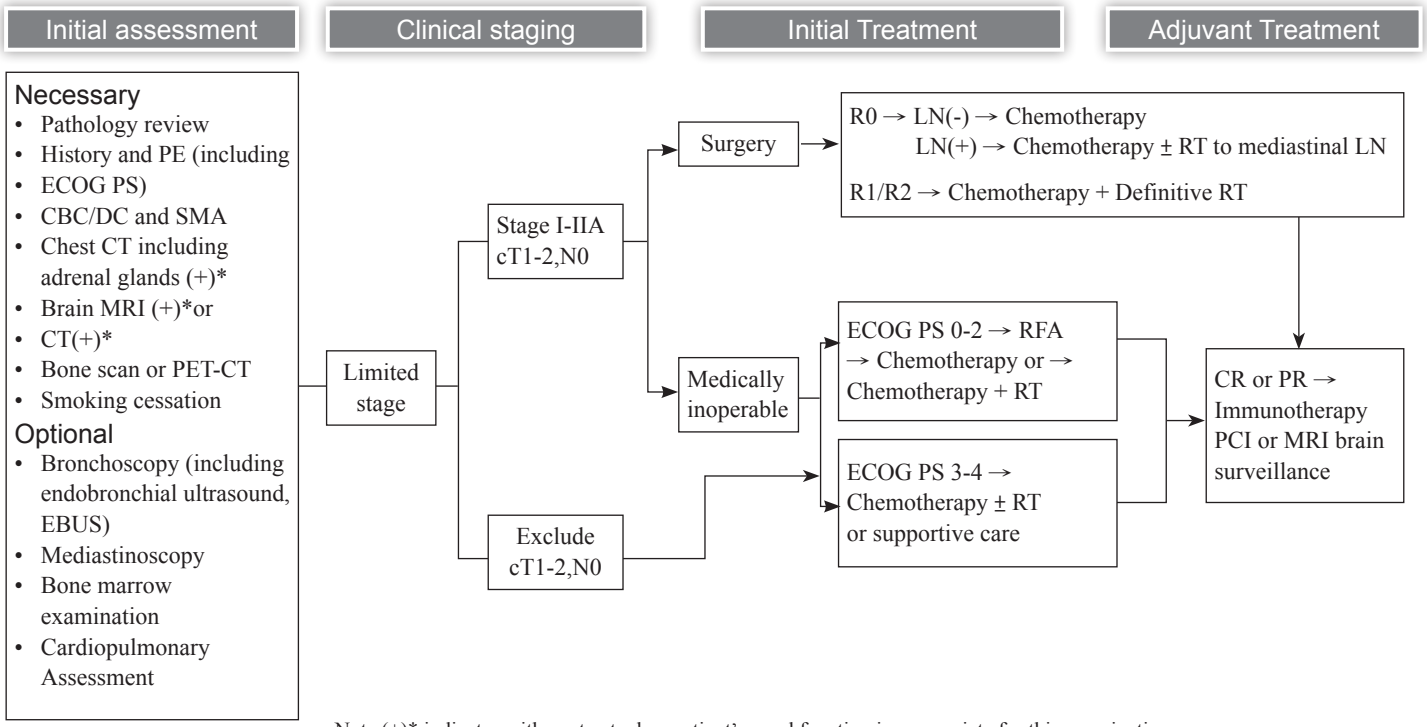
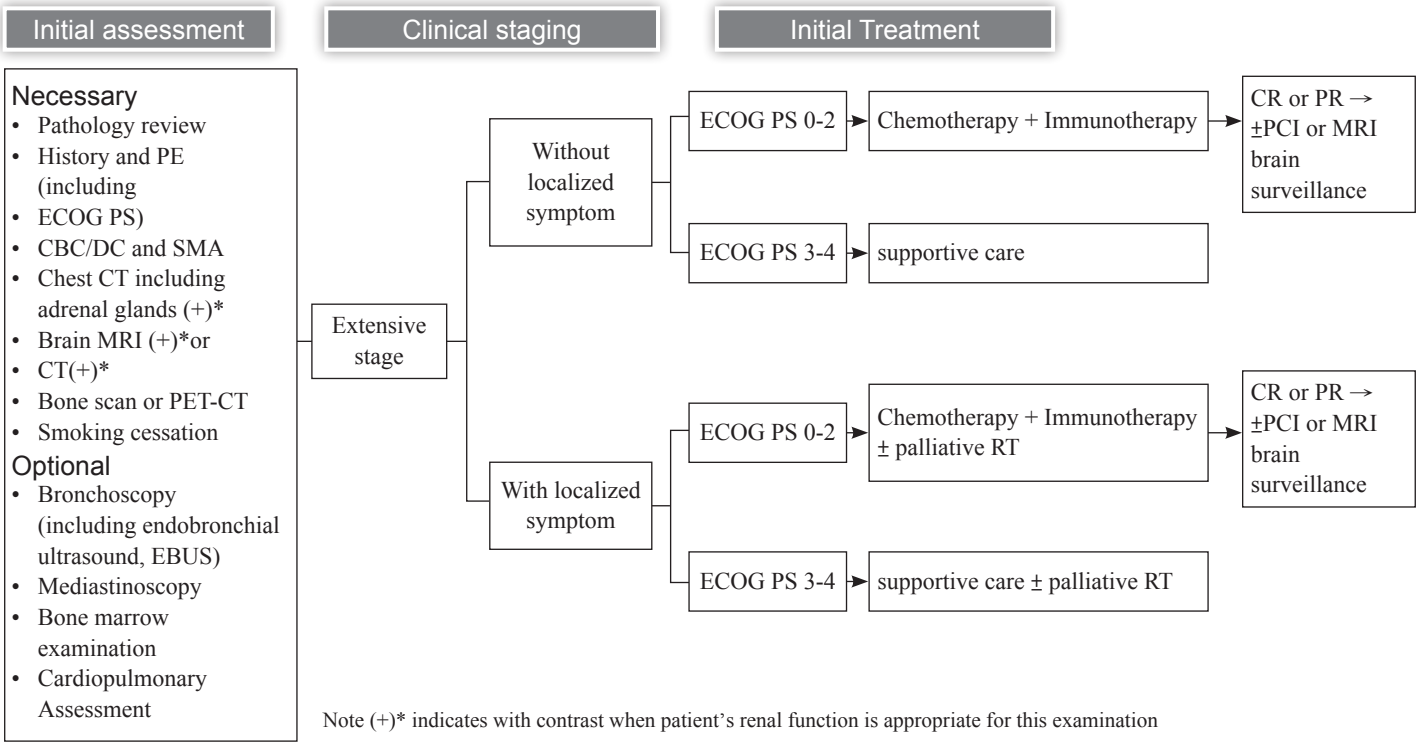
Lung Cancers

