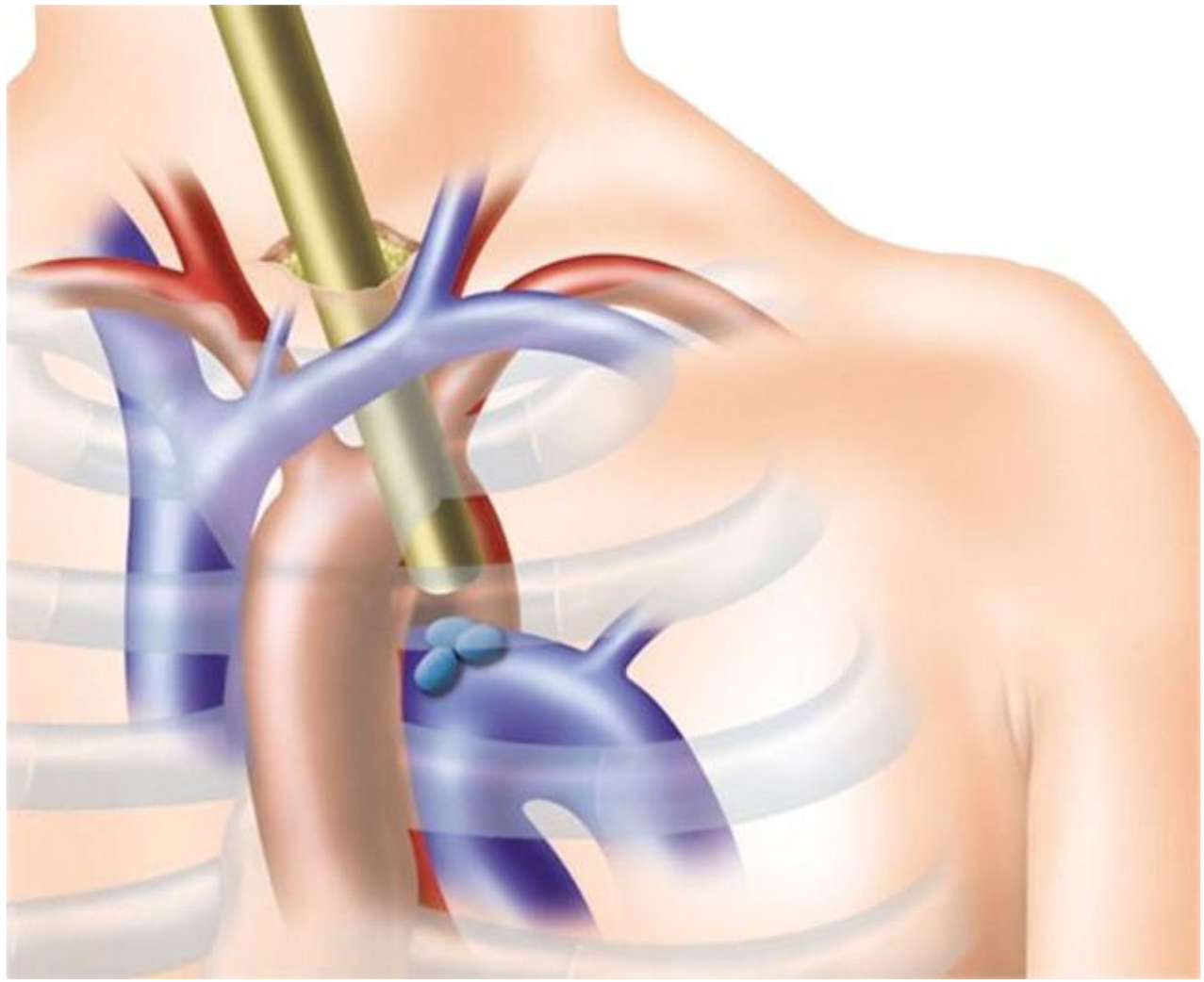
- **10** Hilar
- **11** Interlobar
- **12** Lobar
- **13** Segmental
- **14** Subsegmental

