Assessment of Operability and Resectability in Lung Cancer

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KEYWORDS

• Lung cancer • Operability • Resectability • Mediastinal node map

KEY POINTS

- Factors to consider in operability and resectability.
- Patient-related factors and tumor-related factors and surgery-related factors to consider.
- Attention to details on operability and resectability necessary in the preoperative care of the patients.
- Mediastinal lymphatic staging.

INTRODUCTION

Distinction is made between operability and resectability. The terms are not synonymous and should not be confused. A resectable tumor is one in which there is no technical barrier to surgical excision. An operable tumor is one in which various parameters identify surgical excision as the most appropriate treatment. A tumor may be considered technically resectable, yet deemed inoperable because of other criteria, such as the extent of lymph node involvement, cell type, distant metastases, prohibitively high surgical risk in a compromised patient, distant metastases, and so forth. In many cases, operability implies that resection offers some prospect for cure. The opinion is shared by many that there are rarely indications for deliberate, palliative resection in patients with bronchial carcinoma. In an occasional case, benefit may follow a palliative resection for obstructed or infected lung, or for relief of disabling hypertrophic pulmonary osteoarthropathy.[1–3] Troublesome hemoptysis is almost always controlled by radiotherapy.

OPERABILITY AND RESECTABILITY

In the Introduction to *Surgery and Basic Surgical Principles*, the terms operability and resectability are not synonymous.[1] The patient may be operable on the basis of treatable disease, operative risk, and surgical diagnosis. The disease may be resectable on the basis of cure rate and risk factors.

Surgical diagnosis is based on a sound knowledge of anatomy, physiology, and pathology, a specific clinical history and examination with confirmation by imaging and operative surgery. It is unnecessary to learn what can be deduced, and thus, surgery concerns defining the basic facts on which the consequences of a disease process can be built. The actual operation in surgery is but one part of the process of surgical care: diagnosis, preoperative care and postoperative management being of equal importance in differing circumstances. No matter how good the operation, if it is performed for the wrong diagnosis, the benefit to the patient will be limited or void. In other situations, such as the patient who

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Thorac Surg Clin 31 (2021) 379–391
https://doi.org/10.1016/j.thorsurg.2021.07.008

presents as a surgical emergency in association with severe illness, a common occurrence in this era of the elderly patient, skilled preoperative resuscitation and management can turn a high-risk procedure into a routine operation. Similarly, the very ill patient can be salvaged by expert postoperative management.

Operability

Assessment

The assessment of operability requires consideration of the following factors:

1. Exclusion of detectable extrathoracic and distant metastases
2. Determination of the presence or absence of superior mediastinal lymph node metastases
3. Definition of the histologic or cell type, whenever possible
4. Evaluation of operative risk

Distant metastases History and physical examination may alert the physician to the presence of hematogenous metastases, particularly to brain, bone, and skin. Liver metastases are common and, unfortunately, are frequently "silent." Computed tomography (CT) and PET are sensitive in detecting metastases to the liver, adrenal glands, and bone. There is less reliance on serum alkaline phosphatase level for detecting liver metastases. There is now rarely a need for small laparotomy or laparoscopy for direct examination of the liver. Metastatic spread to the brain is best detected by CT or MRI.

Lymphatic spread There is accumulating evidence that superior mediastinal lymph node involvement influences prognosis profoundly and adversely in most cases. Paulson and Urschel[2] reported a 6% 5-year survival in 251 patients with superior mediastinal lymph node involvement managed by resection. Bergh and Schersten[4] reported similar survival statistics in such cases and make an important observation relating prognosis to the extent of lymph node involvement observed: if tumor had invaded the capsule of the node (perinodal spread), then 5-year survival following resection is limited to 4%. If this type of perinodal spread occurs in the superior mediastinum, the 5-year survival is less than 2%. It is recognized that patients with superior mediastinal lymph node involvement show a very high incidence of hematogenous spread, and although the intrathoracic tumor may be eradicated by surgical excision, the majority succumb to distant metastases. The exceptions to this observation are cases with limited, ipsilateral intranodal mediastinal node involvement associated with a favorable cell type (squamous cell carcinoma) in which more favorable survival statistics are achieved following resection, sometimes combined with radiotherapy.

Cell type The histologic or cell type profoundly affects the prognosis, with well-differentiated squamous cell tumors at the favorable end of the scale, adenocarcinoma in an intermediate position, and small cell carcinoma with such an unfavorable prognosis that many surgeons will not recommend resection if this cell type is identified on needle biopsy. In a randomized, multicenter trial conducted by the British Medical Research Council, it was clearly shown that chemotherapy and radiotherapy were preferable to surgical excision in cases of small cell carcinoma: there were no 2-year survivors following resection in this series, and the mean survival in resected cases was 7 months.

It may be difficult, however, to identify the cell type with certainty before thoracotomy. The pathologist may have difficulty in precisely defining the cell type from sputum analysis or from material obtained by percutaneous needle aspiration lung biopsy. If doubt exists, it is preferable to operate on such patients provided there is no involvement of superior mediastinal lymph nodes. If, however, the pathologist states that the biopsy material shows unequivocal small cell carcinoma, it is then recommended to treat with radiotherapy or chemotherapy as primary treatment. If the primary tumor is, in fact, small and of the small cell type, it will respond favorably to the treatment and disappear radiologically within 4 to 6 weeks of completing irradiation.