《 Small cell lung cancer guideline -1 》



Note (+)* indicates with contrast when patient's renal function is appropriate for this examination

《 Small cell lung cancer guideline - 2 》



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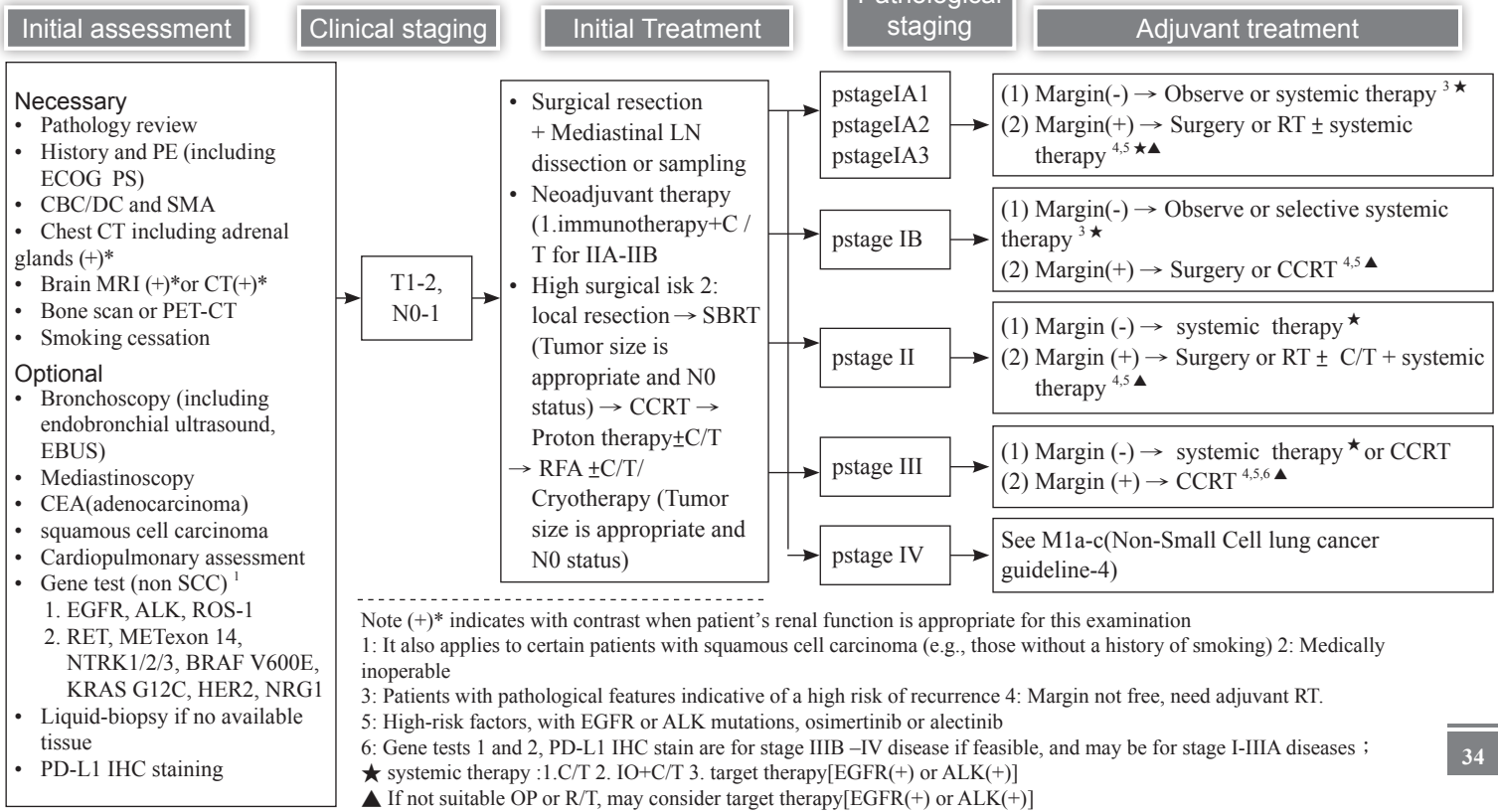
《 Non-Small cell lung cancer guideline -1 》



