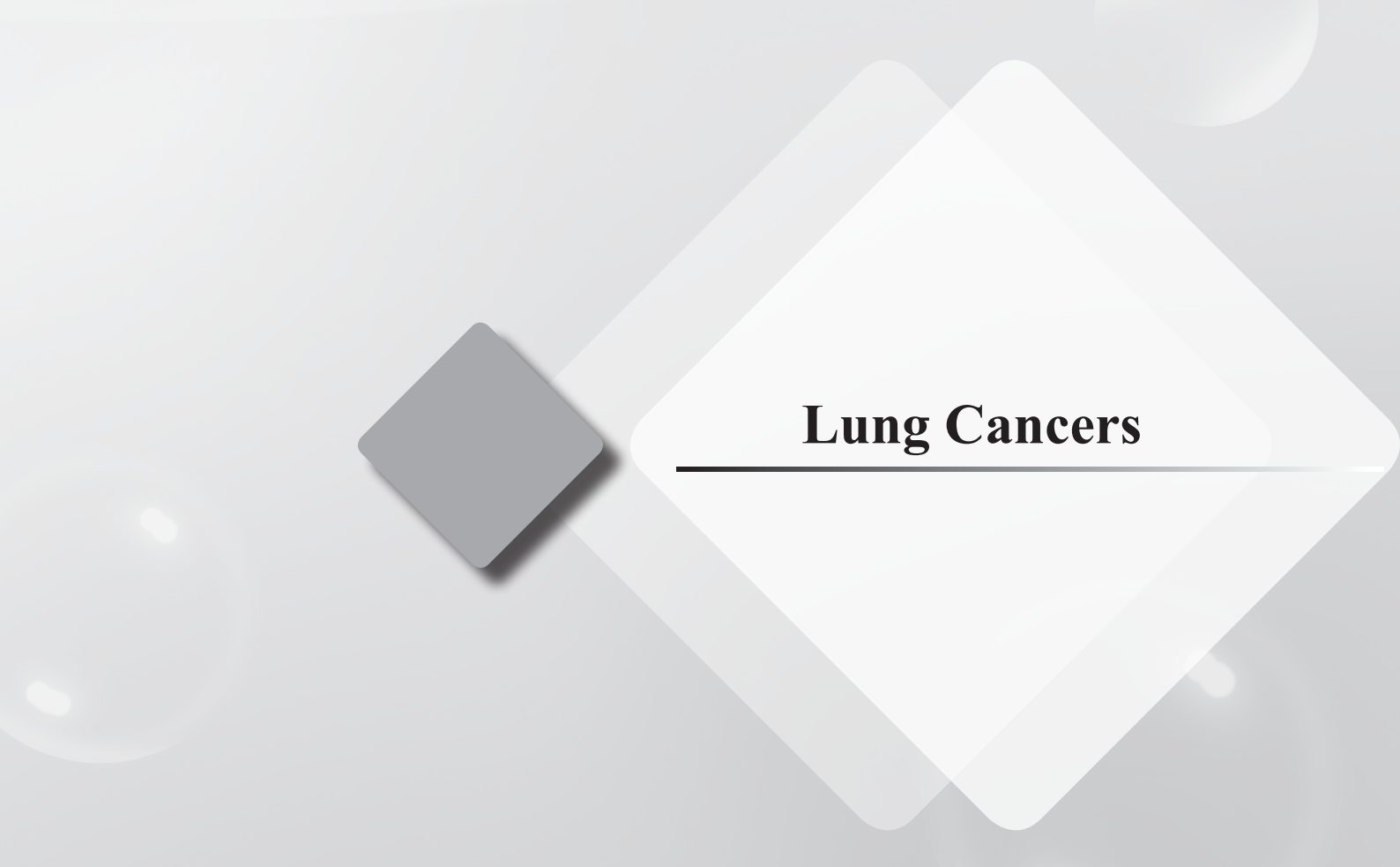