Operative risk There has been a relatively greater increase in the incidence of lung cancer in patients in the sixth, seventh, and eighth decades during recent years, and there is an increasing trend to resect bronchogenic carcinoma in the elderly. At 1 time, it was suggested that no patient over the age of 70 was likely to tolerate pulmonary resection, but this approach is no longer accepted. With careful preoperative selection, patients in the seventh and even in the eighth decades may be operated on with reasonably low levels of morbidity and mortality. This attitude has been favorably affected by the increasing preference for lobectomy (rather than pneumonectomy) and lung-saving bronchoplastic procedures in the management of lung cancer.

It is clear from the report by Golebiowski[5] that careful selection of patients over the age of 70 years requiring pulmonary resection should be

assessed for coexisting disease with the particular risks of postoperative gastrointestinal hemorrhage, cardiac arrhythmias, heart failure, and venous thrombosis with pulmonary embolism. It is clear that the decision to operate on the elderly may be a difficult judgment requiring a more extensive preoperative assessment, and ultimate selection will vary with differing rates at which individuals age and deteriorate.

Pulmonary functional reserve Resection must not result in a "pulmonary cripple" or fatal postoperative failure. Pulmonary function tests are increasingly precise and sophisticated, but there is little practical information reported that will help the surgeon with his decision about management in the patient with marginal respiratory reserves. A recent study by Legge and Palmer[6] analyzes the results of a variety of preoperative pulmonary function tests in relation to the incidence of postoperative respiratory failure in 225 patients with bronchial carcinoma undergoing thoracotomy. In this series, 13 developed postoperative respiratory failure, and 6 of the 13 died of this complication. The following function tests were significantly related to the incidence of respiratory failure: a higher incidence of airway obstruction with low forced expiratory volume in first 1 second (FEV_1)/forced vital capacity ratio less than 1.0, higher mean levels of $PaCO_2$, higher respiratory rate and lower tidal volumes, low arterial oxygenation, and low maximum oxygen consumption (MVO_2) less than 10 mL/kg/min.

Mediastinoscopy The influence of superior mediastinal lymph node involvement on prognosis in patients with bronchogenic carcinoma has already been discussed. Cervical mediastinoscopy provides reasonably precise information about the site and degree of superior mediastinal lymph node involvement. The experience with this procedure at the Toronto General Hospital began in 1961. The information obtained has been so useful that mediastinoscopy is adopted as a routine part of the preoperative assessment in patients with presumably operable lung cancer in 1963. The only exceptions to such routine application are in patients with early occult tumors or peripheral tumors less than 1.5 cm in diameter.

Technique for mediastinoscopy Mediastinoscopy is done under general anesthesia with endotracheal intubation and is combined with bronchoscopy. The useful application of cervical mediastinoscopy requires considerable experience and a clear understanding and familiarity with the lymphatic drainage of the lung. In general, the procedure should be done by the surgeon who will subsequently do the resection.

Anterior subcarinal (station 7), tracheobronchial (station 10), and paratracheal nodes (station 4) are accessible for biopsy at mediastinoscopy. Some superior mediastinal nodes are inaccessible in this operation: anterior mediastinal nodes, which lie in front of the aortic arch and its major branches (station 5) and subaortic lymph nodes lying inferolateral to the subaortic window and low, posterior subcarinal nodes (station 7). Tumors in the left upper lobe or left hilum may spread through the anterior mediastinal lymphatic chain, and cervical mediastinoscopy is least useful in assessing lymphatic spread for tumors in this location. This is of particular importance because the left upper lobe is the largest of all pulmonary lobes, and approximately 35% of the primary tumors arise in this location. For these reasons, additional exploration may be indicated in patients with left hilar or left upper lobe tumors when the cervical mediastinoscopy is negative. With the cervical mediastinoscopy incision still open (previous biopsies having been assessed by frozen section), left anterior mediastinotomy is added to access the anterior mediastinal nodes, identified by palpation and biopsied using the mediastinoscope for access.

Complications of mediastinoscopy
1. Right pneumothorax
2. Left recurrent nerve palsy
3. Significant bleeding
4. Bronchomediastinal fistula
5. Postoperative death

Results Most patients with "positive" mediastinoscopy are considered inoperable. These include small cell carcinoma and non–small cell carcinoma with perinodal and extranodal extension of tumor with fixation to the surrounding mediastinal structures, high right paratracheal nodes and subcarinal nodes, and subinnominate and preaortic lymph nodes. There are reports in the literature that indicate a favorable prognosis in patients managed by resection of squamous cell carcinoma with ipsilateral superior mediastinal node involvement. It is frequently stated that mediastinal node involvement can be determined using the noninvasive technique of CT and PET.

Comparison of mediastinoscopy and computed tomography It is frequently stated that superior mediastinal lymph node involvement can be determined using the noninvasive technique of CT. The criterion for positive CT is a lymph node that is larger in size by more than 1.5 cm supported by finding of a hypermetabolic "hot" lymph node. These findings permit targeted lymph node biopsy

at mediastinoscopy or by needle aspiration at ultrasound bronchoscopy or enlarged cervical lymph node at ultrasound.

