Surgical Treatment of Lung Cancer

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Abstract

In this chapter, we discuss the preoperative evaluation that is necessary prior to surgical resection, stage-specific surgical management of lung cancer, and the procedural steps as well as the indications to a variety of surgical approaches to lung resection.

Keywords

Non-small-cell lung cancer · Mediastinal staging · Small-cell lung cancer · Synchronous lung cancer · Metachronous lung cancer · Oligometastatic disease · Surgery · Lung resection

Contents

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1 Introduction

Surgery, with curative intent, is the major treatment modality for early-stage non-small-cell lung cancer (NSCLC). The primary goal of surgical treatment is twofold: (1) the complete resection of the tumor along with its regional lymphatic drainage and (2) tumor staging which will determine perioperative treatment and prognosis. The principal goal of resection is to obtain an R0 resection with negative microscopic and gross margins. In general, incomplete resection with microscopic (R1) or macroscopic (R2) margin positivity does not confer an overall survival benefit. *En bloc* resection of any adjacent tissue should be performed when possible, and margins should be assessed intraoperatively to ensure negativity.

2 Preoperative Evaluation

2.1 Radiographic Staging

Clinical staging for patients suspected to have lung cancer requires radiologic assessment for extent of disease workup with chest, abdomen, and pelvic CT scanning or whole-body PET/CT scanning with intravenous contrast. The use of PET/CT for preoperative staging has been shown to reduce the total number of thoracotomies and the number of futile thoracotomies for NSCLC stage IIIA, IIIB, IV, or benign lung lesions [1]. Although there has been no clear evidence that the use of PET/CT affects overall mortality [1], there has been routine use of preoperative PET/CT at many centers. Brain MRI with intravenous gadolinium to assess for brain metastases is more sensitive than CT and is generally obtained only in symptomatic or clinical stage II or III patients. While earlier detection of distant metastases has not been shown to provide survival benefit, detection of multiple occult metastases would prevent unnecessary lung surgery. With the exception of the brain and certain bony metastases, pathologic confirmation of the suspected metastatic focus with tissue diagnosis should be obtained. Chest MRI with intravenous gadolinium is helpful in patients with paravertebral or superior sulcus tumors to rule out neuroforaminal invasion and to assess for brachial plexus and subclavian vessel involvement. Although the National Comprehensive Cancer Network (NCCN) guidelines suggest consideration for obtaining somatostatin receptor scintigraphy (octreotide scan) preoperatively for patients with a neuroendocrine tumor (e.g., carcinoid tumor), the clinical utility of this scan is questionable [2]. Although the majority of bronchial neuroendocrine tumors express somatostatin receptors, octreotide scans have limited specificity due to positivity in other tumors, granulomas, and autoimmune diseases, and therefore, its use as a preoperative extent of disease workup is limited [3, 4].

2.2 Tissue Diagnosis

The diagnosis of lung cancer requires pathologic evaluation of biopsied tissue. While a pathologic diagnosis can be made based on cytology or tissue samples, in general a tissue biopsy (core needle or surgical specimen) is preferable to cytology samples (fluid, sputum, bronchoscopic washings or brushings, or fine needle aspirates) due to the higher likelihood for distinguishing histologic subtypes of lung cancer and also allowing genetic analysis of the cancer for driver mutations. However, depending on the size, location, and clinical suspicion for primary lung cancer, a tissue diagnosis is not always necessary prior to surgical intervention. In situations where there is high clinical suspicion for lung cancer and radiographic appearance highly suspicious for primary bronchogenic carcinoma, tissue diagnosis is not required prior to invasive staging and surgery. In these patients, surgery would provide a tissue diagnosis, staging, and definitive resection of the tumor. It is acceptable to obtain a transbronchial or transthoracic needle biopsy for tissue diagnosis. Endobronchial and centrally located lesions are preferably biopsied bronchoscopically with endobronchial or transbronchial technique. More peripheral lesions are generally biopsied by a CT-guided transthoracic needle approach. In limited situations, there is a role for endoscopic ultrasound (EUS) biopsy of the mediastinal lymph nodes with a transesophageal needle biopsy technique to obtain a diagnosis. However, any needle biopsy has an attendant false negativity and a negative or non-diagnostic pathologic finding should not deter the high clinical concern for underlying malignancy and need for surgery for diagnostic and therapeutic purposes.

2.3 Physiologic Pulmonary Evaluation

Physiologic workup for pulmonary and cardiac risk profile is required as part of the preoperative evaluation. To determine pulmonary reserve, complete pulmonary function testing that includes diffusing capacity for carbon monoxide (DLCO) is required. Forced expiratory volume in one second (FEV_1) and DLCO are the most commonly used parameters to predict operative suitability and perioperative morbidity and mortality. The British Thoracic Society (BTS) suggests that patients with a preoperative FEV_1 in excess of 2L (or >80 % predicted) generally tolerate pneumonectomy [5]. Patients with FEV_1 and DLCO >60 % are suitable for lobectomy. Patients with a preoperative FEV_1 or DLCO <60 % of predicted are at increased risk of developing postoperative respiratory complications but are still considered surgical candidates [5]. With the advent of video-assisted thoracic surgery (VATS), it is unclear if this population is at higher risk of complications and mortality based on PFT results [6, 7]. Patients with compromised pulmonary function with FEV_1 or DLCO <60 % should undergo quantitative lung perfusion (QLP) scan to better estimate postoperative pulmonary function based on measurements of lung perfusion to upper, mid, and lower lung zones [7]. Patients with a predicted postoperative FEV_1 and DLCO >40 % are considered at acceptable risk for lobectomy [5]. High-risk subjects with <40 % should undergo cardiopulmonary exercise testing (CPET) that measures maximal oxygen consumption/uptake (VO2 max). CPET has been shown to be a better predictor of postoperative complications than resting cardiac and pulmonary function. A VO2 max of at least 15 mL/kg/min is suitable risk for a lobectomy [8].

If the estimated predicted postoperative FEV_1 is <35–40 %, performing lung resection is extremely high risk with some studies demonstrating postoperative mortality as high as 50 %, and the tumors are generally considered unresectable [9, 10]. However, based on National Emphysema Treatment Trial (NETT), a subgroup of patients was identified with FEV_1 or DLCO >20 % that were deemed to be of acceptable risk for lung volume reduction surgery [11]. On this basis, there are select patients where surgical resection may be offered with predicted postoperative FEV_1 or DLCO as low as 20 %. But this is considered controversial.

2.4 Cardiac Evaluation

As part of a cardiac evaluation, a transthoracic echo (TTE) should be performed to evaluate for right ventricular systolic pressures (RVSP) and pulmonary hypertension. If there is any evidence of pulmonary hypertension and the patient is being considered for a pneumonectomy, then a right heart catheterization should be performed. Pneumonectomy is contraindicated in the presence of pulmonary hypertension. Pulmonary hypertension can also be identified in patients with main pulmonary artery diameter of >3 cm [12]. These patients should also be considered for right heart catheterization. A stress test is done in patients with suspected or known CAD or based on age and functional status as per the ACC/AHA guidelines [13]. If there is evidence of coronary disease requiring intervention, the treatment proposed must be evaluated based on the tumor histologic type and aggressiveness and risk and benefits of delaying surgery versus other oncologic treatment options.

2.5 Mediastinal Staging

Staging of the mediastinal lymph nodes entails radiologic (PET/CT scan) and pathologic (tissue biopsy) approaches. It is our preference to biopsy the mediastinal lymph nodes almost universally except for:

(1) peripheral <1-cm invasive adenocarcinomas,
(2) low-grade neuroendocrine carcinomas (aka typical carcinoid tumor) with negative PET/CT imaging,
(3) small pure ground glass lesions which are suspected to be adenocarcinoma in situ or minimally invasive adenocarcinomas.

It is our practice that preoperative staging of the mediastinum can be omitted for patients with small (<1 cm) peripheral tumors and suspected stage 1A (T1N0M0) disease. These patients are usually staged intraoperatively with VATS mediastinal lymph node biopsies. Invasive mediastinal staging is required for most patients of suspected stage IB, II, and III NSCLC. NSCLCs include lymph nodes that are enlarged on CT (e.g., >1 cm), and PET-avid lymph nodes regardless of their size are suspected to be involved with cancer. We do not use PET/CT as our only modality for evaluating the mediastinum. PET/CT has higher sensitivity and specificity than CT for staging the mediastinum (71 vs. 43 %, respectively), but it commonly has false-negative results in the subcarinal lymph nodes (level 7) and the AP window lymph nodes (level 5 and 6). In addition, many false-positive results occur [14].

We typically submit all patients to mediastinal staging with cervical mediastinoscopy (CM) as this is the gold standard for mediastinal lymph node staging with a false-negative rate of 5.5 % and mortality and morbidity rates of 0.005 and 1.07 %, respectively [15]. Anterior mediastinotomy is typically reserved for patients with left upper lobe tumors as the drainage pattern usually involves the aortopulmonary window (APW) lymph nodes. Extended cervical mediastinoscopy (ECM) is another way to access and pathologically evaluate APW lymph nodes. A retrospective analysis of 55 patients with NSCLC is compared with PET/CT and ECM and found a higher sensitivity (69 vs. 53 %) and negative predictive value (89 vs. 83 %) with ECM [16]. The main advantage of ECM is that when accessing the APW, it avoids the surgical risk and morbidity associated with a left anterior mediastinoscopy in addition to a CM. However, there are a limited number of centers with the expertise to perform ECM.