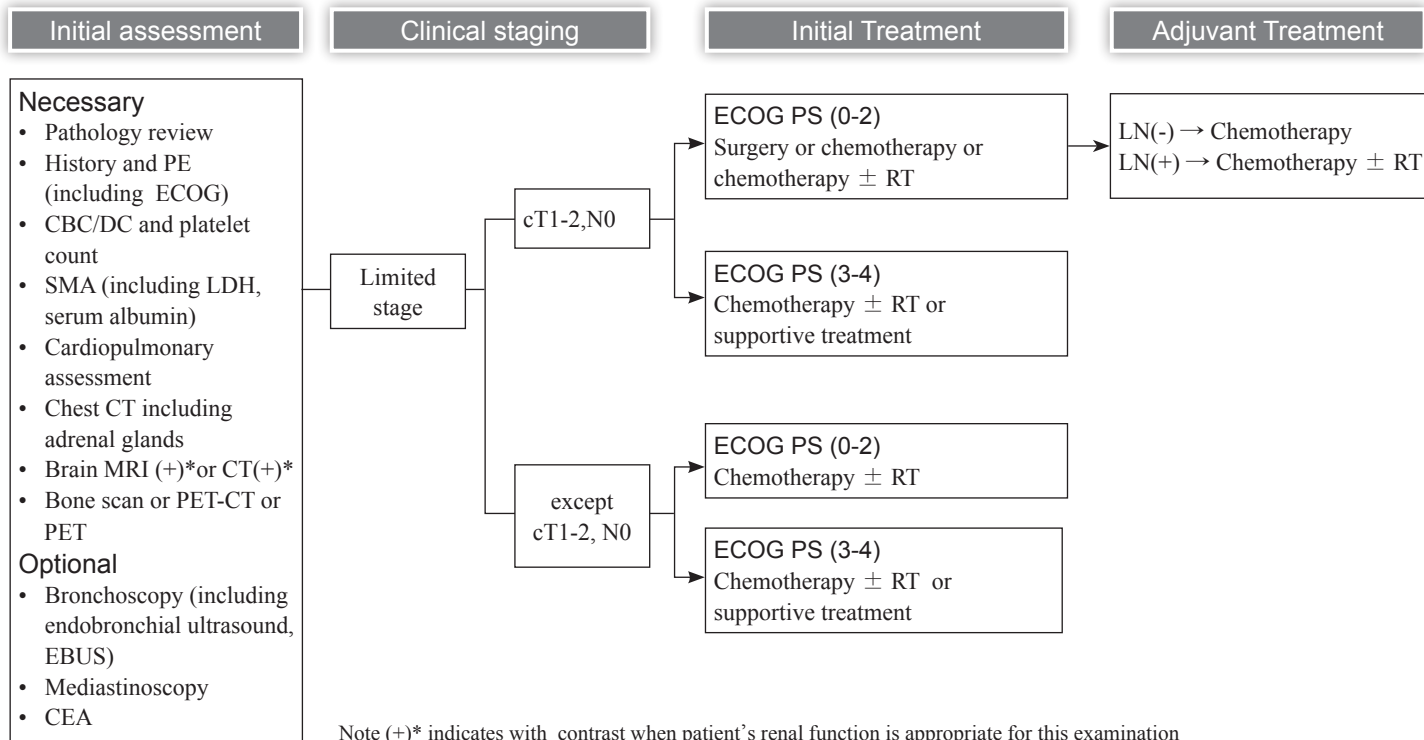