Journal of Thoracic Oncology


1
1
1
2R
2L
4R
4R
N2
4L
6
5
N1
10
7
7
7
10
N3
11
11
8
8
9
9

Video-Mediastinoscopy





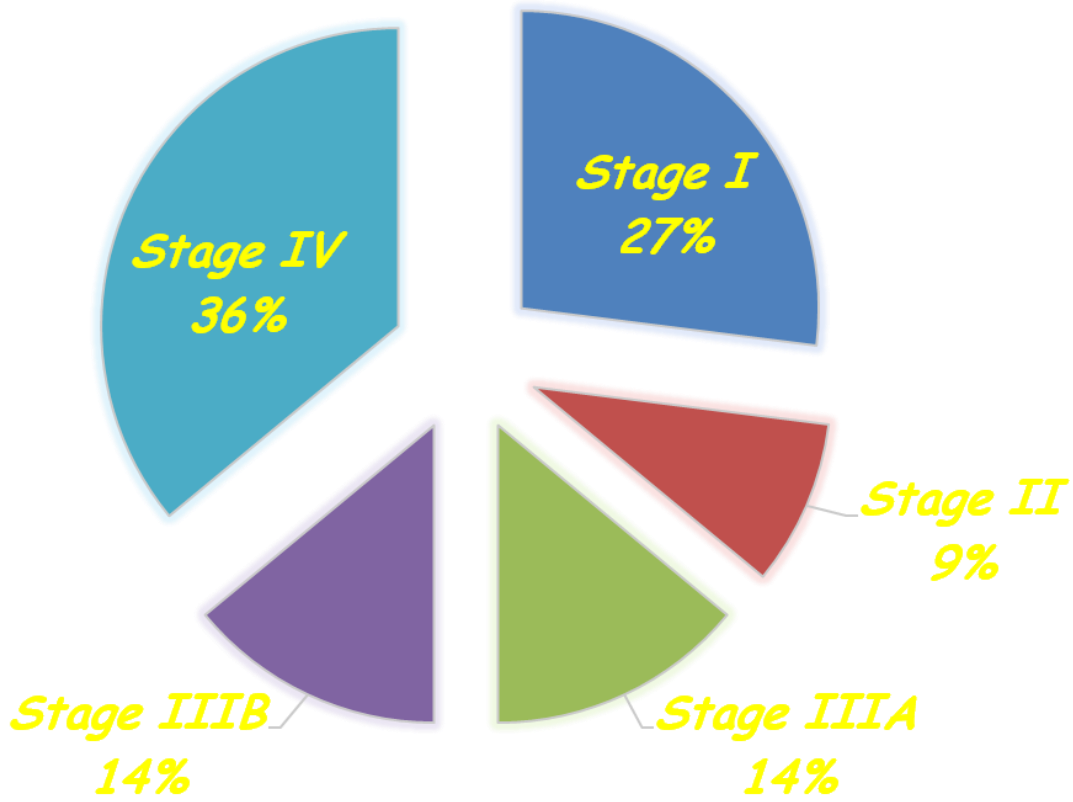
Thoracic Surgery Clinics 2010; 20:195-206

Distant Metastasis (M)

M classification		M component on CT
M0		No distal metastasis
M1	M1a	Intrathoracic metastasis
		Pleural effusion
		Pericardial effusion
		Contralateral lung nodules/pleural nodules
	M1b	Single extrathoracic metastasis in a single organ
	M1c	Multiple extrathoracic metastasis

8th TNM staging system

		N0	N1	N2	N3
M0	Tis	0			
	T1mi	IA1			
	T1a	IA1	IIB	IIIA	IIIB
	T1b	IA2	IIB	IIIA	IIIB
	T1c	IA3	IIB	IIIA	IIIB
	T2a	IB	IIB	IIIA	IIIB
	T2b	IIA	IIB	IIIA	IIIB
	T3	IIB	IIIA	IIIB	IIIC
	T4	IIIA	IIIA	IIIB	IIIC
M1a	Tx	IVA	IVA	IVA	IVA
M1b	Tx	IVA	IVA	IVA	IVA
M1c	Tx	IVB	IVB	IVB	IVB


Stage I
27%
Stage II
9%
Stage IIIA
14%
Stage IIIB
14%
Stage IV
36%

5-Year OS.