Endobronchial ultrasound (EBUS) with transbronchial needle aspiration (EBUS-TBNA) has emerged as a less invasive, non-surgical approach to obtain tissue from lymph nodes in the mediastinum. EBUS has been shown to have similar sensitivity, negative predictive value, and diagnostic accuracy as CM, 81, 91, and 93 %, and 79, 90, and 93 %, respectively [17]. However, in a study looking specifically at patients suspected of having N2 disease, 28 % of patients with negative EBUS-TBNA had positive lymph nodes on CM [18]. Given the discrepancy in results, it is still unclear how EBUS-TBNA should be incorporated into current algorithms for mediastinal staging. At our institution, it is typically used as a primary diagnostic modality in patients with high clinical suspicion of N2 disease. It is otherwise used as an adjunct to the CM.

Some centers have added endoscopic ultrasound (EUS) to EBUS-TBNA to improve the diagnostic accuracy. In a study of 138 patients, the combination of EUS plus EBUS had higher sensitivity and negative predictive value 93 and 97 %, respectively, compared with sensitivity and negative predictive value of EBUS-TBNA (76 and 91 %, respectively) and EUS-TBNA (79 and 91 %, respectively) [19]. EUS plus EBUS also had higher sensitivity and higher negative predictive value for detecting lymph nodes for patients without lymph node enlargement on chest CT [19].

3 Surgery and Small-Cell Lung Cancer (SCLC)

Surgical resection has a limited role in small-cell lung carcinoma (SCLC). SCLC comprises 15 % of lung cancers and is considered aggressive with early development of systemic disease. Local treatment alone has been associated with poor survival. In 1969, the British Medical Research Council study reported a 5-year follow-up study of 144 potentially operable patients with SCLC diagnosed preoperatively on bronchial biopsy. Of the 144 patients, 71 were allocated randomly to surgery and 73 to radiation. The survival rates for the surgery series and the radiotherapy series were 4 and 10 % at 24 months, 3 and 7 % at 48 months, and 1 and 4 % at 60 months, respectively [20]. The study demonstrated extremely poor survival for both treatment groups defining that local treatment alone was inadequate for SCLC.

However, surgical resection does have a role in multimodality treatment of early-stage SCLC with chemotherapy and/or radiation. The National Cancer Institute's Surveillance Epidemiology and End Results (SEER) database from 1988 to 2004 identified 205 patients who underwent lobectomy without radiation for stage I SCLC and reported 3- and 5-year overall survival was 58.1 and 50.3 %, respectively [21]. The benefit of surgery for early-stage SCLC was also demonstrated by the International Association for the Study of Lung Cancer (IASLC) Lung Cancer Study Project. The IASLC database included 349 patients post-resection and staged pathologically with reported 5-year survival rates for patients with pathologic stage I, II, and III SCLC of 48, 39, and 15 %, respectively [22]. Based on this study, patients with SCLC with pathologic absence of mediastinal nodal involvement and distant metastasis should be considered for resection if they are low-surgical-risk candidates.

Given the poor long-term survival with surgery alone historically, adjuvant chemotherapy is given to patients who have undergone a complete resection of pathologically stage I, II, or IIIA SCLC [21]. Patients found to have unsuspected N2 metastasis following resection should receive adjuvant mediastinal radiation. While adjuvant mediastinal radiation is considered in N2 disease, patients with pathologically negative N1 and N2 lymph nodes are generally not given radiation. However, the data on adjuvant radiation following lobectomy for early-stage SCLC are limited and unreliable. The role of prophylactic cranial irradiation is unclear following surgical resection of early-stage SCLC. Based on established data for limited stage SCLC treated with definitive chemoradiation, prophylactic cranial irradiation (PCI) is considered in the adjuvant setting following resection. However, there are no reliable data that addressed the role of PCI after surgical resection for SCLC.

4 Non-Small-Cell Lung Cancer (NSCLC)

4.1 Stage IA

In patients with stage I and II NSCLC, surgical resection is the treatment of choice. Clinical staging based on radiographic findings is limited requiring restaging following pathologic results from invasive mediastinal staging and resection. Stage I and II patients comprise about 30 % of NSCLC patients [23]. Surgical resection alone is the standard of care for stage IA patients.

The location of the tumor dictates the anatomic resection and surgical approach. Intraparenchymal lesions are best treated with surgical lobectomy, while lesions that are central and abutting the bronchus may require sleeve resection or pneumonectomy. Sublobar resection (segmentectomy or wedge resection) is considered in patients with marginal lung function or high-risk surgical candidates. Sublobar resection should be limited to tumors less than 3 cm.

4.2 Stage IB

In patients with stage IB, it is controversial whether tumors should be treated with adjuvant chemotherapy. The CALGB trial demonstrated that adjuvant chemotherapy with carboplatin and paclitaxel provided improved disease-free survival in patients with stage IB tumors in initial reports [24]. However, at 74 months, the difference in survival was not statistically significant. This has been the only study that has showed a potential benefit of adjuvant chemotherapy in stage IB tumors, which may be limited to patients with tumors greater than 4 cm. The ANITA trial demonstrated a benefit of adjuvant therapy in stage II NSCLC tumors [25]. It is our practice that these patients receive adjuvant chemotherapy.

4.3 Stage IIB

In patients with chest wall invasion stage IIB (T3N0), en bloc chest wall resection with ribs should be performed. It is associated with a 40 % five-year survival. However, five-year survival decreases to 12 % if there is any mediastinal lymph node involvement [26]. For this reason, it is crucial to have adequate mediastinal staging prior to surgical resection. Multiple studies have demonstrated improved survival in stage IIB NSCLC and are discussed with most patients [27, 28].

4.4 Stage III NSCLC

4.4.1 Stage IIIA (e.g., T3N1/T4N1)

If the patient has stage IIIA disease based on the involvement of the chest wall or proximal airways or due to the presence of satellite nodules within the same lobe as the primary tumor, they are candidates for surgical resection followed by adjuvant chemotherapy. These patients have a better prognosis than patients with stage IIIA secondary to mediastinal N2 nodal involvement [29]. The primary exceptions to this treatment are superior sulcus (Pancoast) tumors with hilar lymph node involvement. Patients with Pancoast tumors are typically treated with neoadjuvant chemoradiation followed by surgery [30].

4.4.2 Stage IIIA with N2 Disease

Patients with clinically resectable stage IIIA (T3N2) disease have been the only group of patients found to benefit from neoadjuvant chemotherapy or chemoradiation. It is our practice that these patients are staged cervical mediastinoscopy first and reserve EBUS for mediastinal restaging after neoadjuvant therapy to evaluate for persistent N2 disease. If there is no evidence of mediastinal disease or the patient is downstaged to N1 (N2 negative), then the patient is considered a candidate for surgical resection with increased survival if lobectomy is performed versus pneumonectomy [29, 31]. While it is controversial whether the induction should be chemotherapy alone or chemoradiation, when pneumonectomy is technically required, preoperative radiation should be omitted due to the attendant high risk of perioperative mortality associated with pneumonectomy following chemoradiation. It is our preference to offer preoperative chemotherapy alone and then perform pneumonectomy should there be any clearance of N2 disease on mediastinal restaging for low-risk patients [31, 25]. Based on the ANITA trial, adjuvant radiation should be considered in these patients.

4.5 Stage IIIB and IV NSCLC

Patients with stage IIIB or stage IV NSCLC are typically not candidates for resection and should be treated with definitive chemotherapy or chemoradiation.

4.6 Special Situations

4.6.1 Extended Resections

Resectable T4N0-1 lesions are uncommon, and most T4 lesions (mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, or carina) are generally treated with definitive chemoradiation therapy. Patient selection is of critical importance. Surgery for T4 disease is contraindicated in the presence of N2 involvement (stage IIIB) or if a complete resection is not possible.

When carefully staged and selected, some patients with T4 (N2 negative) tumors appear to benefit from resection as part of the treatment as opposed to chemoradiotherapy alone [31–33].

4.6.2 Synchronous NSCLC

Patients that present with synchronous multiple primary lung cancer (MPLC) pose a variety of clinically important diagnostic and therapeutic dilemmas. Patients presenting with more than one pulmonary nodule at the same time must fulfill strict criteria to be classified as having synchronous MPLC. Based on the American College of Chest Physicians guidelines, the following are the considerations that define synchronous lung cancers [34]:

1. Both lesions must be malignant and must arise independently in the lung.
2. The second lesion cannot be assumed to represent a second primary lung cancer. A benign nodule, infectious process, or metastasis from an extrapulmonary site must be excluded.
3. The second malignant lesion must not represent a metastasis from the first lung lesion. Accepted criteria for distinction include different histology or origin from separate focus of carcinoma in situ. It has same histology but anatomically distinct, without involvement of the mediastinum (N2, N3, negative) and without systemic metastases.
4. Absence of systemic disease.