Resectability

The hospital exists for the sake of the patients. The very word "*hospital*" (Latin, *hospitium*) means a place where guests are received. As a hospital is a house of hospitality, all patients within the walls of a hospital should therefore be treated as guests; this is a basic and changeless concept that has prevailed for centuries. In the Introduction by the late Hamilton Bailey on *Pye's Surgical Handicraft*, one of the first medical books published by John Wright & Sons Ltd, Mr Pye had put into the hands of the profession a work of exceptional merit.[7]

Selectivity is the basis of surgical treatment for bronchogenic carcinoma in order to avoid unwarranted, injudicious exploratory thoracotomy and resection, both of which carry significant operative risks without benefit to the patient's survival.[2] Distinction should be made between *operability* (patient factors) and *resectability* (tumor factors). *Preoperative clinical staging* reflects in prognosis, facilitates the choice of treatment, correlates well with survival after resection, and clarifies the results of selected treatment. *Postoperative pathologic staging* is precise after detailed analysis of the resected lung and lymph node specimens and is used to determine prognosis, likely cure rate, and the need for adjuvant therapy.

The *4 treatment options* are as follows: (a) Surgery with or without induction chemoradiotherapy in the operable patients with limited and potentially curable disease; (b) Definitive combined chemotherapy and radiotherapy in patients with locally advanced but treatable and controllable disease even if it is incurable; (c) Palliative radiotherapy or chemotherapy alone in patients with advanced incurable disease; and (d) Targeted immunotherapy on the basis of molecular markers.

Major advances have been made in resectability of lung cancer by complete pretreatment assessment of the patient and classification of the lesion according to the cell type and extent and stage of lymph node involvement, systemic staging, attention to details in the international pathologic classification of lung cancer into small cell or non–small cell types, mutation and molecular staging of lung cancer, accuracy in the histologic assessment by pulmonary pathologists, thorough preoperative and intraoperative lymphatic staging in the mediastinum by the surgeon, and safe conduct of the operation. By the means of advances made over time, a decision can be made with better than 90% accuracy regarding resectability with benefit and to the extent of resection necessary. The use of all available means of preoperative assessment has increased surgical salvage and with moderate increase in 5 years.

Resectability in lung cancer surgery needs careful attention, taking into consideration the following: attention to details, surgical skills and knowledge, diagnosis, precision in surgical techniques, and precision in the operation.

Surgical treatment

There are clinical situations in which patients stand to benefit by resection when the preoperative cardiopulmonary assessment is favorable, and the tumor is localized and resectable with intent to cure with acceptable operative risk. However, there are situations with a concomitant reduction in the number of useless resections or unnecessary thoracotomies for inoperable tumors.

Non–small cell lung cancer with resectable extrathoracic metastases

There are limited situations in lung cancer in which resection of primary tumor and metastases is feasible. One of these is the presence of solitary brain metastasis with absence of lymphatic spread in the thorax and the primary tumor that is technically resectable. Another situation that arises is when solitary adrenal gland metastasis becomes evident after the primary tumor has been surgically controlled. Lung cancer that has resulted in metastases to the bone, liver, and lung are not amenable to surgical treatment.

Mediastinoscopy

Mediastinoscopy may occasionally be useful in determining resectability of the primary lesion for tumors in 2 locations. Superior sulcus tumors may be examined directly on either the right or the left side at the time of mediastinoscopy by deliberately breaching the mediastinal pleura and entering the pleural space lateral to the trachea. It is then possible to palpate or directly observe the gross extent of involvement of vertebral bodies by tumor. Second, bulky tumors in the right upper lobe may fix and distort the right lateral wall of the trachea and be considered inoperable on the basis of radiography and bronchography.

Preoperative angiography

Evaluation of the pulmonary arteries is obtainable by preoperative angiography. Pulmonary angiography may be in determining resectability and is useful for tumors in the right superior mediastinum, left hilum, and lobar arteries. It provides less precise information about pulmonary veins and heart. Such information may clearly obviate an unnecessary thoracotomy, or it may indicate

the feasibility of lobectomy, lobectomy with sleeve resection of the bronchus, or even lobectomy with sleeve resection of both bronchus and pulmonary artery. Involvement of the superior vena cava with proximity to the large tumor mass in the right upper lobe may be evident on contrast-enhanced CT or on angiogram precluding operation and pulmonary resection.

Thoracic spine invasion

Superior sulcus cancer extending within the confines of the thoracic inlet may directly extend into vertebral bodies of the upper thoracic spine, precluding surgical intervention. Similarly, lung cancer arising in the paravertebral gutter may invade the chest wall and extend into the extrathoracic muscles, preventing tumor resection with intent to cure.

Factors to Consider in Operability and Resectability

Operability and resectability in bronchial carcinoma require attention to details before making surgical decision with respect to the following[1]:

1. *Patient-related factors*: patient characteristics, functional status and general heath, and operative risk factors for specific treatment.
2. *Tumor-related factors*: tumor characteristics, classification of the tumor according to the histologic type, and extent and stage of the disease at presentation.
3. *Surgery-related factors*: the type of surgical procedure, extended or limited pulmonary resection; standard lobectomy or sleeve lobectomy, standard pneumonectomy or sleeve pneumonectomy or carinal pneumonectomy; segmentectomy; en bloc chest wall resection with pulmonary resection; resection of superior sulcus tumor with or without subclavian vascular reconstruction, en bloc partial or total superior vena cava resection with pulmonary resection and reconstruction, whether the operation is elective or emergent; surgical skills and experience of the operating surgeon; and the skills of the anesthetist.[8]