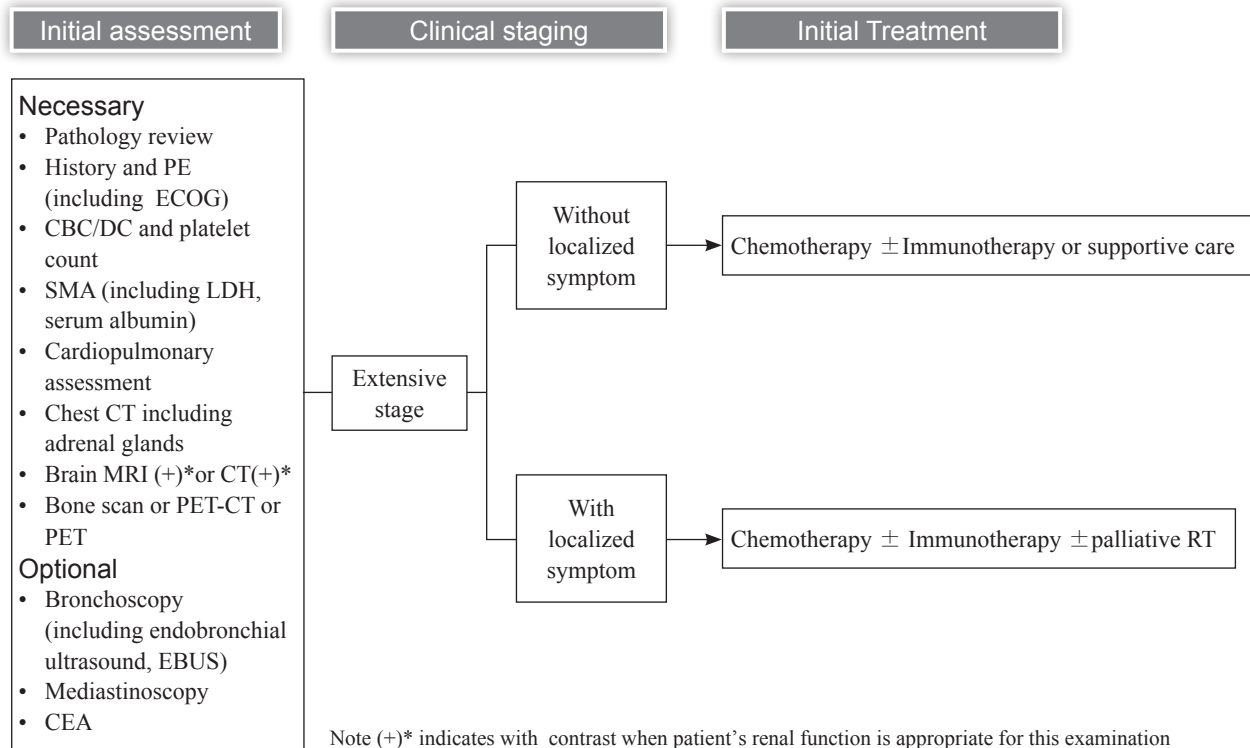
Lung Cancers

《 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 》



臺北癌症中心
TMU Taipei Cancer Center



《 Non-Small cell lung cancer guideline - 2 》

Initial assessment

Necessary

- Pathology review
- History and PE (including ECOG)
- CBC/DC and platelet count
- SMA (including LDH, serum albumin)
- Cardiopulmonary assessment
- Chest CT including adrenal glands
- Brain MRI (+)*or CT(+)*
- Bone scan or PET-CT or PET
- Gene test 1*. EGFR, ALK, ROS-1
- Gene test 2** RET, MET exon 14, NTRK1/2/3, BRAF V600E, KRAS G12C, HER2
- PD-L1

Optional

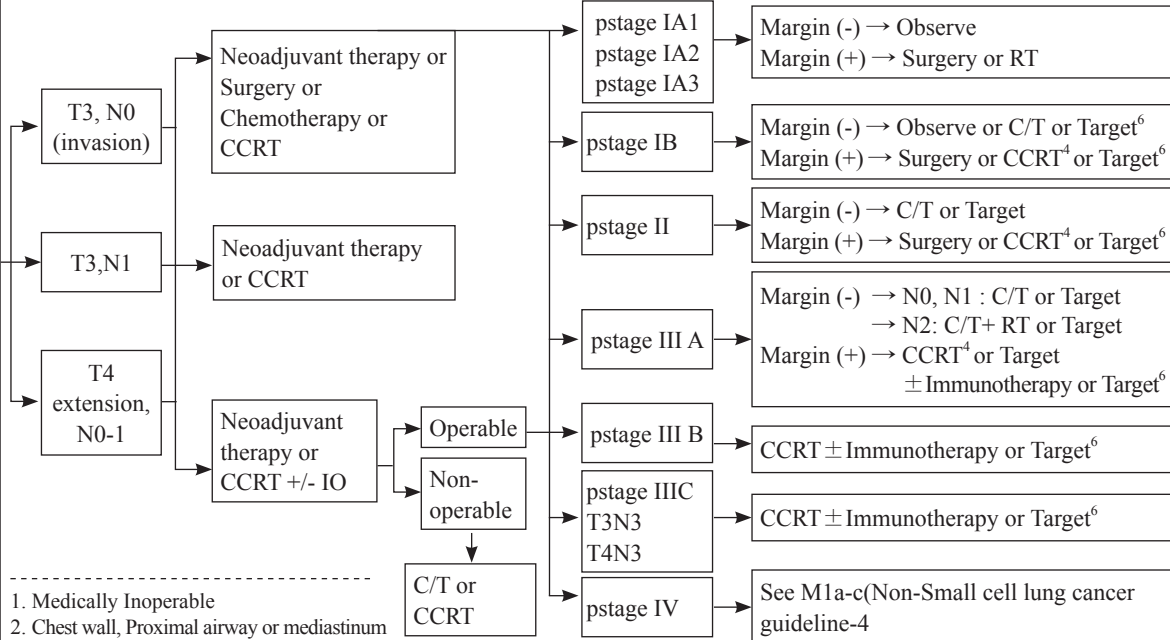
- Bronchoscopy (including endobronchial ultrasound, EBUS)
- Mediastinoscopy
- CEA (adenocarcinoma)
- SCC (squamous cell carcinoma)
- TPMI gene profile test