Patients with MPLC with N1 involvement of NSCLC should be considered for surgical resection if feasible. Some patients may be candidates for surgical resection of the primary with N1 nodal involvement and non-operative local management of the other primary malignancy if surgical resection is not feasible. MPLC with the same histology and N2 nodal involvement are generally treated as stage IV disease since a single malignant process is likely responsible for all the lesions and clinical carries a poorer prognosis compared to absent mediastinal involvement.

Surgery is a standard approach for treatment in patients with synchronous MPLC. Surgical planning is based on sufficient pulmonary reserve after resection. However, limited pulmonary reserve may require a patient to undergo a sublobar resection (e.g., segmentectomy) of one or both lesions, or limited resection to one lesion and definitive non-operative local therapy such as radiation or ablation. Patients with a satellite lesion in the same lobe as the primary lung cancer have a good prognosis and should be managed as dictated by the primary tumor alone.

4.6.3 Oligometastatic Disease

Oligometastatic disease is relatively common in NSCLC and does not always lead to widespread metastatic disease. Mediastinal staging is extremely important in this patient group as any positive mediastinal lymph nodes are a contraindication to resection.

(a) ***Brain metastasis***

Limited brain metastases can be managed aggressively with surgical resection. The use and benefit of directed therapy toward brain metastases has coincided with improved neurosurgical and radiosurgical techniques. Surgery is reserved for patients with limited number (1–3) of metastases. These patients benefit from a combination of stereotactic radiosurgery (if less than 3 cm or in a surgical inaccessible location) and/or surgical resection in addition to whole-brain radiation. Patients whose treatment included surgery had significantly fewer local recurrences (20 vs. 52 %), significantly improved survival (40 vs. 15 weeks), and a better quality of life [35]. Whole-brain radiation is primarily used to decrease risk of recurrence. The patients with stable extracranial disease had increased survival (median 12 months) [36]. In patients with >3 brain metastases, whole-brain radiation is the standard approach. Our practice is the local treatment of solitary brain metastasis (either surgically or with radiation) and resection of the primary lung cancer in mediastinal lymph node-negative patients with chemotherapy, preferably preoperative to the lung resection. Although there have been reports of lung cancer resection with oligometastatic brain lesions, the existing information suggests poorer prognosis with oligometastatic disease.

(b) ***Isolated Adrenal metastasis***

The adrenal gland is a common site of metastasis in NSCLC. Diagnosis should not be based exclusively on imaging findings as one study found that 4 of 14 suspected adrenal metastases were cortical adenomas [37]. Histologic confirmation is absolutely necessary.

Surgical resection in isolated adrenal metastasis from lung cancer should be considered in selected patients. Patients with metachronous adrenal metastases survived longer than those with synchronous adrenal metastases [38]. Favorable prognostic characteristics are R0 resection, long disease-free interval, and no other metastasis. In a study from the Massachusetts General Hospital, among 37 patients with isolated adrenal metastases, the five-year survival was 34 % in the adrenalectomy group versus 0 % in the non-operative group [39], thus emphasizing the important survival benefit of surgical resection. Our practice is surgery of solitary adrenal metastasis and resection of the primary lung cancer in mediastinal lymph node-negative patients with chemotherapy, preferably preoperative to the lung resection. Usually, patients are given systemic therapy first, followed by lung resection and finally adrenalectomy.

(c) ***Metachronous NSCLC***

Although many patients are treated successfully for NSCLC, approximately one-third of recurrences will be isolated from the ipsilateral thorax [40]. A complete metastatic workup should guide further therapy. Selected patients with the same type of cancer in a different lobe of the lung may benefit from aggressive surgical resection. According to the American College of Chest Physicians guidelines and recommendations, the survival results after resection for either a synchronous presentation or a metachronous presentation with an interval of <4 years between tumors are variable and generally poor, suggesting that many of these patients may have had a pulmonary metastasis rather than a second primary lung cancer [41]. Although a thorough and careful evaluation of these patients is warranted to differentiate between metastatic disease from a second primary lung cancer, distinguishing criteria have not been defined in the literature [41]. Surgical resection should be considered in appropriately selected patients as it can prolong survival [42]. A retrospective study of 161 patients at the Mayo Clinic with metachronous NSCLC revealed a 5-year overall survival rate of 61 % calculated from the time of the second resection with improved survival and freedom from recurrence with tumors less than 2 cm [43]. If recurrence is restaged clinically a stage I or II, then re-resection should be considered. If the patient is not a candidate for additional surgery, definitive radiation or ablation should be the primary modality of treatment particularly in patients with a long disease-free interval. If the recurrence is restaged clinically as stage III with nodal involvement, then definitive chemoradiation should be considered [44].

(d) ***Synchronous Squamous cell carcinoma (SCC) of the head and neck and the lung***

Synchronous SCC of the head and neck with solitary SCC of the lung presents a very difficult diagnostic and therapeutic dilemma. If the tumors are found metachronously, then the treatment is based on established clinical criteria. For synchronous tumors, pan endoscopy and cervical mediastinoscopy are necessary for adequate staging. If there is no evidence of mediastinal disease, then surgical resection is warranted as this prolongs survival. In a retrospective study of 2964 patients with SCC of the head and neck, 27 patients were found to have synchronous SCC of the lung. Of those who had surgery with curative intent, the 5-year disease-free survival was 51 % if the mediastinum was radiographically negative compared to 13 % in patients who were surgical candidates but elected to treat with palliative therapy [45].

The appropriate sequence of surgery is still unclear. If the head and neck tumor will be treated with radiation, then it is reasonable to proceed with the thoracic resection first. However, if both tumors require surgery, then proceeding with the resection of the head and neck tumor to ensure a patent airway is a reasonable approach.

5 Surgical Options and Approaches

5.1 Types of Incisions

Lung resection, such as a lobectomy, can be performed through a thoracotomy (most common) or a median sternotomy. A posterolateral thoracotomy (Fig. 1) is a

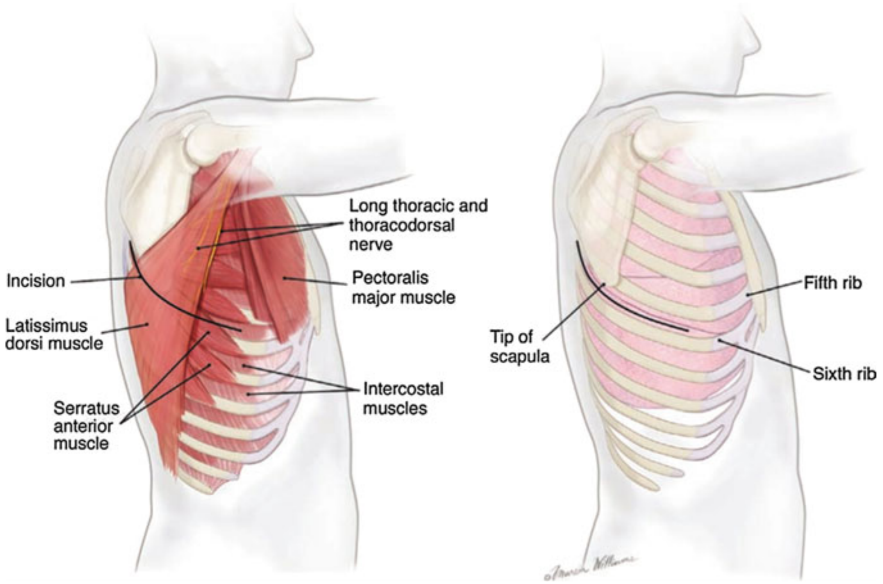


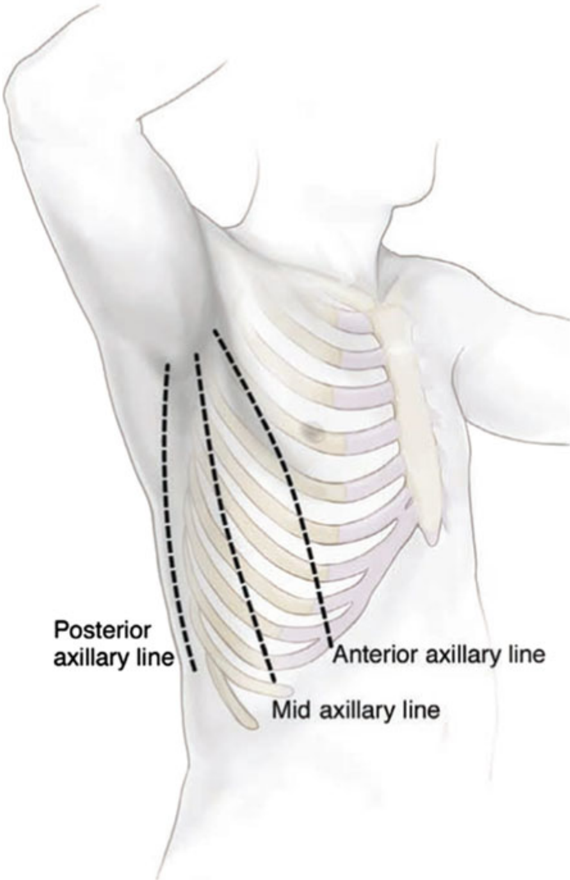
Fig. 1 Posterolateral thoracotomy

commonly used incision for lung resection. This incision is carried from the mid-point between the spine and the posterior border of the scapula to one fingerbreadth below the inferior tip of the scapula and then extended anteriorly the same distance toward the inframammary crease. The serratus anterior muscle is usually preserved and retracted anteriorly. For the standard pulmonary resection, the chest cavity is reached by entering through an intercostal space that provides the best access for the procedure to be performed (4th interspace for upper lobe lesions and 5th interspace for lower lobe lesions) [46]. The posterior muscle-sparing thoracotomy is preferred when possible as it spares all chest wall muscles by using the auscultatory triangle as the landmark. The initial skin incision is identical to the traditional thoracotomy. Subcutaneous skin flaps are created superiorly and inferiorly. The latissimus dorsi muscle is identified and mobilized from the underlying serratus muscle for its entire length. The serratus muscle is then elevated. A rib can be partially excised to facilitate spreading and to avoid rib fractures.