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1: It also applies to certain patients with squamous cell carcinoma (e.g., those without a history of smoking) 2: Medically inoperable

3: Patients with pathological features indicative of a high risk of recurrence 4: Margin not free, need adjuvant RT.

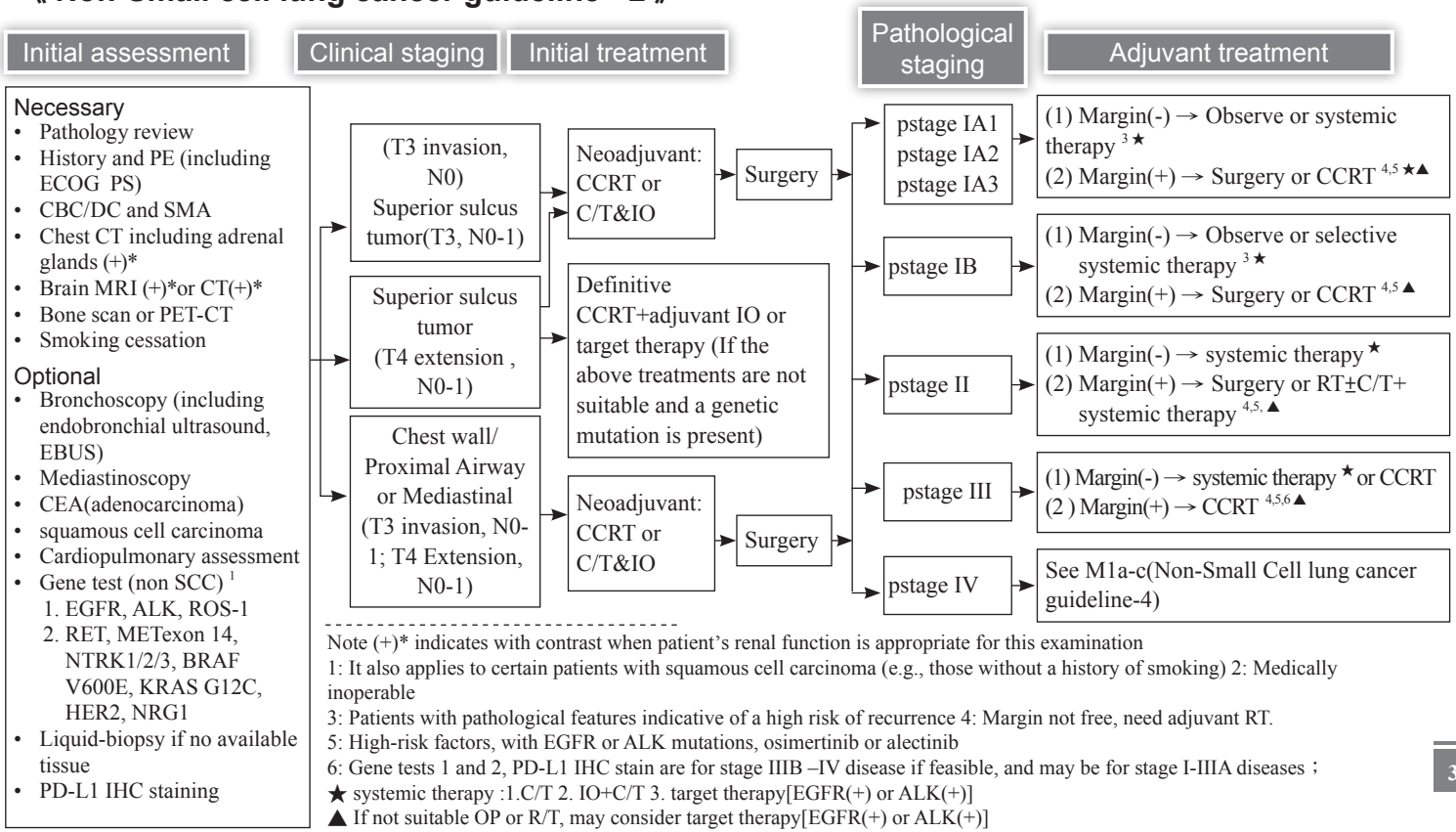
5: High-risk factors, with EGFR or ALK mutations, osimertinib or alectinib