From the above thoughtful considerations, patients are classified into the 4 following groups regarding management:

i. The patient may be considered to be *medically operable* and localized lung *cancer resectable* with intent to cure by an operation.
ii. The patient may be considered to be *medically inoperable*, but the lung cancer found to be localized and *potentially resectable* and yet the treatment recommended would have to be nonsurgical with intent to control and cure with concurrent chemotherapy and radiotherapy.
iii. The patient may be considered to be *medically operable,* but lung cancer is found to be *locally advanced and unresectable*, but still treatable, and the recommended treatment would have to be with concurrent chemotherapy and radiotherapy with intent to control and cure.
iv. The patient may be deemed to be *medically inoperable* and lung *cancer unresectable* in which case only palliative treatment is feasible.

PREPARATION AND PLANNING OF OPERATION FOR LUNG CANCER

The objectives of these notes are to stress the principles underlying the management of lung cancer and other thoracic malignancies, and from these considerations to outline a routine scheme for management, which will be followed easily by all staff. It is hoped that by adherence to this routine, adequate and efficient management of all cases will be obtained, in the very important matter of preoperative preparation as well as in the postoperative management.

It is recognized that although the routine will be most suitable for most cases, there will in special circumstances be cases requiring different management. Such special instructions will be given only by the surgeon in charge and should not be embarked upon without his or her specific instructions. It is hoped that the routine outlined will be a sound basis for preoperative and postoperative care and as such will be of value to the surgical and nursing staff in the routine management of thoracic surgical cases. It will also be of help in teaching the young doctors who wish to embark on a surgical career.

The guiding principle that must be followed is outlined in **Table 1**. *Selectivity is the basis of surgical treatment* for bronchogenic carcinoma in order to avoid unwarranted, injudicious exploratory thoracotomy and resection, both of which carry significant operative risks, without benefit to the patient's survival.[2] Selection is based on complete pretreatment evaluation of the patient's functional status, general medical condition, perioperative cardiac risk, pulmonary function tests, and medical condition; when thoughtfully used, resection rates, adverse events, perioperative morbidity and mortality rates, survival figures, and total salvage should improve.

Attention to Details on Operability and Resectability Necessary in the Preoperative Care of the Patients

Surgical intuition becomes important when faced with having to make a surgical decision in the

Table 1
Clinical predictors of risk for lung surgery

Predictors	Clinical Determinants
A. Major risk factors	*Worrisome*
"Major"	Increasing age >80 y Reduced functional capacity by cardiopulmonary exercise testing (CPET): MVO_2 < 10 mL·kg·min[6] Low FEV_1 < 1.2 L Calculated postoperative (ppo) FEV_1 < 0.8 L Low diffusion capacity (diffusing capacity of the lungs for carbon monoxide [DLCO]) at rest <25 mL·min·mm Hg (<75%); as low as 5 mL·min·mm Hg in pulmonary fibrosis Modified Medical Research Council *dyspnea scale*: 0–4 *Grade 3:* Breathlessness stops walking after ~100 m or a few minutes *Grade 4:* Breathless when dressing or not able to leave the house Type of elective operation Standard pneumonectomy Carinal pneumonectomy Tracheal carinal resection En bloc lung and chest wall resection En bloc superior vena cava resection with pulmonary resection Continuous supplemental O_2 Unstable coronary artery syndrome Low ejection fraction <35 (normal from 55% to 80%) Decompensated congestive heart failure *Severe valvular aortic stenosis* usual definition criteria: ■ Mean transvalvular gradient >40 mm Hg. ■ Aortic valve area (AVA) <1 cm^2 ■ Peak aortic jet velocity >4.0 m/s Critical valvular aortic stenosis usual definition criteria: ■ High fixed cardiac output ■ Mean transvalvular gradient >80 mm Hg. ■ AVA < 0.5 cm^2 *Assessment of aortic stenosis severity* should integrate the flow-gradient pattern to the classic measurement of AVA: Normal flow/high gradient and AVA < 1 cm^2: benefit from aortic valve replacement (AVR) Low flow/high gradient and AVA <1 cm^2 benefit from AVR Pulmonary arterial hypertension: mean PAP > 24 mm Hg BMI > 30 Low arterial blood gases PaO_2 < 70 mm Hg Low oxygen saturation <70%
B. Intermediate risk factors	*Cautious*

(*continued on next page*)

Table 1
(*continued*)

Predictors	Clinical Determinants
"Intermediate"	Chronic lung disease: Panacinar emphysema, interstitial pulmonary fibrosis, pulmonary sarcoidosis, asbestosis, silicosis, recurrent pneumonia, fibrosing alveolitis Diffuse bronchiectasis Age 70–79 y Active cigarette smoker $\geq$1 ppo for 20 y Reduced functional capacity by cardiopulmonary exercise test (CPET): MVO_2 < 15 mL·kg·min[6] FEV_1 1.2–1.5 L Ejection fraction <50 BMI 25–29.9 Significant cardiac arrhythmias: >5 PVCs documented before the operation, bundle branch block, uncontrolled atrial fibrillation
C. Minor risk factors	*Acceptable*
"Minor"	Modified Medical Research Council *dyspnea scale*: 0–4 *Grade 0:* No breathlessness *Grade 1:* Breathless when hurrying or walking up a hill Age 60–69 y Ex-smoker Normal functional capacity MVO_2 > 20 mL·kg·min[6] FEV_1 > 1.5 L for lobectomy FEV_1 > 2.0 L for pneumonectomy BMI 18.5–24.9 Ejection fraction >55% (55%–80%) and mean 67% Diffusion capacity (DLCO) at rest 25–30 mL·min·mm Hg (>90%) *Type of elective operation:* Standard lobectomy Sleeve lobectomy Segmental resection Wedge resection Normal pulmonary artery pressure: 25/8 mm Hg and mean pulmonary arterial pressure 15 mm Hg