Clinical staging

Initial treatment

Pathological staging

Adjuvant treatment



1. Medically Inoperable
2. Chest wall, Proximal airway or mediastinum
3. Superior sulcus tumor
4. Margin not free, need adjuvant RT
5. High-risk factors, with EGFR mutations, osimertinib(optional)
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

《 Non-Small cell lung cancer guideline - 3 》

Initial assessment

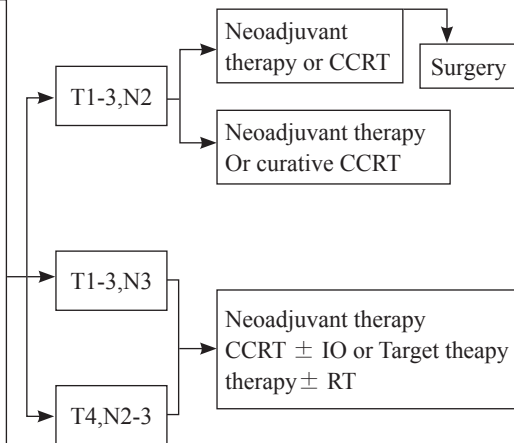
Necessary

- Pathology review
- History and PE (including ECOG)
- CBC/DC and platelet count
- SMA (including LDH, serum albumin)
- Cardiopulmonary assessment
- Chest CT including adrenal glands
- Brain MRI (+)*or CT(+)*
- Bone scan or PET-CT or PET
- Gene test 1*: EGFR,ALK, ROS-1
- Gene test 2**:
RET, MET, exon 14,
NTRK1/2/3, BRAF V600E,
KRAS G12C, HER2
- PD-L1

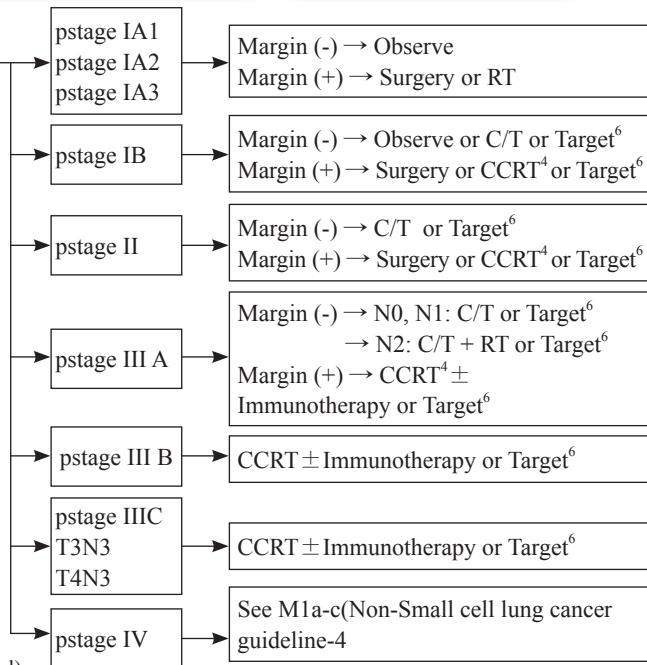
Optional

- Bronchoscopy (including endobronchial ultrasound, EBUS)
- Mediastinoscopy
- CEA (adenocarcinoma)
- SCC (squamous cell carcinoma)
- TPMI gene test