6: Gene tests 1 and 2, PD-L1 IHC stain are for stage IIIB –IV disease if feasible, and may be for stage I-IIIA diseases；

★ systemic therapy :1.C/T 2. IO+C/T 3. target therapy[EGFR(+) or ALK(+)]

▲ If not suitable OP or R/T, may consider target therapy[EGFR(+) or ALK(+)]

《 Non-Small cell lung cancer guideline - 2 》



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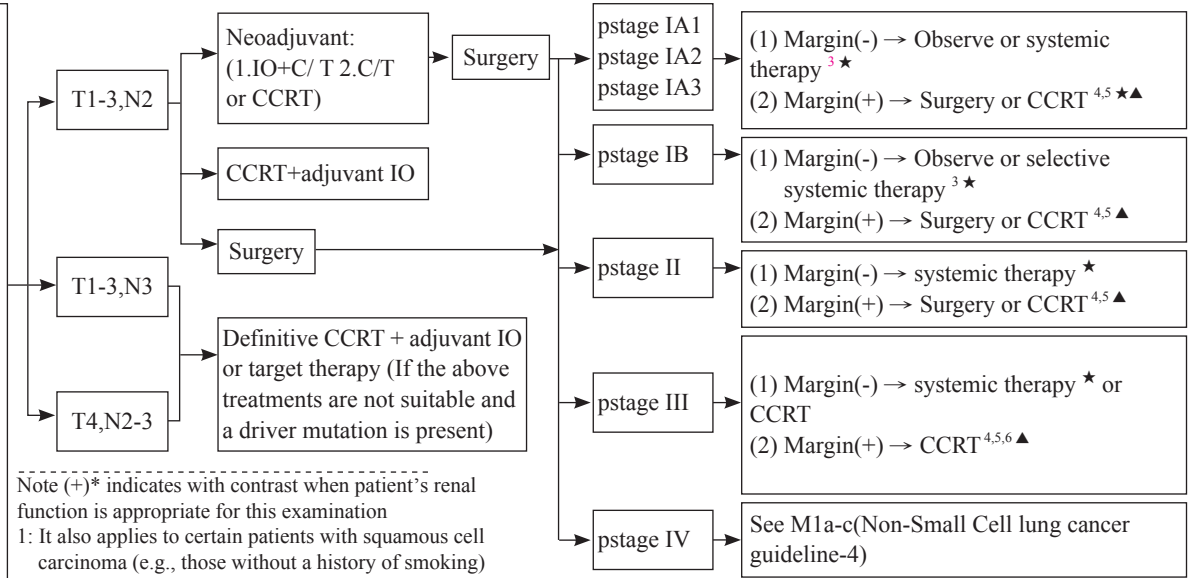
Initial assessment | Clinical staging | Initial treatment | Pathological staging | Adjuvant treatment