An axillary thoracotomy, or limited lateral thoracotomy (Fig. 2), can be used for upper or middle lobe resections or procedures confined to the anterior mediastinum or hilum. The incision is carried through the anterior aspect of the serratus muscle parallel to its fibers to the level of the 4th intercostal space. Care must be taken not to damage the long thoracic nerve posteriorly. With experience, this incision can be used for most situations. Since no muscle is divided, it can also be the least painful of the thoracotomy incisions.

The anterior thoracotomy (Fig. 3) is used to approach lesions in the anterior and middle thoracic cavity. An incision is made in the inframammary crease along the

Fig. 2 Axillary thoracotomy



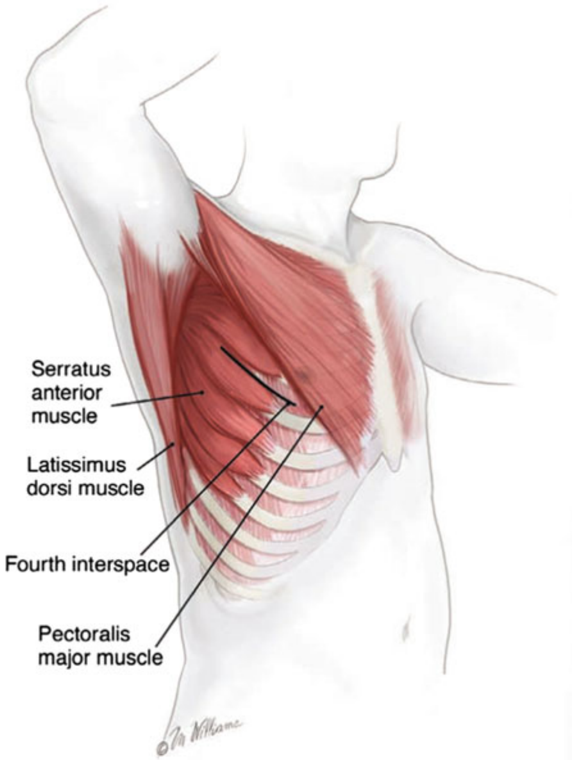
5th rib. The pectoralis major muscle is divided at its insertion into the medial chest wall. The serratus anterior muscles are then incised to expose the 4th and 5th ribs with the chest cavity entered at the 4th intercostal space. Lateral serratus fibers are spared to avoid long thoracic nerve injury [46].

5.2 Types of Surgical Resection

5.2.1 Wedge Resection

Several studies indicate that wedge resections for NSCLC are associated with higher local recurrence rates compared to lobectomy. Wedge resections are reserved for small peripheral lesions in patients with impaired cardiopulmonary reserve that are not candidates for lobectomy or segmentectomy [47–49]. Minimally invasive approaches such as VATS wedge resections are the standard of care that achieve shorter hospital stay and less patient morbidity than an open operation [50]. More

Fig. 3 Anterior thoracotomy



importantly, the 5-year survival rates are the same for patients with T1N0 lesions who underwent wedge resection whether by VATS or thoracotomy [51]. There is also no difference in disease-free survival when comparing wedge resection to anatomic lobectomy of stage IA patients [52]. Criteria for wedge resection that have been suggested include the following:

(1) Tumors less than 2 cm in diameter (T1a lesion);
(2) Tumors located in outer third of lung and approachable by wedge resection by staple, electrocautery, or laser;
(3) No endobronchial extension;
(4) Frozen section evidence of negative pathological resection margins; and
(5) Intraoperative mediastinal and hilar nodal staging [51].

Recurrences vary with tumor size and nodal involvement. For node-negative patients with T1 and T2 tumors, the long-term local recurrence occurs in 5–12 %, whereas distant metastasis occurs in 7–30 % of patients. Failure rates increase with the presence of hilar or mediastinal nodal disease. In N1 and N2 disease, several studies show the local failure rate ranges from 9–28 % to 13–17 %, respectively, while distant metastasis occurs in 22–61 % of patients [53–55]. Interestingly, if recurrence occurs with initially clear margins, this is thought to reflect an aggressive, metastatic tumor phenotype rather than surgical failure leading to metastatic disease [51, 56–59].

A number of strategies have been shown to decrease local recurrence after wedge resections. External beam radiation has had promise, but in a prospective multi-institutional clinical trial of high-risk patients treated with post-wedge resection “postage stamp” radiotherapy, the results were less promising [47]. The phase III Alliance trial that enrolled 224 patients found no difference in local recurrence or survival between sublobar resection alone and sublobar resection combined with intraoperative placement of iodine-125 seeds. Local progression occurred in only 17 patients (8 %) overall, there was no significant difference between the two treatment arms, and the three-year overall survival rate was 71 % in each treatment arm. The median follow-up was 4.4 years [60].

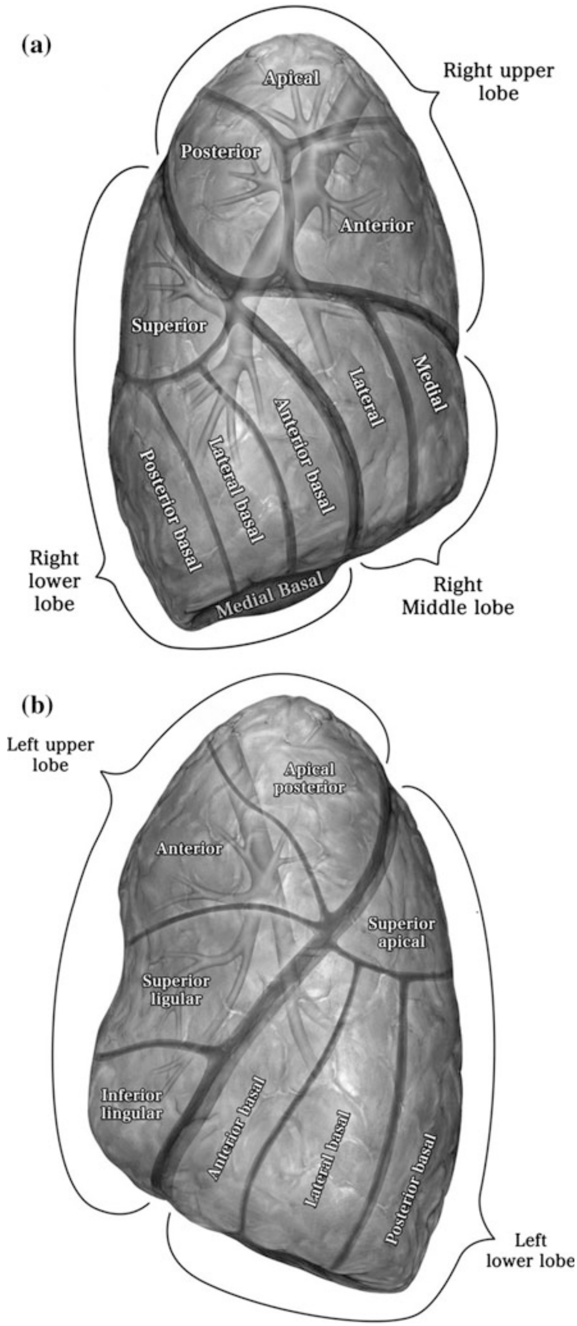
5.2.2 Segmentectomy

Segmentectomy (Fig. 4) has been reserved for resection of selected NSCLC. These include stage I and II NSCLC in patients with impaired lung function, as a lung preservation operation in patients with synchronous or metachronous lung cancer, and for peripheral stage I lung cancer [61]. Retrospective studies have shown segmentectomies to confer equivalent survival rates to lobectomy in selected patients. Major complications include prolonged air leaks (5–16 %) and a higher rate of recurrence (11–16 vs. 5 % for lobectomy) [47, 62–65]. As expected, increased recurrence (22 %) was seen in segmentectomies with margins less than 1–2 cm as well as proximity to the hilum [66, 67]. With underlying pulmonary compromise, segmentectomies were associated with a 30-day mortality benefit of 1.1 versus 3.3 % for lobectomy [66]. This is supported by findings that segmentectomy results in better residual pulmonary function than lobectomy [68]. Thoracoscopic resection has been shown to result in shorter hospital stay as well as lower thirty-day mortality compared to the open approach [69]. Due to the improved tolerance of patients to adjuvant therapy, thoracoscopic segmentectomy may also yield better survival than the open technique [70]. Commonly performed segmentectomies include lingula-sparing left upper lobectomy, lingulectomy, superior segmentectomy, and basilar segmentectomy. Less commonly performed segmentectomies include anterior or posterior upper lobe segmentectomies [71].