Survival rates by TNM grouping				
	Clinical stage		Pathologic stage	
	MST	5-year (%)	MST	5-year (%)
IA	60	50	119	73
IB	43	43	81	58
IIA	34	36	49	46
IIB	18	25	31	36
IIIA	14	19	22	24
IIIB	10	7	13	9
VI	6	2	17	13

Prognosis by TNM stage grouping, modified from Goldstraw et al. [2]. *MST* median survival time in months. 5-year overall survival

Treatment of NSCLC

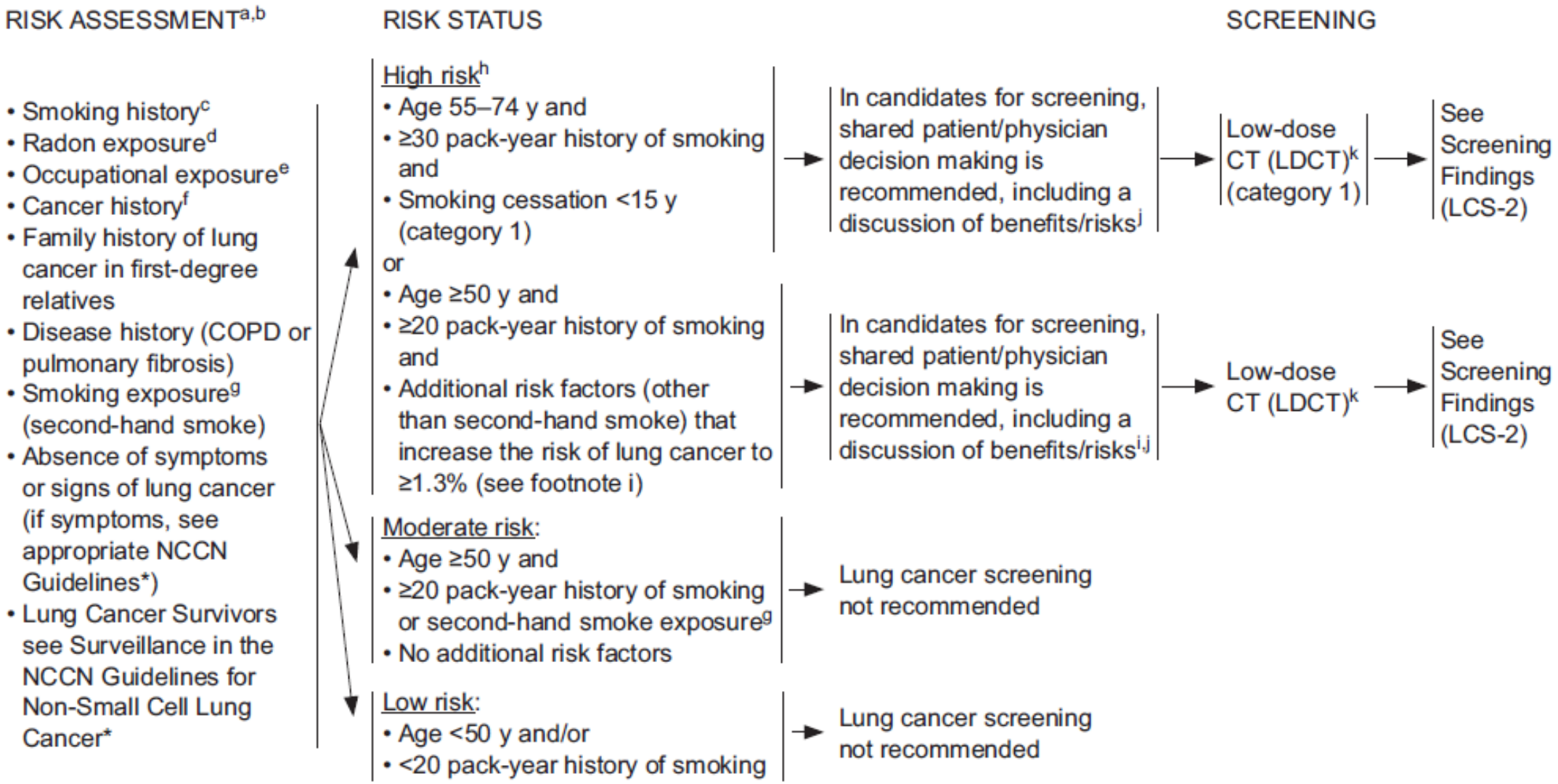
- Stage IA = Surgery
- Stage IB = Surgery ± Chemotherapy
- Stage IIA and IIB = Surgery + Chemotherapy
- Stage IIIA = Chemotherapy ± Surgery ± Radiotherapy
- Stage IIIB = Radiochemotherapy
- Stage IV = Palliative chemotherapy