Necessary
- Pathology review
- History and PE (including ECOG PS)
- CBC/DC and SMA
- Chest CT including adrenal glands (+)*
- Brain MRI (+)*or CT(+)*
- Bone scan or PET-CT
- Smoking cessation

Optional
- Bronchoscopy (including endobronchial ultrasound, EBUS)
- Mediastinoscopy
- CEA(adenocarcinoma)
- squamous cell carcinoma
- Cardiopulmonary assessment
- Gene test (non SCC) [1]
  1. EGFR, ALK, ROS-1
  2. RET, METexon 14, NTRK1/2/3, BRAF V600E, KRAS G12C, HER2, NRG1
- Liquid-biopsy if no available tissue
- PD-L1 IHC staining



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《 Non-Small cell lung cancer guideline - 4 》

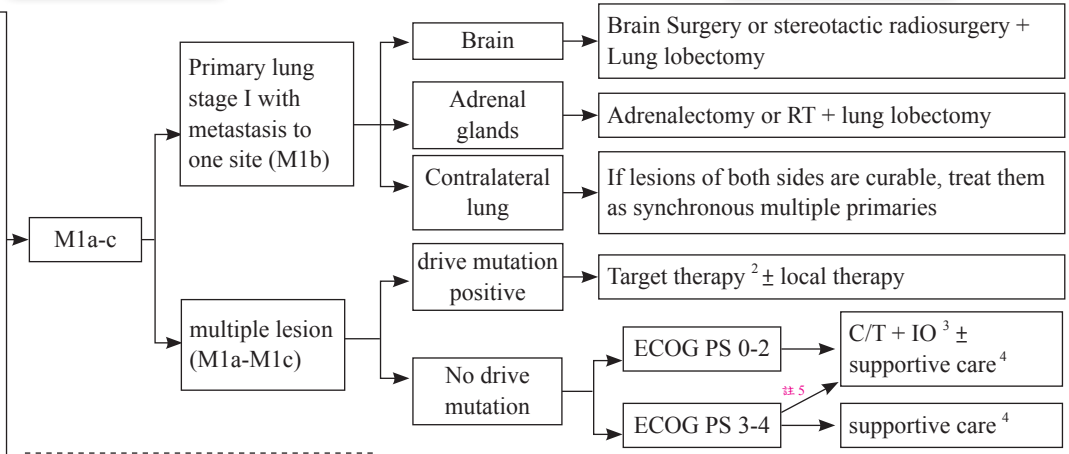
Initial assessment

Necessary
- Pathology review
- History and PE (including ECOG PS)
- CBC/DC and SMA
- Chest CT including adrenal glands (+)*
- Brain MRI (+)*or CT(+)*
- Bone scan or PET-CT
- Smoking cessation
- Gene test 1 (non SCC) [1]
  1.EGFR, ALK, ROS-1
- PD-L1 IHC staining

Optional
- Bronchoscopy (including endobronchial ultrasound, EBUS)
- Mediastinoscopy
- CEA(adenocarcinoma)
- squamous cell carcinoma
- Cardiopulmonary assessment
- Gene test 2 (non SCC) [1]
  RET, MET exon 14, NTRK1/2/3, BRAF V600E, KRAS G12C, HER2, NRG1
- Liquid-biopsy if no available tissue

Clinical staging

Initial Treatment



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1: It also applies to certain patients with squamous cell carcinoma (e.g., those without smoking history)

2: 1.EGFR exon 19 deletion or exon 21 L858R mutations-->EGFR TKI, osimertinib preferred; C/T+Osimertinib
2. EGFR S768I, L861Q, and/or G719X mutations-->Afatinib preferred
3. EGFR exon 20 insertion mutation-->C/T+Amivantamab
4. ALK rearrangement-->Alectinib or Brigatinib or Lorlatinib or Ceritinib
5. ROS1 rearrangement-->Entrectinib or Crizotinib or Repotrectinib
6. BRAF V600E mutation-->Dabrafenib+Trametinib
7. NTRK1/2/3 gene fusion-->Larotrectinib or Entrectinib or Repotrectinib
8. METex14 skipping mutation-->Capmatinib or Tepotinib
9. RET rearrangement-->Selpercatinib or Pralsetinib
10.KRAS G12C-->Sotorasib
11.HER2 mutation-->Trastuzumab deruxtecan

3: (1) PD-L1 ≥ 50% can consider mono IO
(2)PS 2 can consider mono chemo
(3)PD-L1 < 1% squamous cell carcinoma can chemo alone

4: Local palliative radiotherapy for local symptoms

5: If PS 3-4 is caused by cancer, consider active treatment

《Appendix》

- If there are suitable clinical trials, patients are encouraged to participate.