Abbreviation: ppo, predicted postoperative pulmonary function; PVCs, premature ventricular contractions.

preoperative care.[8] The clinician must ask himself or herself the following questions before every operation, which must only be performed once each question has been answered satisfactorily:

A. HAS THE DIAGNOSIS BEEN FIRMLY ESTABLISHED?
   a. With modern techniques of imaging and tissue biopsy, this can be done in the vast majority of cases.
   b. Occasionally, an exploratory operation is necessary if the possibility of serious disease cannot be confidently ruled out, but this must be an exception.

B. IS AN OPERATION NECESSARY?
   1. *Operations have certain indications*, which must be present before an operation is justified.
   2. *Operation is potentially dangerous* and is only indicated if the risks of the disease are greater than the risks of the operation. For this, one must know the following:
      1. Natural history of the disease
      2. Risk of the operation
   3. *Would you have the operation* if you were in the patient's position?
   4. *If in doubt*:
      a. Seek a second opinion
      b. Reevaluate the case later
   5. It is not justifiable to perform an operation merely on the possibility that it may be necessary: there must be a reasonable probability, or preferably certainty that it is required.

C. IS THE PATIENT FIT FOR THE OPERATION AND ANESTHETIC? IF NOT, MAKE HIM FIT and examine and improve functions of the different body organ systems: heart, lung, kidneys, and liver before committing to an operation.

a. Heart: normalize cardiac function after appropriate cardiac investigations
b. Lungs: improve lung function after investigations to minimize risk for postoperative atelectasis, bronchitis, and pneumonia
c. Kidneys: restore renal function
d. Liver: investigate and prepare liver function if required
e. Bladder-neck obstruction: if significant, this must be treated before operation
f. Hemoglobin level: restore adequate hemoglobin level before operation if low
g. Serum proteins: estimate and rule out protein deficiency
h. Serum electrolytes: should be corrected before an operation
i. Control sepsis: clear up infection before operation
j. Colon preparation: must be done before operation on the colon to reduce risk
k. Previous cortisone therapy: cortisone replacement to sustain the patient during and after the operation
l. Reduce risk for postoperative deep vein thrombosis by prophylaxis anticoagulation

D. WHEN IS THE BEST TIME FOR OPERATION?
a. In general, if an operation is well indicated, it should be done without undue delay
b. Reasons for postponing an operation
1. To improve the patient's state of fitness: operate as soon as maximal improvement has taken place.
2. To allow inflammatory reaction to subside and so make operation easier: operate when maximal improvement has taken place.
3. The benefits of delay must be judged against the possible harm of progression of the disease: careful judgment and possible compromise required to balance out these 2 factors.

E. WHEN IS THE BEST TIME FOR OPERATION?
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3. The benefits of delay must be judged against the possible harm of progression of the disease: careful judgment and possible compromise required to balance out these 2 factors.

F. WHO SHOULD PERFORM THE OPERATION?
1. Someone with the training to perform the operation competently.
2. In emergencies, this may have to be compromised.

NECESSARY POSTOPERATIVE CARE

A. MAINTAIN PATIENT DURING RECOVERY[8]:
1. Immediate postoperative period in the postanesthesia care unit
a. Until recovered from respiratory and circulatory disturbances of the anesthetic and operation
b. Maintain open airway
c. Maintain circulation
2. Intermediate postoperative period in the ward

B. PREVENT COMPLICATIONS:
1. Abdominal distension
2. Pulmonary complications
3. Deep vein thrombosis
4. Fluid and electrolyte imbalance
5. Wound infection
6. Urinary retention

C. EARLY RECOGNITION AND PROMPT TREATMENT OF COMPLICATIONS:
1. Postoperative fever
2. Pulmonary atelectasis
3. Deep vein thrombosis
4. Fluid and electrolyte imbalance
5. Wound infection
6. Coronary thrombosis
7. Urinary retention
8. Sudden postoperative collapse may be due to the following:
a. Complications of the operation:
i. Hemorrhage
ii. Infection (septicemia)
iii. Fluid and electrolyte disturbances
iv. Massive tissue damage and metabolic disturbances
b. Major organ failure
i. Heart (coronary thrombosis)
ii. Lungs (atelectasis, pneumonia, or pulmonary thromboembolism)
iii. Adrenal gland insufficiency (hypoadrenal response)
iv. Kidneys (uremia)
v. Liver failure
vi. Brain (cerebrovascular accident)

OPERABILITY

Assessment

The assessment of operability requires consideration of the following factors:

1. Exclusion of detectable extrathoracic and distant metastases
2. Determination of the presence or absence of superior mediastinal lymph node involvement
3. Definition of the histologic or cell type, whenever possible
4. Evaluation of operative risk
5. Determination of the local extent of the tumor growth within the lung and direct invasion within the chest involving the bony chest wall, mediastinal structures, phrenic nerve on the pericardium and the brachial plexus in the thoracic inlet, and central extension through the intervertebral foramen and produce epidural compression of the spinal cord

Distant metastases

History and physical examination may alert the physician to the presence of hematogenous metastases, particularly to brain, bone, and skin. Liver metastases are common and, unfortunately, are frequently "silent." Metastatic liver involvement no longer requires laparoscopy or a small laparotomy for direct examination of the liver in equivocal cases now because PET is available for systemic staging at all distant sites except for the brain. PET is a noninvasive method for systemic staging of cancer, and it provides more reliable and accurate information about staging and planning of treatment for lung cancer. MRI of the head is most frequently required for completeness of staging of primary lung cancer for determining presence of intracranial metastases if the patient has suggestive neurologic symptoms and signs, if the cancer appears to be at an advanced unresectable stage in the lung, and in the high-surgical-risk patient in the absence of neurologic symptoms in order to plan for the most appropriate treatment.

Lymphatic spread

There is now accumulated evidence that superior mediastinal lymph node involvement by lung cancer influences prognosis profoundly and adversely in most cases.[9] The 5-year survival rate in patients with documented preoperative superior mediastinal lymph node metastases managed by resection has been reported to be as low as 6% (4% to 9%), and even worse at 4% following resection if tumor has invaded the capsule of the lymph node (perinodal spread). If this type of perinodal spread occurs in the superior mediastinum, the 5-year survival is less than 2%. When the preoperative staging cervical mediastinoscopy is normal and the presence of lymphatic metastases are discovered in the mediastinal lymph nodes during pulmonary resection, the 5-year cure rate is no higher than 25% to 30%.

Cell type and histologic grading

The histologic or cell type and the degree of differentiation, defined in 3 grades: well differentiated, poorly differentiated, and undifferentiated, profoundly affect the prognosis; with well-differentiated squamous cell tumors at the favorable end of the scale; adenocarcinoma in an intermediate position; and small cell carcinoma at the most unfavorable end of the scale. Small cell lung cancer is frequently described in 3 stages: very limited truly stage I disease (potentially surgical), limited intrathoracic disease within the ipsilateral hemithorax (nonsurgical), and extensive advanced disease (nonsurgical) associated with such an unfavorable prognosis and outcome, that it is not recommended for surgical resection if this cell type is identified. There is 1 exception to the rule in small cell lung cancer when surgery is considered for treatment when it is a true very limited stage I disease and complete staging is favorable, including normal brain MRI, normal mediastinal nodal staging, and normal systemic staging with PET scan.

The recommended treatment for localized primary non–small cell lung cancer is surgery; for small cell cancer, it is chemotherapy for extensive systemic disease and chemotherapy combined with radiotherapy for limited intrathoracic disease.

Operative risk

There has been a relatively greater increase in the incidence of lung cancer in patients in the fourth to eighth decades of life during recent years, and there is an increasing trend to resect bronchial carcinoma in the elderly patients in the sixth, seventh, and eighth decades. The increase in the incidence is due to change in the distribution of the 2 cell types with adenocarcinoma spectrum disorder with variable cure rate in this heterogeneous group of 4 descriptors becoming more common than the squamous cell cancer.

The factors that have been identified to be associated with increased surgical risk are advanced age older than 80 years, in those with compromised pulmonary function owing to diffuse emphysematous lung disease, interstitial pulmonary fibrosis, and pulmonary artery hypertension, and in those with marginal heart function from congestive heart failure owing to coronary artery disease, valvular heart disease, and cardiomyopathy.

Although limited pulmonary resections may be well tolerated in elderly patients even over the age of 80 years with low operative mortality, the risk will be increased if more extensive pulmonary resection is undertaken, including standard and sleeve pneumonectomy and pulmonary resection with en bloc chest wall resection.

With careful preoperative selection, patients in the seventh and even in the eighth decades may be operated on with reasonably low levels of morbidity and mortality. This attitude has been favorably affected by the increasing preference for limited resections with wedge, segment, standard lobectomy, and lung-saving sleeve lobectomy rather than performing high-risk pneumonectomy in the management of lung cancer; pneumonectomy in itself is considered to be a disease from loss of a significant amount of lung function.

It is clear that the decision to operate on the elderly patient may be a difficult judgment requiring a more extensive preoperative assessment and preparation, and ultimate selection will vary with the differing rates at which individuals age with reduction in physiologic function and deteriorate.

The postoperative complications are prolonged air leak, empyema, significant hemothorax, deep vein thrombosis and pulmonary embolism, cardiac arrhythmias, respiratory failure, pneumonia, bronchopleural fistula, and wound infection.

Pulmonary functional reserve

Pulmonary resection must *not* result in a "pulmonary cripple" or suffer fatal postoperative respiratory failure. The risk is the highest with pneumonectomy, which compromises half of the total lung capacity. The adequacy of lung function before operation should be established before subjecting the patient to lung resection. Pulmonary function tests have become increasingly precise and sophisticated now with the ability to determine more accurately the postoperative exercise capacity from cardiopulmonary exercise test measuring MVO_2 and the acceptable low risk is when it is greater than 20 mL/kg/min.[10] However, there is little practical information that will help the surgeon with the decision about management in the patient with compromised lung function and marginal respiratory reserve. The following pulmonary function test results are significantly related to high incidence of postoperative respiratory failure and morbidity and mortality: a higher incidence of airway obstruction, higher mean levels of arterial $PaCO_2$ greater than 45 mm Hg, higher resting respiratory rate and lower tidal volumes, and reduced calculated postoperative $FEV_1 < 1$ L, higher Vd/Vt ratio on exercise, and reduced $MVO_2 < 15$ mL/kg/min on exercise testing.