WHO classification of tumors of the lung

- Squamous cell carcinoma
- Adenocarcinoma
- Large cell carcinoma
- Adenosquamous carcinoma
- Sarcomatoid carcinoma
- Salivary gland-type tumors
  - Mucoepidermoid carcinoma
  - Adenoid cystic carcinoma
  - Epithelial myoepithelial carcinoma
- Neuroendocrine Tumors
  - SCLC
  - Large cell neuroendocrine carcinoma
  - Carcinoid tumor
    - Typical
    - Atypical

https://www.pathologyoutlines.com/topic/lungtumorWHO.html

Lung Cancer Screening



Approximate sensitivity and specificity of diagnostic and staging investigations

Test	Sensitivity (%)	Specificity (%)
PET-CT	85–90	80–90
SPECT	65–90	75–85
Transthoracic needle aspiration	85–90	90–95
EUS-FNA	85–95	99
EBUS-TBNA	85–95	99
Bronchoscopy ± biopsy	70–90	90–95
Non-ultrasound-guided TBNA	40–70	99
Neck ultrasonography	80–90	99
Thoracoscopy	90–95	90–95
Mediastinoscopy	78–95	100

EBUS, endobronchial ultrasound; EUS, endoscopic ultrasound; FNA, fine needle aspiration; SPECT, single-photon emission CT; TBNA, transbronchial needle aspiration.

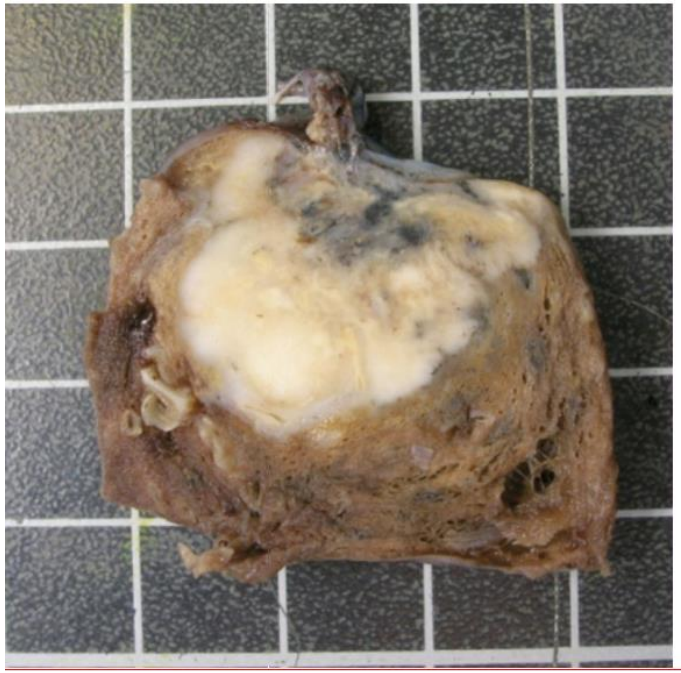
Prognosis

- Stage of the disease
- Completeness of the surgical resection
- Age
- Gender
- SUV of the PET/CT
- Diffuse bone marrow uptake in the absence of focal bone mets.

Squamous cell carcinoma

- 25% of lung cancers.
- More frequently diagnosed with endobronchial biopsy duo to its central location in the majority of cases.
- Large tumors may undergo central necrosis with cavity formation.
- Less distant mets.
- More locoregional recurrence after surgery.

Adenocarcinoma



- 40% of lung cancers.
- Peripheral adenocarcinoma with a V-shaped area of fibrosis with anthracotic pigmentation.
- Has a tendency for peripheral locations (75%).
- Diffiuse or lobar pneumonia with preservation of underlying lung architecture is typical for mucinous adenocarcinoma with lepidic growth pattern.
- Locoregional recurrence is less.
- Tend to mets. early.
- Derived from the mucus-producing cells of the bronchial epithelium.

Small cell lung cancer

- 13% of all lung cancers
- About 80% are centrally located.
- Aggressive tendency to metastasize.
- It often spreads early to mediastinal lymph nodes and distant sites, especially bone marrow and brain.
- Appears to arise in cells derived from the embryologic neural crest.
- Microscopically, these cells appear as sheets or clusters of cells with dark nuclei and little cytoplasm.