5.2.3 Lobectomy

Open lobectomy has been the standard of care of early-stage NSCLC for many years. However, VATS lobectomy has emerged as an excellent alternative to open lobectomy and is now the standard of care for surgically amenable tumors. Comparable complication [72–74] and survival [73, 75, 76] rates between VATS and open lobectomies can be achieved. VATS lobectomies have several advantages over traditional open techniques. These include decreased postoperative pain [77, 78], lower chest tube output and duration [73], less blood loss [79], superior pulmonary function [80], shorter hospital stay, and earlier return to normal activities [72, 73]. Equivalent survival at 3 and 5 years has been reported for VATS

Fig. 4 Segments of the lung



lobectomy (90 and 90 %, respectively) and open lobectomy (93 and 85 %) for stage I NSCLC [81–83]. Importantly, patients who underwent VATS lobectomy were more tolerant of adjuvant therapy than their open lobectomy counterparts. Patients undergoing VATS lobectomy experienced fewer delays in chemotherapy and were more likely to tolerate and complete the entire adjuvant chemotherapy regimen. Furthermore, more VATS lobectomy patients received >75 % of their planned regimen without delayed or reduced doses. Long-term outcome differences remain unproven [84]. Although challenging, VATS lobectomy has also found to be feasible and safe after induction therapy [85].

5.2.4 Pneumonectomy

According to the Lung Cancer Study Group report, mortality in "pneumonectomies should carry a risk of less than 7 %, lobectomies less than 3 %, and lesser resections less than 2 %." Risk factors for mortality in pneumonectomies include right-sided pneumonectomies, older age (>70), and low-volume surgical centers. In addition, long-term sequelae of pneumonectomies include pulmonary hypertension, progression of emphysema, and increased right heart pressures during exercise [86, 87]. Pneumonectomies are considered when sleeve resections are considered technically not feasible [88]. Impaired function and shortened long-term survival due to cardiorespiratory compromise have been cited as risks against pneumonectomies in favor of sleeve resection [87, 89]. Patients treated with pneumonectomy have increased operative morbidity and mortality as well as reduced long-term survival compared with patients treated with lobectomy [90–92]. Late death may also be increased by the long-term cardiopulmonary morbidity of pneumonectomies [92]. Life-threatening complications following pneumonectomies are more likely when there is reduced preoperative diffusion capacity, preexisting compromising cardiopulmonary disease, excessive perioperative fluid administration, and a preoperative low hemoglobin [93]. Others have found that after performing a multivariate analysis, pneumonectomy was not an independent determinate of long-term survival [94]. Rather, it was the patient age, preoperative spirometry, and T and N status that determined long-term survival. It has also been argued that pneumonectomies are associated with a lower rate of second primaries compared with lobectomies, presumably because there is less remaining lung tissue at risk for malignancy.

The safety of chemoradiation therapy with pneumonectomy is an important issue for patients with more advanced NSCLC. Single-institution experiences report that chemoradiation induction therapy can be performed with acceptable 30- and 100-day mortality rates of 6 and 10 %, respectively, with good oncologic outcomes [95]. Long-term survival at 1 and 5 years for those receiving neoadjuvant therapy was 74 and 46 % and similar to the surgery-only group with the survival of 72 and 34 % [96]. However, definitive chemoradiation is recommended by some groups in NSCLC stage IIIA patients being considered for pneumonectomy as there is increased mortality in this select patient group, particularly with a right-sided pneumonectomy. Results from other similar reports were, however, less encouraging with 30- and 90-day mortality rates of 12 and 21 %. Survival at 3 and 5 years was 35 and 25 %, respectively [97]. A consistent finding is that right pneumonectomies are associated with significantly greater morbidity and mortality and should be performed with great care [98]. Discrepant results are likely due to the retrospective nature of these studies that are subject to inherent biases. Differences in perioperative management can lead to variations in outcomes such as chest tube drainage, pain control, and fluid balance.

5.2.5 Sleeve Resections

Bronchial sleeve lobectomy was introduced by Sir Clement Price-Thomas in 1947 to allow parenchyma-sparing surgery. Allison subsequently performed the first sleeve lobectomy for bronchogenic carcinoma [99]. Bronchoplastic techniques are used in 3–13 % of resectable pulmonary tumors accompanied [99–101]. The purpose is to provide adequate tumor resection margins while conserving as much healthy lung parenchyma as possible [102]. Sleeve lobectomy has become an alternative to pneumonectomy for patients with marked impairment in pulmonary function, elderly patients, as well as those with serious comorbidities, and should be considered in all patients where technically feasible. In particular, it is the procedure of choice for cancer extending to the left or right upper lobe bronchial orifice and adjacent main stem bronchus or extending to the proximal left lower lobe bronchus. Compared to pneumonectomy, it provides an improved quality of life while achieving superior morbidity, mortality, and long-term survival [99, 103]. Interestingly, in addition to a better quality of life, the long-term cancer control appears to be no different than a pneumonectomy [104]. Sleeve resections have a reported mortality 4 % with survival at 1 and 5 years of 84 and 42 %, respectively. A sleeve lobectomy can reach the same functional result as a standard lobectomy. However, it takes 3–4 months for the reimplanted lobe to completely recover and contribute to residual postoperative pulmonary function [105]. Given that the lifelong risk of developing a second lung cancer is about 2 % per year after the resection, a subsequent lung resection can more safely be performed in patients who previously underwent a sleeve lobectomy versus those who had a prior pneumonectomy [103, 106]. The size of the tumor may limit the technical feasibility of sleeve lobectomy [107]. However, chemotherapy and radiation can downstage tumors in the presence of mediastinal disease to allow bronchoplastic techniques. Although chemotherapy has been associated with decreased mucosal blood flow and healing [108], clinical studies have shown that sleeve lobectomy is still safe after neoadjuvant chemotherapy [101, 109]. Operative mortality is high in patients with serious comorbidities (e.g., poor nutritional status, liver impairment, renal impairment, diabetes, cardiac compromise, peripheral vascular disease, stroke). Elderly patients must be very carefully selected as well [103].

Performance of sleeve resections involves a dissection of bronchus from its adjacent lung and pulmonary vessels at the lobar orifice level (Fig. 5). A bronchotomy is sometimes performed under bronchoscopic guidance to ensure adequate margins. After determining the extent of the tumor, resection is performed *en bloc* with a portion of the airway and sometimes the associated pulmonary artery perfusing the remaining lung. The specimen is then sent for frozen section to confirm

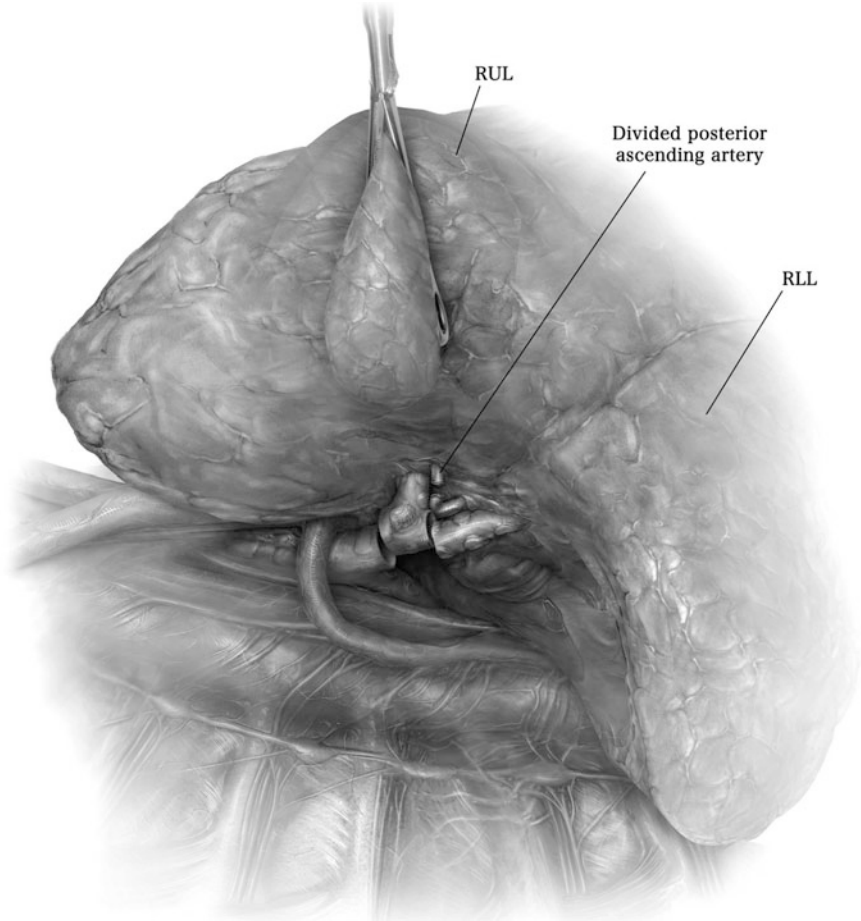


Fig. 5 Sleeve right upper lobectomy

negative margins. An end-to-end anastomosis (Fig. 6) is then performed and covered with a vascularized pleural or pericardial flap (Fig. 7) for protection and prevention of pulmonary vessel erosion by suture knots and to provide extra blood supply to the anastomosis [102, 110]. The most common site of sleeve resection is the right upper lobe [111–117].