Mediastinal lymph node biopsy for staging lung cancer

This surgical procedure to advance surgical care of the patients with lung cancer was the brainchild of late *Dr Frederick Griffith Pearson* of the Toronto General Hospital in Canada. He recognized the value of this procedure, to be diligently learned by a thoracic surgeon, after his visit to the Karolinska Institute in Sweden in 1961 as a visiting postgraduate surgical fellow where he witnessed the procedure and assisted *Dr Eric Carlens*, who was performing *cervical mediastinoscopy.*[11]

Further advances in managing lung cancer came from Japan by *Dr T. Naruke*, who put forward a map of thoracic lymph nodes, deservedly called the internationally accepted Naruke Map, to guide standard nomenclature of the mediastinal lymph nodes to be sampled at cervical mediastinoscopy and to maintain consistency in biopsy of the named lymph nodes.[12]

Then came the most remarkable publication by *Dr H.C. Nohl Oser*[13] in 1972, Consultant Thoracic Surgeon to Harefield, Hillingdon, and West Middlesex Hospitals in London on "An investigation of the anatomy of the lymphatic drainage of the lungs as shown by the lymphatic spread of bronchial carcinoma."[13] This profoundly increased the understanding of the diverse lymph flow in the thoracic region from each lung and from each pulmonary lobe, resulting in advancing mediastinal lymph node staging for lung cancer. The staging-diagnostic value of left anterior mediastinotomy for lymphatic staging of cancer in the left upper lobe and left hilum became accepted.

Cervical mediastinoscopy became the gold standard in the staging of lung cancer on either side in the thorax. Later in time, after publication on the pattern of mediastinal lymphatic drainage by Dr H.C. Nohl Oser[13] in 1972, it was recognized, from this publication, that the different pathway of lymph flow from the left upper lobe and left hilum was different from the rest of the lungs, and this resulted in addition of *left anterior mediastinotomy* to cervical mediastinoscopy for staging left lung cancer in these 2 sites. Diagnostic anterior mediastinotomy was first reported by *Dr Thomas M McNeill and Dr J Maxwell Chamberlain* in 1966 and came to be known as the *Chamberlain Procedure*.[14]

In order to perform safe mediastinal staging by cervical mediastinoscopy and left anterior mediastinotomy requires considerable surgical experience and knowledge of the mediastinal anatomy, and a clear understanding and familiarity with the lymphatic drainage of the lung as described by *Nohl Oser*.[13] In general, the procedure should be done by the experienced senior surgeon who will subsequently perform the pulmonary resection.

Cervical mediastinoscopy and/or left anterior mediastinotomy The adverse influence of superior mediastinal lymph node metastases on prognosis

in patients with bronchial carcinoma is now well recognized. Cervical mediastinoscopy is performed for cancer in the right and left lung, and to which is added, left anterior mediastinotomy when the cancer is in the left upper lobe or left hilum to provide reasonably precise information about the site and extent of superior mediastinal lymph node involvement.[9,15–18] The only exception to routine application of the procedure was when the lung tumor is small in size measuring less than 1.5 cm in diameter and peripherally placed in the lung and there is an absence of enlarged mediastinal lymph nodes (<1.5 cm in size) on CT scan of the chest. The accuracy of staging lung cancer was advanced further in recent times with the advent of the metabolic scan with PET, but it has not eliminated the need for surgical staging of lung cancer, which remains the gold standard for mediastinal nodal staging. PET has been shown to benefit, not only by directing mediastinal lymph node biopsy but also for intrathoracic assessment of the primary lung cancer and for extrathoracic staging at all sites except the brain, for which MRI is necessary.

The standard for precise identification and biopsy of the mediastinal and bronchopulmonary lymph nodes was first described by T. Naruke in Japan (*Naruke Mediastinal Lymph Node Map*)[12] and much later by the *International Association for Staging of Lung Cancer* (IASLC).[15,16] These are now uniformly accepted in the mediastinal lymph node staging, providing accurate information on the number and location of the normal and metastatic superior mediastinal lymph nodes. The fundamental difference is that the Naruke Map is preoperative for guiding mediastinal nodal staging whereas the IASLC Map is for surgical-pathologic staging of the primary tumor and the lymph nodes after pulmonary resection.