Clinical staging

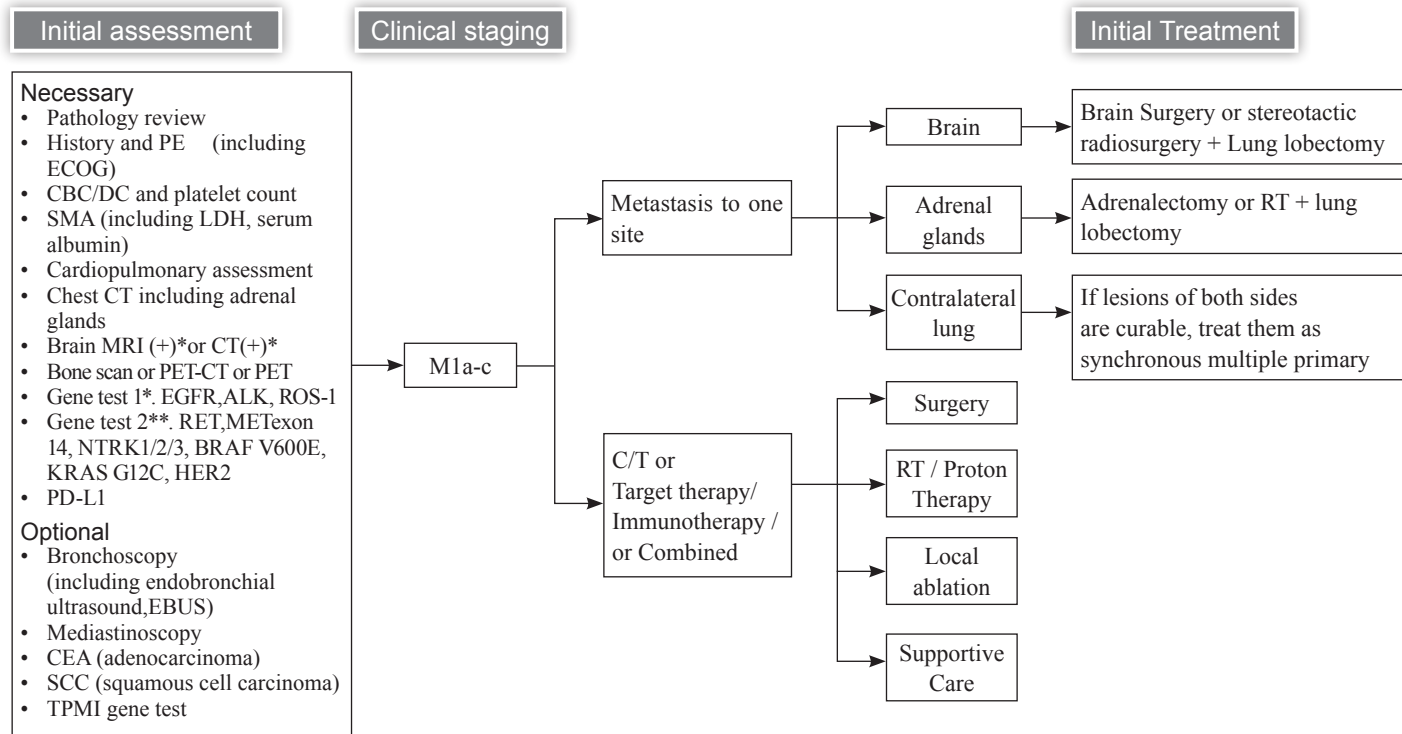


Pathological staging



-
1. Medically Inoperable
 2. Chest wall, Proximal airway or mediastinum
 3. Superior sulcus tumor
 4. Margin not free, need adjuvant RT
 5. High-risk factors, with EGFR mutations, osimertinib(optional)
 6. Gene tests 1 and 2, PD-L1 IHC stain are for stage IIIB-IV diseases if feasible, and may be for stage I-IIIA diseases

《 Non-Small cell lung cancer guideline - 4 》



《 Non-Small cell lung cancer guideline -Appendix 》

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.
- Surgical resection (including wedge resection) is better than tumor ablation (radiofrequency ablation, Microwave ablation, cryotherapy, stereotactic radiotherapy). Everyone considers the line .Patients with radical local treatment should consult their chest cavity during evaluationThe opinion of the oncologist. Surgical removal of high-risk patients consider Yili. For body-oriented radiotherapy, it is recommended that many specialists including radiation oncologists.The team evaluates it.

Principles of surgical treatment of lung cancer

- Before any non-emergency treatment, a complete treatment plan should be completed and necessary The necessary imaging studies.
- Thoracic surgeons should actively participate in multidisciplinary team discussions for lung cancer patients Discussions and meetings (such as multi-specialty comprehensive treatment clinics and/or tumor committees).
- 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 surgery disease. For patients with early stage lung cancer, surgery is an important treatment mode, because In addition, physicians should not only consider the smoking status of patients, and refuse to treat patients.Surgery.