Bronchoplastic procedures have more postoperative complications than standard lobectomies, thereby requiring intensive care monitoring in the immediate postoperative period. Early postoperative issues include partial atelectasis, lobar collapse, pneumonia, air leak, suture erosion of vessels, and transient vocal cord paralysis. Atelectasis commonly results from blood or mucus plugging. Routine postoperative flexible bronchoscopy and bronchial toilet are recommended for preemptive treatment prior to extubation. This also offers an opportunity for the surgeon to confirm the patency of the reconstructed bronchus. Pulmonary clearance

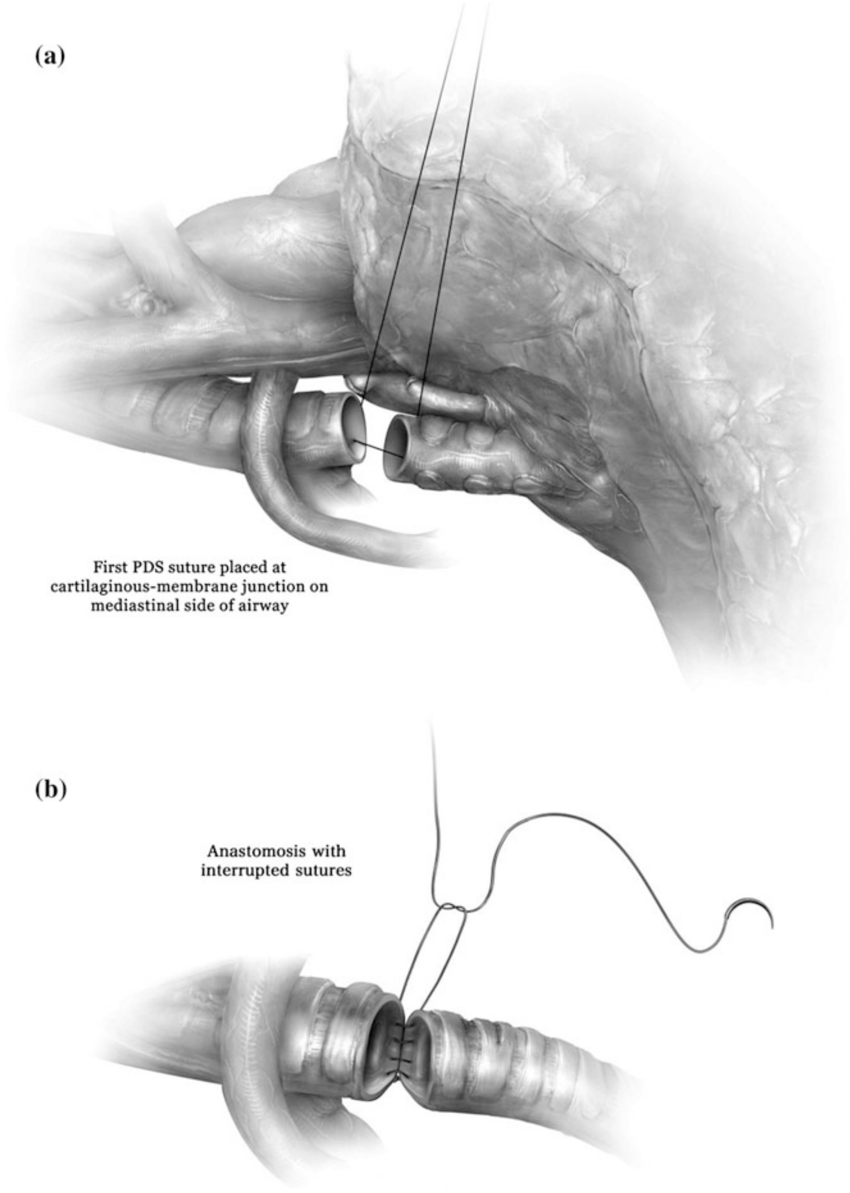


Fig. 6 Sleeve lobectomy anastomosis

mechanisms are compromised postoperatively, especially in elderly patients, so aggressive chest physiotherapy and steam inhalations may help prevent complications [102]. Transection of bronchial lymphatics increases pulmonary fluid and likely contributes to increased risk of infection [110]. Sleeve resection has a

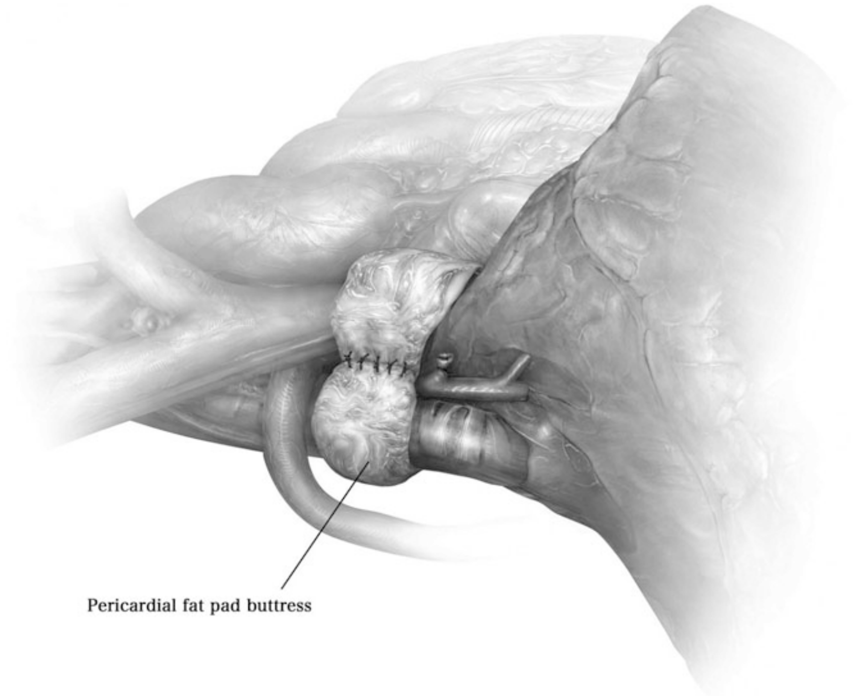


Fig. 7 Pericardial fat pad buttress

morbidity rate of 26.8 % and mortality rate of 5.5 % [101]. Other complications following sleeve resection are bronchoplasty site stenosis and dehiscence, bronchopleural fistulae, and bronchovascular fistulae [103, 104]. Late complications include bronchial stricture, bronchiectasis, bronchopleural fistula, and empyema [99]. The incidence of bronchial anastomotic complications is 6.4 % with a bronchopleural fistula rate of 3 % and a bronchovascular fistula rate of 2.5 %. There is also a 10 % rate of pneumonia following sleeve resection [99]. Predictive factors for postoperative complications include right-sided resections, smoking, and squamous cell carcinomas [118]. Technical points that can assist in minimizing complications include precise dissection and anastomotic technique, avoidance of anastomotic stenosis during initial surgery, preservation of blood supply, using a buttress for the anastomosis, and interpositing healthy tissue between the bronchial and vascular structures [118]. Anastomotic dehiscence or stenosis after sleeve lobectomy can require subsequent completion pneumonectomy [99]. This occurs more frequently in compromised patients [119], pathologic N2 status, as well as those with positive bronchial margins [119, 120]. The use of absorbable suture such as vicryl or PDS has decreased the incidence of bronchial anastomotic complications which can more readily allow postoperative dilatation [121]. Bronchoplastic procedures are technically demanding and have better outcomes by surgeons specializing in general thoracic surgery.

5.2.6 Carinal Resection

Lung cancers in close proximity to or involving the carina are often not amenable to resection. However, complete resection may be possible for a select patient group that does not have dissemination or invasion into vital structures [122, 123]. Utilization of bronchoplastic techniques in these patients can greatly improve outcomes and survival [124]. Several studies have shown that bronchoplastic operations for carinal involvement can be done with an acceptable mortality rate of approximately 16 % [124–130]. Tracheobronchial junction tumors are particularly challenging. While most of these tumors can be resected through the usual right posterolateral thoracotomy, Muscolino et al. used anterior thoracotomy through the fourth intercostal space to perform a right sleeve pneumonectomy. Good exposure, adequate anastomotic visualization, and nodal clearance from the paratracheal and subcarinal areas can be achieved through this incision [106]. Other exposures that have been described include bilateral thoracotomies or sternothoracotomy [128]. Lethal complications of this operation are acute respiratory distress syndrome (ARDS) and non-cardiogenic pulmonary edema. The etiology of post-lung-resection ARDS and is unknown, but this complication is associated with mortality rates as high as 90 % [123, 131]. Nitric oxide has been used to treat this devastating condition with modest success [132]. Anastomotic complications are major complications of bronchoplastic resection of carinal tumors. Most commonly, these result from excessive tension on the anastomosis either from an excessive airway resection or from inadequate mobilization of the remaining lung and trachea. Therefore, carinal resection should be limited to a maximum of 4 cm (measured from proposed tracheotomy to left main stem bronchotomy). Other key factors include preservation of airway vascularity, meticulous anastomotic technique, and careful tissue handling [125]. Prolonged postoperative mechanical ventilation increases mortality, so patients should be extubated immediately after surgery whenever possible [123].