Small cell lung cancer

- The oat-like appearance under the microscope provides the term oat cell carcinoma to this disease.
- Neurosecretory granules are evident on electron microscopy.
- This tumor is staged as:
  - Limited stage (disease restricted to an ipsilateral hemithorax within a single radiation port).
  - Extensive stage (obvious metastatic disease).

Small cell lung cancer

- Most of these tumors are typically not treated by surgery
- Treatment
  - Limited stage: concurrent chemoradiotherapy ± prophylactic cranial irradiation PCI
  - (except in early stages like stages “T1-2N0”surgery has a role in treatment of SCLC)
  - Extended stage: palliative chemotherapy ± (PCI)
- Complete responses may occur in about 30% of patients but relapse is common
- The 5-year survival rate is only 5%.

Large cell carcinoma

- The term is used as a collective name for tumors that can’t be classified as Adenocarcinoma or SCC.
- 10%
- Specific cytologic features of SCC or ACA are lacking.
- Tend to occur peripherally and may metastasize relatively early.
- The histologic features are similar to those of SCLC.

Carcinoid Tumors

- Pulmonary carcinoids are malignant neuroendocrine tumors comprising 1% to 2% of all primary lung tumors and 85% of bronchial gland tumors.

- The treatment of choice for bronchial carcinoids is surgical resection.

- Prognosis is most significantly dependent on histology (typical versus atypical), with typical cases having an excellent long-term prognosis.

Typical carcinoid Tumors

- Constitute approximately 90%
- Tend to be central in location
- The 1999 WHO classification of this group of neoplasms is based on the absence of necrosis and less than two mitoses per high power field (HPF).
- Approximately 10% to 15% metastasize to lymph nodes.

Typical Carcinoids

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- Tend to be central in location
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- Approximately 10% to 15% metastasize to lymph nodes.

Atypical Carcinoids

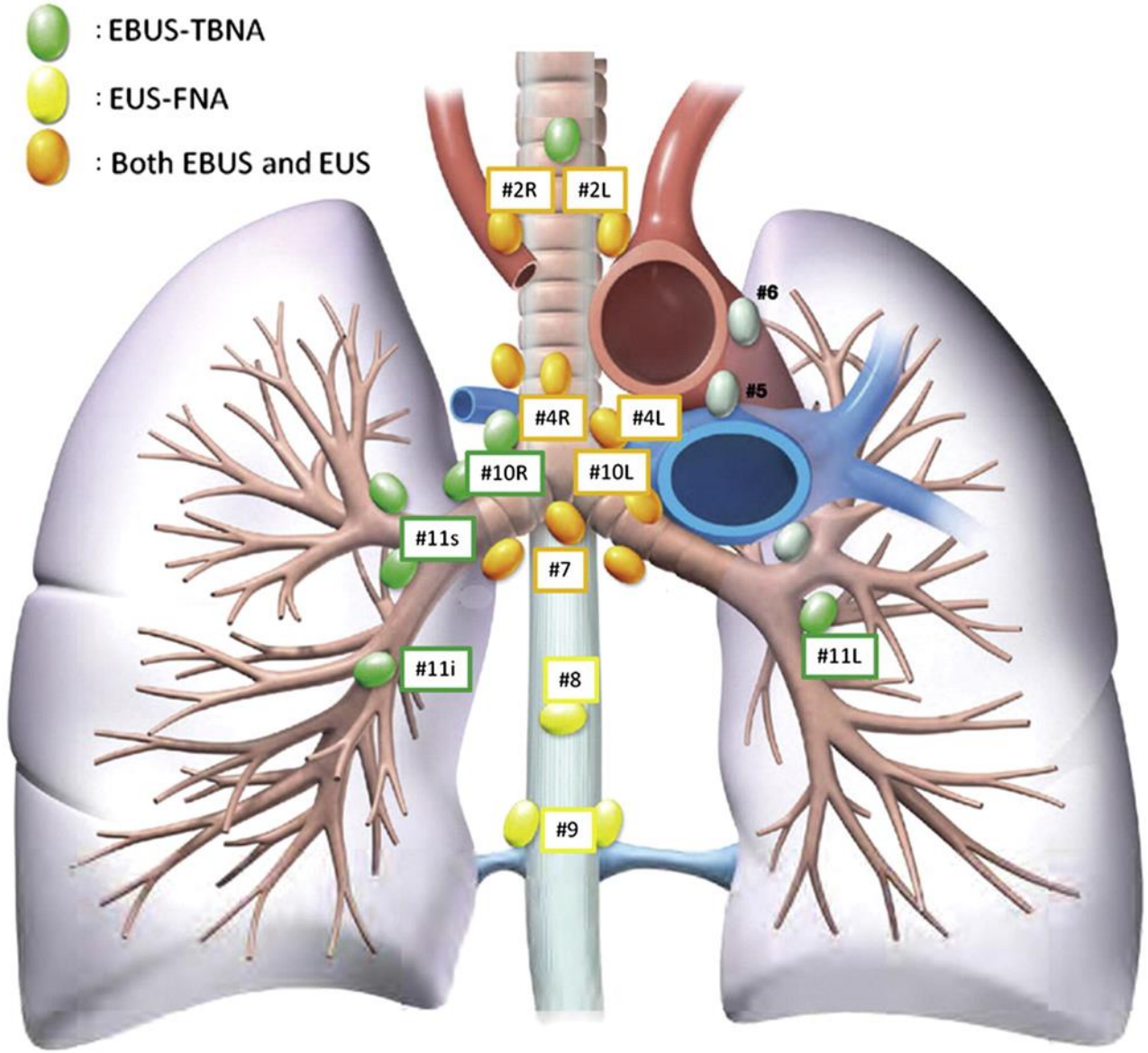
- 10% of bronchial carcinoids
- Usually larger at presentation
- More likely located in the lung periphery
- Presence of 5 to 10 mitoses per HPF is a characteristic
- the 1999 WHO classification includes the presence of necrosis or two to 10 mitoses per HPF
- 20-75% have regional lymph node involvement.