Principles of surgical treatment of lung cancer 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 Sample 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 $\geq 50\%$ are ground glass
- Follow-up imaging examination confirmed that the tumor doubling time is longer (≥ 400 days)

Principles of surgical treatment of lung cancer

- If the patient has no anatomical and surgical contraindications, as long as the swelling is not violated tumor treatment standards and principles of thoracic surgery resection should be strongly recommended (strongly considered) Patients choose minimally invasive video-assisted thoracoscopic surgery (Including robotic arm assisted surgery).
- In high volume centers (high volume centers) and have comparable Experience in thoracoscopic surgery, select certain patients to perform thoracoscopic lobes resection can improve short-term results (pain, length of hospital stay, return to normal function can time) without jeopardizing the prognosis of cancer.
- 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.

Principles of surgical treatment of lung 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. resection margin and lymphatic 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. Radical removal surgery

Principles of surgical treatment of lung cancer

- 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, 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.

Principles of surgical treatment of lung cancer

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 experimental 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.

Principles of surgical treatment of lung cancer

The role of surgery in stage IIIA (N2) patients

- 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.

Principles of surgical treatment of lung cancer

- 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. Vertical diaphragmoscope surgery 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.

Principles of surgical treatment of lung cancer

- 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.

Principles of surgical treatment of lung cancer

- N2-positive patients with a single lymph node and less than 3 cm can be considered diversified treatment including surgery.
- The restaging after induction therapy should include computed tomography +/- positron scans, In order to rule out disease progression or metastasis.
- Patients whose mediastinum is negative after induction therapy have a better prognosis.

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

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

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

1. NCCN Clinical Practice in Oncology:Small Cell Lung Cancer V.2.2022.
2. NCCN Clinical Practice in Oncology:Non-Small Cell Lung Cancer V.6.2022.
3. Takada M, Fukuoka M, Kawahara M, et al. Phase III study of concurrent versus sequential thoracic radiotherapy in combination with cisplatin and etoposide for limited-stage small-cell lung cancer: results of the Japan Clinical Oncology Group Study 9104. *J Clin Oncol.* 2002;15;20(14):3054-3060.
4. Sundstrøm S, Bremnes RM, Kaasa S, et al. Cisplatin and etoposide regimen is superior to cyclophosphamide, epirubicin, and vincristine regimen in small-cell lung cancer: results from a randomized phase III trial with 5 years' follow-up. *J Clin Oncol.* 2002;15;20(24):4665-4672.
5. Rossi A, Di Maio M, Chiodini P, et al. Carboplatin- or cisplatin-based chemotherapy in first-line treatment of small-cell lung cancer: the COCIS meta-analysis of individual patient data. *J Clin Oncol.* 2012 ;10;30(14):1692-1698.
6. Pavel ME, Hainsworth JD, Baudin E, et al. Everolimus plus octreotide long-acting repeatable for the treatment of advanced neuroendocrine tumours associated with carcinoid syndrome (RADIANT-2): a randomised, placebo-controlled, phase 3 study. *Lancet.* 2011 ;10;378(9808):2005-2012.
7. Sholl LM, Xiao Y, Joshi V, et al. EGFR mutation is a better predictor of response to tyrosine kinase inhibitors in non-small cell lung carcinoma than FISH, CISH, and immunohistochemistry. *Am J Clin Pathol.* 2010;133(6):922-934.
8. Mitsudomi T, Morita S, Yatabe Y, et al. Gefitinib versus cisplatin plus docetaxel in patients with non-small-cell lung cancer harbouring mutations of the epidermal growth factor receptor (WJTOG3405): an open label, randomised phase 3 trial. *Lancet Oncol.* 2010;11(2):121-128.
9. Maemondo M, Inoue A, Kobayashi K, et al. Gefitinib or chemotherapy for non-small-cell lung cancer with mutated EGFR. *N Engl J Med.* 2010;24;362(25):2380-2388.
10. Song WA, Zhou NK, Wang W, et al. Survival benefit of neoadjuvant chemotherapy in non-small cell lung cancer: an updated meta-analysis of 13 randomized control trials. *J Thorac Oncol.* 2010;5(4):510-6.
11. Shah AA, Berry MF, Tzao C, et al. Induction chemoradiation is not superior to induction chemotherapy alone in stage IIIA lung
12. Kappers I, van Sandick JW, Burgers SA, et al. Surgery after induction chemotherapy in stage IIIA-N2 non-small cell lung cancer: why pneumonectomy should be avoided. *Lung Cancer.* 2010;68(2):222-227.