6 Summary

Preoperative staging is very important and is considered to be one of the most important prognostic indicators in patients with lung cancer. Once adequately staged, a treatment regimen can be outlined for the patient. It is not uncommon for patients to be told they are unresectable without adequate staging only to be told later that they are surgical candidates. Cardiopulmonary testing is important to risk stratify patients and better estimate their risk of morbidity and mortality from surgery. There are several surgical approaches to surgical resection of a lung cancer. However, minimally invasive surgical approaches such as VATS and robot assistance are increasingly used for pulmonary resections for lung cancer. The T and N status of a surgically resected specimen determines whether it is beneficial to proceed with adjuvant chemotherapy or radiation. Genetic alterations in lung cancer may be able to predict sensitivity to chemotherapy agents and allow for more targeted therapy. Due to the complexity of management, patients with lung cancer should be cared for by general thoracic surgeons and a multidisciplinary team to improve both disease-free survival and overall survival.

Bibliography

1. Fischer B et al (2009) Preoperative staging of lung cancer with combined PET-CT. N Engl J Med 361(1):32–39
2. Reidy-Lagunes DL, Gollub MJ, Saltz LB (2011) Addition of octreotide functional imaging to cross-sectional computed tomography or magnetic resonance imaging for the detection of neuroendocrine tumors: added value or an anachronism? J Clin Oncol 29(3):e74–e75
3. Granberg D et al (2003) Octreoscan in patients with bronchial carcinoid tumours. Clin Endocrinol (Oxf) 59(6):793–799
4. Gustafsson BI et al (2008) Bronchopulmonary neuroendocrine tumors. Cancer 113(1):5–21
5. British Thoracic S, Society of Cardiothoracic Surgeons of Great B, Ireland Working P (2001) BTS guidelines: guidelines on the selection of patients with lung cancer for surgery. Thorax, 56(2):89–108
6. Berry MF et al (2010) Pulmonary function tests do not predict pulmonary complications after thoracoscopic lobectomy. Ann Thorac Surg 89(4):1044–1051; discussion 1051–1052
7. Brunelli A et al (2013) Physiologic evaluation of the patient with lung cancer being considered for resectional surgery: diagnosis and management of lung cancer, 3rd ed: American college of chest physicians evidence-based clinical practice guidelines. Chest 143 (5 Suppl):e166S–e190S
8. Datta D, Lahiri B (2003) Preoperative evaluation of patients undergoing lung resection surgery. Chest 123(6):2096–2103
9. Markos J et al (1989) Preoperative assessment as a predictor of mortality and morbidity after lung resection. Am Rev Respir Dis 139(4):902–910
10. Kearney DJ et al (1994) Assessment of operative risk in patients undergoing lung resection. Importance of predicted pulmonary function. Chest 105(3):753–759
11. Criner GJ, Sternberg AL (2008) National emphysema treatment trial: the major outcomes of lung volume reduction surgery in severe emphysema. Proc Am Thorac Soc 5(4):393–405
12. Karazincir S et al (2008) CT assessment of main pulmonary artery diameter. Diagn Interv Radiol 14(2):72–74
13. Gibbons RJ et al (1997) ACC/AHA guidelines for exercise testing: executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Exercise Testing). Circulation 96(1):345–354
14. Cerfolio RJ et al (2003) The role of FDG-PET scan in staging patients with nonsmall cell carcinoma. Ann Thorac Surg 76(3):861–866
15. Lemaire A et al (2006) Nine-year single center experience with cervical mediastinoscopy: complications and false negative rate. Ann Thorac Surg 82(4):1185–1189; discussion 1189–1190
16. Metin M et al (2011) The role of extended cervical mediastinoscopy in staging of non-small cell lung cancer of the left lung and a comparison with integrated positron emission tomography and computed tomography: does integrated positron emission tomography and computed tomography reduce the need for invasive procedures? J Thorac Oncol 6(10):1713–1719
17. Yasufuku K et al (2011) A prospective controlled trial of endobronchial ultrasound-guided transbronchial needle aspiration compared with mediastinoscopy for mediastinal lymph node staging of lung cancer. J Thorac Cardiovasc Surg 142(6):1393–400 e1
18. Defranchi SA et al (2010) Mediastinoscopy in patients with lung cancer and negative endobronchial ultrasound guided needle aspiration. Ann Thorac Surg 90(6):1753–1757

19. Wallace MB et al (2008) Minimally invasive endoscopic staging of suspected lung cancer. JAMA 299(5):540–546
20. Miller AB, Fox W, Tall R (1969) Five-year follow-up of the medical research council comparative trial of surgery and radiotherapy for the primary treatment of small-celled or oat-celled carcinoma of the bronchus. Lancet 2(7619):501–505
21. Yu JB et al (2010) Surveillance epidemiology and end results evaluation of the role of surgery for stage I small cell lung cancer. J Thorac Oncol 5(2):215–219
22. Vallieres E et al (2009) The IASLC lung cancer staging project: proposals regarding the relevance of TNM in the pathologic staging of small cell lung cancer in the forthcoming (seventh) edition of the TNM classification for lung cancer. J Thorac Oncol 4(9):1049–1059
23. Groome PA et al (2007) The IASLC lung cancer staging project: validation of the proposals for revision of the T, N, and M descriptors and consequent stage groupings in the forthcoming (seventh) edition of the TNM classification of malignant tumours. J Thorac Oncol 2(8):694–705
24. Strauss GM et al (2008) Adjuvant paclitaxel plus carboplatin compared with observation in stage IB non-small-cell lung cancer: CALGB 9633 with the cancer and leukemia group B, radiation therapy oncology group, and north central cancer treatment group study groups. J Clin Oncol 26(31):5043–5051
25. Douillard JY et al (2006) Adjuvant vinorelbine plus cisplatin versus observation in patients with completely resected stage IB-IIIA non-small-cell lung cancer (adjuvant navelbine international trialist association [ANITA]): a randomised controlled trial. Lancet Oncol 7 (9):719–727
26. Doddoli C et al (2005) Lung cancer invading the chest wall: a plea for en-bloc resection but the need for new treatment strategies. Ann Thorac Surg 80(6):2032–2040
27. Winton T et al (2005) Vinorelbine plus cisplatin vs. observation in resected non-small-cell lung cancer. N Engl J Med 352(25):2589–2597
28. Arriagada R et al (2004) Cisplatin-based adjuvant chemotherapy in patients with completely resected non-small-cell lung cancer. N Engl J Med 350(4):351–360
29. Jaklitsch MT et al (2006) Nodal downstaging predicts survival following induction chemotherapy for stage IIIA (N2) non-small cell lung cancer in CALGB protocol #8935. J Surg Oncol 94(7):599–606
30. Detterbeck FC (1997) Pancoast (superior sulcus) tumors. Ann Thorac Surg 63(6):1810–1818
31. Albain KS et al (2009) Radiotherapy plus chemotherapy with or without surgical resection for stage III non-small-cell lung cancer: a phase III randomised controlled trial. Lancet 374 (9687):379–386
32. Detterbeck FC et al (2003) Lung cancer, special treatment issues. Chest 123(1 Suppl):244S–258S
33. DiPerna CA, Wood DE (2005) Surgical management of T3 and T4 lung cancer. Clin Cancer Res 11(13 Pt 2):5038s–5044s
34. Kozower BD et al (2013) Special treatment issues in non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American college of chest physicians evidence-based clinical practice guidelines. Chest 143(5 Suppl):e369S–e399S
35. Patchell RA et al (1990) A randomized trial of surgery in the treatment of single metastases to the brain. N Engl J Med 322(8):494–500
36. Noordijk EM et al (1994) The choice of treatment of single brain metastasis should be based on extracranial tumor activity and age. Int J Radiat Oncol Biol Phys 29(4):711–717
37. Lucchi M et al (2005) Metachronous adrenal masses in resected non-small cell lung cancer patients: therapeutic implications of laparoscopic adrenalectomy. Eur J Cardiothorac Surg 27 (5):753–756
38. Porte H et al (2001) Resection of adrenal metastases from non-small cell lung cancer: a multicenter study. Ann Thorac Surg 71(3):981–985
39. Raz DJ et al (2011) Outcomes of patients with isolated adrenal metastasis from non-small cell lung carcinoma. Ann Thorac Surg 92(5):1788–1792; discussion 1793