Carcinoid Tumors

- **Clinical Presentation**
  - Peripheral: asymptomatic
  - Central: cough, hemoptysis, wheezing and recurrent infection
  - Carcinoid syndrome <5%
  - Cushing's syndrome
- **Diagnosis**
  - CT scan
  - Octreotide scan
  - Bronchoscopy

Thank You

Key points in surgical management of lung cancer
1. Completely remove the tumor and all intrapulmonary lymphatic drainage. **Anatomical: Segmentectomy, lobectomy, sleeve resection and pneumonectomy** ***Non-anatomical:* Sublobar resection**
2. Take care not to transgress the tumor during resection in order to avoid tumor spillage.
3. Make an effort to perform en-bloc resection of adjacent or invaded structures rather than discontinuous resection.
4. Perform frozen section analysis on the bronchial margin and any other margins in close proximity to the tumor.
5. Remove or sample all accessible mediastinal lymph node stations for pathologic evaluation


: EBUS-TBNA
: EUS-FNA
: Both EBUS and EUS
#2R
#2L
#6
#5
#4R
#4L
#10R
#10L
#11s
#7
#11i
#8
#11L
#9

Lung Cancer Metastases

- LC with metastases is characterized as stage IV (any T, any N, M1).
- LC most commonly metastasize to the pulmonary and mediastinal lymph nodes (LN) (lymphatic spread).
- *Hematogenous spread* of LC is indiscriminate, and virtually all areas of the body are at risk.
- There is a particular predilection for NSCLC to spread to the adrenal glands, lung, bone, and brain

Lung Cancer Metastases

- The biology of lymphatic and hematogenous metastasis is different and a lack of mediastinal or hilar nodal involvement by no means precludes the ability of a NSCLC to metastasize systemically.
- Patients with these “skip” metastases are not uncommon.
- SCLC is the most aggressive tumor to metastasize to the LN. Typically, the pattern of spread is first to the hilar LN and then into the mediastinal (usually ipsilateral) LN.

Lung Cancer Metastases

- Tumors of the left lower lobe that metastasize to the mediastinal nodes involve *the contralateral* mediastinum in about 25% of patients.
- ACA is more likely to metastasize to the *CNS*, but SCCA may as well.
- Bone metastases are usually osteolytic. LC is the second most common cause of bone metastasis after breast cancer.
- Metastases rarely occur distal to the elbow or distal to the knee.

Pathology

- Slight preponderance of right lung because
  1. Right lung has ≈ 55% of the lung parenchyma
  2. More favorable anatomic path for carcinogens to travel through the downwardly acutely angled right main-stem bronchus.
- Upper lobes > Lower lobes.
- The blood supply is from the bronchial arteries.