Principles of surgical treatment of lung cancer

Evaluate

- It should be provided by those who have passed specialist certification and whose main practice item is lung cancer surgery. The cavity surgeon decides whether the tumor can be removed surgically and performs related surgical staging, and lung resection.
- Computerized tomography and positron radiography for staging should be completed within 60 days before surgery.
- For patients who are eligible for surgery, surgical resection is the preferred local treatment option (superior to other modalities such as radiofrequency ablation, cryotherapy, and stereotactic body radiotherapy). Every patient being considered for curative local therapy should consult a thoracic surgical oncologist during evaluation. For high-risk patients who are not suitable for surgical resection and are being considered for stereotactic body radiotherapy, evaluation by a multidisciplinary team that includes a radiation oncologist is recommended.
- Before any non-emergency treatment, a complete treatment plan should be completed as well as the necessary imaging studies.
- Thoracic surgeons should actively participate in multidisciplinary team discussions for lung cancer patients such as multi-disciplinary comprehensive treatment clinics and/or tumor board.
- Patients who actively smoke should be given counseling and smoking cessation assistance. Even if smoking would slightly increase postoperative complications, but smoking should not be regarded as a contraindication to surgical disease. For patients with early stage lung cancer, surgery is an important treatment mode. In addition, physicians should not only consider the smoking status of patients and refuse to treat patients.

Resection

- For most patients with non-small cell lung cancer, anatomical lung resection is the first choice.
- Sublobectomy (nodal segment resection and wedge resection) should reach the lung parenchymal margin 2 cm or more or the size of the nodule.
- Unless the technology is impossible feasibility, in the case of surgery without significantly increasing the risk of surgery, N1 and N2 should be dealt with biopsy of lymph nodes.
- Nodular resection (preferred) or wedge resection, It can be applied to some specific patients for the following reasons:
  - Poor pulmonary reserve or due to other serious comorbidities cannot accept lobectomy
  - Peripheral nodules ≤ 2 cm, and meet at least one of the following criteria:
    - The histological type is pure adenocarcinoma in situ (AIS)
    - CT examination shows that nodules ≥ 50% are ground glass opacity (GGO)
    - Follow-up imaging examination confirmed that the tumor doubling time is longer (≥ 400 days)
- If the patient has no anatomical and surgical contraindications, as long as it does not violate oncology treatment standards and principles of thoracic surgery, video-assisted thoracoscopic surgery should be strongly recommended, including robotic-assisted thoracic surgery.
- In high volume centers (high caseload centers) and have comparable experience in thoracoscopic surgery, select certain patients to perform thoracoscopic lobectomy can improve short-term results (pain, length of hospital stay, return to normal function can time) without jeopardizing the prognosis of cancer.
- T3 (invasion) and T4 locally expanded tumors require en-bloc resection there are tissue structures involved in the tumor,
- with the goal of achieving negative margins.

Margins and lymph node assessment

- If the anatomical position is appropriate and the resection margin can be negative, anatomic resection (lobectomy) that preserves lung tissue is better than pneumonectomy surgery.
- N1 and N2 lymph nodes are removed and their locations are marked (at least 3 lymph nodes at N2 station sampling or complete lymph node dissection) should be an example of lung cancer resection line component.
- Patients with stage IIIA (N2) should undergo regular ipsilateral mediastinal lymphatics when undergoing resection
- familiar removal surgery.
- Complete resection requires negative surgical margins, systemic lymphatic dissection or sampling, and the highest mediastinal lymph nodes were negative. If the margin is positive, there is no removal of positive lymph nodes, or positive pleural or pericardial effusion, defined for incomplete resection. Complete resection is classified as R0. If the pathological microscopy is positive, it is R1, and the residual tumor visible to the naked eye is R2.
- Patients whose postoperative pathological stage is stage II or above should be referred to thoracic tumors section for evaluation.
- Patients with stage IB may be referred to the Department of Thoracic Oncology, and patients with stage IIIA may be considered referral to the Department of Radiation Oncology.