Cervical mediastinoscopy Cervical mediastinoscopy is performed under general anesthesia with endotracheal intubation for mediastinal lymph node staging for right and left lung cancers in all of the pulmonary lobes and is combined with bronchoscopy. Lymph flow from the right lung is ipsilateral to the right side in 96% and to the contralateral left side in 4%. Lymph flow from the left lung is not the same as from the right lung. It differs in that the lymph flow is to the contralateral side from the left lower lobe in 25% and from the left hilum and upper lobe in 12%. For left lung cancer, left anterior mediastinotomy is added to the cervical mediastinoscopy, with negative lymph node biopsies, when the cancer is in the left upper lobe or in the left hilum because of a different lymphatic drainage pathway through the anterior lymphatic chain in stations 5 and 6 lymph nodes. In this situation, lymphatic spread to the contralateral mediastinal lymph nodes must be determined first by cervical mediastinoscopy by sampling paratracheal lymph nodes. Contralateral lymphatic spread from the left lung occurs through subcarinal station 7 lymph node and pretracheal station 3 lymph nodes, particularly from the left lower lobe (25%) and left upper lobe (12%).[9,17–23]

Anterior subcarinal (station 7, N2), tracheobronchial lymph node (station 10, N1), paratracheal lymph nodes (ipsilateral N2 stations 4 and 2 and contralateral N3 stations 4 and 2), and pretracheal lymph node (station 3) are *accessible* for biopsy at cervical mediastinoscopy. The superior mediastinal lymph nodes, which are *not accessible* for biopsy at cervical mediastinoscopy include the anterior mediastinal nodes, which lie in front of the aortic arch and its major branches (station 6) and the subaortic lymph nodes lying inferolateral to the subaortic window (station 5). Access to these specific lymph nodes for sampling will require left anterior mediastinotomy. The low, posterior subcarinal nodes (station 7) are *not accessible* by either of the procedures and will require video-assisted thoracoscopic surgical technique for sampling.

Left anterior mediastinotomy Left anterior mediastinotomy is performed for mediastinal lymphatic staging for bronchial cancer in the left upper lobe or left hilum after cervical mediastinoscopy and frozen section analysis of the mediastinal lymph nodes has ruled out ipsilateral and contralateral lymphatic spread of cancer. Diagnostic anterior mediastinotomy was introduced in 1966 by *Thomas McNeill and J. Maxwell Chamberlain.*[14] The lymphatic drainage from these 2 sites in the left lung takes a different route through the anterior mediastinal lymphatic vessels; first into the subaortic (station 5) lymph node in the aortopulmonary window and from station 5 lymph nodes into the lymph nodes located along the inferior phrenic nerve (station 6) in front of the transverse aortic arch. Cervical mediastinoscopy does not permit access to these 2 lymph node stations and is least useful in assessing lymphatic spread for cancer in these locations. There is an increased tendency for cancer in these locations to spread to the contralateral mediastinal lymph nodes through a different lymphatic route passing through the subcarinal station 7 and pretracheal station 3 lymph nodes; cervical mediastinoscopy should always be performed first with frozen-section analysis of the contralateral sampled lymph nodes (stations 7, 10R, 4R, 3, 2R) and ipsilateral lymph nodes (10L, 4L). It is important to remember that 10R and 10L once were considered mediastinal N2 stations, and now these nodes are considered N1

stations. If there is no evidence of cancer spread at cervical mediastinoscopy, then left anterior mediastinotomy[16] should be added for sampling anterior mediastinal lymph nodes in stations 5 and 6.

For these reasons, additional mediastinal exploration is indicated in patients when the lung cancer is in the left hilum or left upper lobe. There is a higher incidence of contralateral lymphatic spread of primary lung cancer from these 2 sites in the left lung. In this case, left anterior mediastinotomy should be combined with cervical mediastinoscopy. With the cervical mediastinoscopy incision still open, and the sampled mediastinal lymph node biopsies proven to be negative for metastases by frozen section, this rules out N3 lymphatic spread.

Cervical mediastinoscopy became the gold standard in the staging of lung cancer on either side. Later in time, after publication on the pattern of mediastinal lymphatic drainage by Dr Nohl Oser in 1972, it was recognized that the pathway of lymph flow from the left upper lobe and left hilum was different from the rest of the lungs, and this resulted in adding left anterior mediastinotomy concomitantly to cervical mediastinoscopy for staging left lung cancer in these 2 sites.

Mediastinoscopy by cervical approach and left anterior mediastinotomy were reported in the International Association for the Study of Lung Cancer (IASLC)[9,10] and Clinical predictors of risk for Lung Cancer Surgery.[5,18,20]

SUMMARY

Lung cancer is a lethal disease, and chronic cigarette smoking is the most common cause. The selection of treatment is based on the histologic cell type, accurate staging, and adequacy of cardiopulmonary functional reserve. The risk for surgery is highest in patients over the age of 80 years.

The *TNM Cancer Staging System* was introduced in France by *Pierre Denoix* in 1940.[24] It describes the *extent of cancer anatomically* and it is globally accepted as

- TUMOR: local
- NODE: regional
- METASTASES: distant

Cancer staging is important in the patient care because

- It determines *Treatment*
- It determines *Prognosis*
- It is an important component of *Cancer Research* and *Advances in Treatment*

CLINICAL CARE POINTS

- Factors to consider in assessment of operability: exclusion of detectable extrathoracic and distant metastases; determination of the presence of superior mediastinal lymph node metastases; definition of the histologic cell type, evaluation of operative risk.
- Pulmonary functional reserve.
- Complications of mediastinoscopy.
- Factors to consider in resectability: non-small cell lung cancer, mediastinoscopy, preoperative angiography, thoracic spine invasion, mediastinoscopy, preoperative angiography, patient-related factors, tumor-related factors, surgery-related factors.
- Attention to details in the preoperative patient care.
- Clinical predictors of risk for lung surgery.

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