The role of surgery in stage IIIA (N2) patients

- The role of surgery in pathologically diagnosed N2 patients remains to be clarified.so far, there have been two randomized Phase III clinical trials exploring this topic. Both reports show that surgery failed to increase the overall number of patients in this group survival rate. However, patients in this group are quite heterogeneous (heterogeneity), the discussion group believes that these two trials are related to the N2 population the lack of a more refined evaluation of the heterogeneity leads to in some specific situations, the oncological benefit of surgery to patients cannot be confirmed.
- Whether mediastinal lymph gland metastasis or not, the prognosis of the disease and treatment decisions has a profound impact, so whether the patient has N2 disease, it must be treated as far as possible, it is determined by imaging and aggressive staging.
- If the patient is found to be occult-positive during the operation the N2 lymph nodes should undergo the original tumor resection, supplemented by the mediastinal cavity Lymph node dissection. If N2 disease is found in a patient receiving VATS, you can consider stopping the operation and allowing the patient to undergo induction therapy before undergoing the operation; However, continuing the original surgery is also a treatment option.
- The role of surgery in the treatment of patients with positive N2 lymph nodes should be initiating treatment previously, it was evaluated by a multi-disciplinary team including thoracic surgeons.
- If the N2 lymph node is suspected to be positive in imaging studies, N3 will be greatly increased the possibility of a positive lymph node. Therefore, the pathological evaluation of the mediastinum must include the subcarinal lymph nodes and the contralateral lymph nodes of the trachea. Mediastinoscopy can complete the pathological evaluation and staging of mediastinal lymph nodes.
- Bronchoscopy ultrasound and upper gastrointestinal endoscopy ultrasound can be used as auxiliary minimally invasive technology to help. Even if these assessments are performed, it is important that in the end before making treatment decisions, properly assess the location and slices of mediastinal lymph nodes number, and record that the contralateral lymph gland is negative.
- Although it is feasible to repeat mediastinoscopy, compared with the initial mediastinoscopy, the technical difficulty is high and the accuracy is low. One possible strategy is to initially perform EBUS ($\pm$ EUS) during the pre-treatment assessment and retain mediastinoscopy, after neoadjuvant treatment, lymph nodes were re-staged using mediastinoscopy.

- N2-positive patients with a single lymph node and less than 3 cm can be considered diversified treatment including surgery.
- The restaging after neoadjuvant therapy should include computed tomography +/- positron scans. In order to rule out disease progression or metastasis.
- Patients whose mediastinum is negative after neoadjuvant therapy have a better prognosis.
- Among NCCN member institutions, one-third use neoadjuvant chemoradiotherapy, while the remaining two-thirds use neoadjuvant chemotherapy alone.

  Postoperative radiotherapy (if radiotherapy was not given preoperatively) appears to result in similar overall survival. Neoadjuvant chemoradiotherapy is associated with a higher rate of pathological complete response and a higher proportion of mediastinal lymph node negativity, but at the cost of increased acute toxicity and higher treatment expenses.
- When the radiation dose of neoadjuvant chemoradiotherapy is lower than that used for standard definitive treatment, every effort should be made to minimize interruptions in radiotherapy that may occur due to surgical evaluation.

  A treatment interruption exceeding one week is considered unacceptable.
- When timely surgical evaluation cannot be performed, neoadjuvant chemoradiotherapy should not be used as a treatment strategy. Another option, in selected cases and with the agreement of a thoracic surgeon, is to complete a definitive dose of radiation first, followed by re-evaluation and consideration of surgery.

  If the surgeon or tumor board is uncertain about the feasibility or safety of resection after definitive radiotherapy, consultation with thoracic surgery experts at a high-caseload medical center may be considered.

  During resection, soft tissue flap coverage of the bronchial stump within the previous radiation field may also be considered.
- Data from a large multi-institutional trial indicate that pneumonectomy after neoadjuvant chemoradiotherapy carries a higher risk of complications and mortality.

However, it remains unclear whether this risk also applies to patients who receive neoadjuvant chemotherapy alone.
In addition, experience from several single-institution studies has demonstrated the safety of pulmonary resection after neoadjuvant therapy. Moreover, there is no evidence that adding radiotherapy to neoadjuvant chemotherapy improves outcomes in patients with resectable stage III (N2) disease

《 Lung cancer follow up (5 years follow up program)》

(一) Small cell Lung cancer

First 3 years: H&P + Chest CT(including liver and adrenal gland)±Brain MRI±Bone scan 3-6 monthly
After 3 years: H&P + Chest CT(including liver and adrenal gland)±Brain MRI±Bone scan 6 monthly

(二) Non-small cell lung cancer after surgery

First 2 years: 3-6 monthly, H & P + CXR + Chest CT±Brain MRI±Bone scan
After 2 years: 6 monthly, H & P + CXR + Chest CT±Brain MRI±Bone scan
After 5 years: 12 monthly, H & P + CXR + Chest CT±Brain MRI±Bone scan

(Note: For AIS or MIA, a longer follow-up interval may be considered)

《Appendix》AJCC TNM staging system, 9th edition

T/M	Categories and Descriptors	N0	N1	N2a	N2b	N3
T1	T1a ≤ 1 cm	IA1	IIA	IIB	IIIA	IIIB
	T1b >1 to ≤ 2 cm	IA2	IIA	IIB	IIIA	IIIB
	T1c >2 to ≤ 3 cm	IA3	IIA	IIB	IIIA	IIIB
T2	T2a Visceral pleura / central invasion	IB	IIB	IIIA	IIIB	IIIB
	T2a >3 to ≤ 4 cm	IB	IIB	IIIA	IIIB	IIIB
	T2b >4 to ≤ 5 cm	IIA	IIB	IIIA	IIIB	IIIB
T3	T3>5 to ≤ 7 cm	IIB	IIIA	IIIA	IIIB	IIIC
	T3 Invasion	IIB	IIIA	IIIA	IIIB	IIIC
	T3 Same lobe separate tumor nodules	IIB	IIIA	IIIA	IIIB	IIIC
T4	T4>7 cm	IIIA	IIIA	IIIB	IIIB	IIIC
	T4 Invasion	IIIA	IIIA	IIIB	IIIB	IIIC
	T4 Ipsilateral separate tumor nodules	IIIA	IIIA	IIIB	IIIB	IIIC
M1	M1a Contralateral tumor nodules	IVA	IVA	IVA	IVA	IVA
	M1a Pleural / pericardial effusion, nodules	IVA	IVA	IVA	IVA	IVA
	M1b Single extrathoracic metastasis	IVA	IVA	IVA	IVA	IVA
	M1c1 Multiple metastases in 1 organ system	IVB	IVB	IVB	IVB	IVB
	M1c2 Multiple metastases in >1 organ systems	IVB	IVB	IVB	IVB	IVB

《 Reference 》

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一、Treatment field

1. Gross primary lung tumor or lung tumor bed
2. Gross node area
3. High risk elective node area
4. Prophylactic whole brain

二、Dose prescriptions

Non-small cell lung cancer

◎ Neoadjuvant radiotherapy

47 Gy (45~54 Gy/25~30 fractions

◎ Adjuvant radiotherapy

1. Residual lung tumor or lung tumor bed： 60~64 Gy/30~32 fractions or 66~70 Gy /33~35 fractions
2. High risk area： 50~54 Gy/25~30 fractions
3. fraction size：1.8~2.0Gy

◎ Definitive RT

1. Conventional RT

   Gross lung tumor：60-64 Gy/30-32 fractions 或 66-70 Gy/33-35fractions
2. SABR

   30 Gy (25~34 Gy)/1fraction、52Gy(45-60Gy)/3Fx、49Gy(48-50Gy)/4Fx、52Gy(50-55Gy)/5Fx、65Gy(60-70Gy)/8-10Fx(hypofractions)

   Have to use IGRT technique

Small cell lung cancer

◎ Lung tumor

Total dose 62 Gy (60~64 Gy)/30~32 fractions or 68 Gy (66~70 Gy) /33~35 fractions or 45~60Gy/30~40 fractions(BID) or 65Gy/26 fractions or 40Gy/15fraction

◎ Prophylactic whole brain irradiation
Total dose：25 Gy (24~26 Gy)/12~13 fractions or 28 Gy (26~30 Gy) /13~15 fractions[註2] ，once daily, 5-6 fractions per week
[註2]Suggestion 25 Gy/10 fractions；If extensive stage suggestion 20 Gy/5 factions

三、RT technique：

When use IMRT techniques, including VMAT, image guidance can be considered. Different IMRT techniques have been accepted, including sequential boost and simultaneous integrated boost (SIB).

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