40. Younes RN, Gross JL, Deheinzelin D (1999) Follow-up in lung cancer: how often and for what purpose? Chest 115(6):1494–1499
41. Shen KR et al (2007) Special treatment issues in lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition). Chest 132(3 Suppl):290S–305S
42. Hamaji M, Ali SO, Burt BM (2015) A meta-analysis of resected metachronous second non-small cell lung cancer. Ann Thorac Surg 99(4):1470–1478
43. Hamaji M et al (2013) Surgical treatment of metachronous second primary lung cancer after complete resection of non-small cell lung cancer. J Thorac Cardiovasc Surg 145(3):683–690; discussion 690–691
44. Harpole DH Jr et al (1995) Stage I nonsmall cell lung cancer. A multivariate analysis of treatment methods and patterns of recurrence. Cancer 76(5):787–796
45. Kuriakose MA et al (2002) Simultaneously presenting head and neck and lung cancer: a diagnostic and treatment dilemma. Laryngoscope 112(1):120–123
46. Nesbitt JC, Wind GG (2003) Thoracic surgical oncology: exposures and techniques. Lippincott Williams & Wilkins, Philadelphia
47. Miller JI, Hatcher CR Jr (1987) Limited resection of bronchogenic carcinoma in the patient with marked impairment of pulmonary function. Ann Thorac Surg 44(4):340–343
48. Pastorino U et al (1991) Limited resection for Stage I lung cancer. Eur J Surg Oncol 17 (1):42–46
49. Ginsberg RJ, Rubinstein LV (1995) Randomized trial of lobectomy versus limited resection for T1 N0 non-small cell lung cancer. Lung Cancer Study Group. Ann Thorac Surg 60 (3):615–622; discussion 622–623
50. Landreneau RJ et al (1993) Postoperative pain-related morbidity: video-assisted thoracic surgery versus thoracotomy. Ann Thorac Surg 56(6):1285–1289
51. Landreneau RJ et al (1997) Wedge resection versus lobectomy for stage I (T1 N0 M0) non-small-cell lung cancer. J Thorac Cardiovasc Surg 113(4):691–698; discussion 698–700
52. El-Sherif A et al (2006) Outcomes of sublobar resection versus lobectomy for stage I non-small cell lung cancer: a 13-year analysis. Ann Thorac Surg 82(2):408–415; discussion 415–416
53. Feld R, Rubinstein LV, Weisenberger TH (1984) Sites of recurrence in resected stage I non-small-cell lung cancer: a guide for future studies. J Clin Oncol 2(12):1352–1358
54. Thomas P, Rubinstein L (1990) Cancer recurrence after resection: T1 N0 non-small cell lung cancer. Lung Cancer Study Group. Ann Thorac Surg 49(2):242–246; discussion 246–247
55. Pairolero PC et al (1984) Postsurgical stage I bronchogenic carcinoma: morbid implications of recurrent disease. Ann Thorac Surg 38(4):331–338
56. Siegfried JM et al (1994) Ability to culture resectable non-small cell lung carcinomas is correlated with recurrence. Ann Thorac Surg 58(3):662–666; discussion 667
57. Kessler R et al (1996) Blood vessel invasion is a major prognostic factor in resected non-small cell lung cancer. Ann Thorac Surg 62(5):1489–1493
58. Harpole DH Jr et al (1996) Angiogenesis and molecular biologic substaging in patients with stage I non-small cell lung cancer. Ann Thorac Surg 61(5):1470–1476
59. Johnson JR et al (1995) Successful xenotransplantation of human lung cancer correlates with the metastatic phenotype. Ann Thorac Surg 60(1):32–36; discussion 36–37
60. Fernando HC et al (2014) Impact of brachytherapy on local recurrence rates after sublobar resection: results from ACOSOG Z4032 (Alliance), a phase III randomized trial for high-risk operable non-small-cell lung cancer. J Clin Oncol 32(23):2456–2462
61. Deslauriers J et al (1989) Carcinoma of the lung. Evaluation of satellite nodules as a factor influencing prognosis after resection. J Thorac Cardiovasc Surg 97(4):504–512
62. Kutschera W (1984) Segment resection for lung cancer. Thorac Cardiovasc Surg 32(2):102–104
63. Bonfils-Roberts EA, Clagett OT (1972) Contemporary indications for pulmonary segmental resections. J Thorac Cardiovasc Surg 63(3):433–438

64. Jensik RJ, Faber LP, Kittle CF (1979) Segmental resection for bronchogenic carcinoma. Ann Thorac Surg 28(5):475–483
65. Bennett WF, Smith RA (1979) Segmental resection for bronchogenic carcinoma: a surgical alternative for the compromised patient. Ann Thorac Surg 27(2):169–172
66. Schuchert MJ et al (2007) Anatomic segmentectomy in the treatment of stage I non-small cell lung cancer. Ann Thorac Surg 84(3):926–932; discussion 932–933
67. Sienel W et al (2007) Frequency of local recurrence following segmentectomy of stage IA non-small cell lung cancer is influenced by segment localisation and width of resection margins—implications for patient selection for segmentectomy. Eur J Cardiothorac Surg 31 (3):522–527; discussion 527–528
68. Martin-Ucar AE et al (2005) A case-matched study of anatomical segmentectomy versus lobectomy for stage I lung cancer in high-risk patients. Eur J Cardiothorac Surg 27(4):675–679
69. Houck WV, Fuller CB, McKenna RJ Jr (2004) Video-assisted thoracic surgery upper lobe trisegmentectomy for early-stage left apical lung cancer. Ann Thorac Surg 78(5):1858–1860
70. Atkins BZ et al (2007) Pulmonary segmentectomy by thoracotomy or thoracoscopy: reduced hospital length of stay with a minimally-invasive approach. Ann Thorac Surg 84(4):1107–1112; discussion 1112–1113
71. D'Amico TA (2008) Thoracoscopic segmentectomy: technical considerations and outcomes. Ann Thorac Surg 85(2):S716–S718
72. Sugiura H et al (1999) Long-term benefits for the quality of life after video-assisted thoracoscopic lobectomy in patients with lung cancer. Surg Laparosc Endosc Percutan Tech 9(6):403–408
73. McKenna RJ Jr, Houck W, Fuller CB (2006) Video-assisted thoracic surgery lobectomy: experience with 1,100 cases. Ann Thorac Surg 81(2):421–425; discussion 425–426
74. Hoksch B et al (2003) Complication rate after thoracoscopic and conventional lobectomy. Zentralbl Chir 128(2):106–110
75. Sugi K et al (2003) Intrathoracic bleeding during video-assisted thoracoscopic lobectomy and segmentectomy. Kyobu Geka 56(11):928–931
76. Kaseda S, Aoki T (2002) Video-assisted thoracic surgical lobectomy in conjunction with lymphadenectomy for lung cancer. Nippon Geka Gakkai Zasshi 103(10):717–721
77. Walker WS (1998) Video-assisted thoracic surgery (VATS) lobectomy: the Edinburgh experience. Semin Thorac Cardiovasc Surg 10(4):291–299
78. Giudicelli R et al (1994) Major pulmonary resection by video assisted mini-thoracotomy. Initial experience in 35 patients. Eur J Cardiothorac Surg 8(5):254–258
79. Demmy TL, Curtis JJ (1999) Minimally invasive lobectomy directed toward frail and high-risk patients: a case-control study. Ann Thorac Surg 68(1):194–200
80. Nakata M et al (2000) Pulmonary function after lobectomy: video-assisted thoracic surgery versus thoracotomy. Ann Thorac Surg 70(3):938–941
81. Onaitis MW et al (2006) Thoracoscopic lobectomy is a safe and versatile procedure: experience with 500 consecutive patients. Ann Surg 244(3):420–425
82. Sugi K, Kaneda Y, Esato K (2000) Video-assisted thoracoscopic lobectomy achieves a satisfactory long-term prognosis in patients with clinical stage IA lung cancer. World J Surg 24(1):27–30; discussion 30–31
83. Walker WS et al (2003) Long-term outcomes following VATS lobectomy for non-small cell bronchogenic carcinoma. Eur J Cardiothorac Surg 23(3):397–402
84. Bonadonna G et al (1995) Adjuvant cyclophosphamide, methotrexate, and fluorouracil in node-positive breast cancer: the results of 20 years of follow-up. N Engl J Med 332(14):901–906
85. Petersen RP et al (2006) Thoracoscopic lobectomy: a safe and effective strategy for patients receiving induction therapy for non-small cell lung cancer. Ann Thorac Surg 82(1):214–218; discussion 219
86. van Meerbeeck JP, Damhuis RA, Vos de Wael ML (2002) High postoperative risk after pneumonectomy in elderly patients with right-sided lung cancer. Eur Respir J 19(1):141–145

87. Burrows B et al (1960) The postpneumonectomy state: clinical and physiologic observations in thirty-six cases. Am J Med 28:281–297
88. Baumann M, Stamatis G, Thomas M (2001) Therapy of localized non-small cell lung cancer (take home messages). Lung Cancer 33(Suppl 1):S47–S49
89. Gaissert HA et al (1996) Survival and function after sleeve lobectomy for lung cancer. J Thorac Cardiovasc Surg 111(5):948–953
90. Ginsberg RJ et al (1983) Modern thirty-day operative mortality for surgical resections in lung cancer. J Thorac Cardiovasc Surg 86(5):654–658
91. Rocco PM et al (1996) Long-term outcome after pneumonectomy for nonsmall cell lung cancer. J Surg Oncol 61(4):278–280
92. Paulson DL, Reisch JS (1976) Long-term survival after resection for bronchogenic carcinoma. Ann Surg 184(3):324–332
93. Bernard A et al (2001) Pneumonectomy for malignant disease: factors affecting early morbidity and mortality. J Thorac Cardiovasc Surg 121(6):1076–1082
94. Kim DJ et al (2007) Long-term survival following pneumonectomy for non-small cell lung cancer: clinical implications for follow-up care. Chest 132(1):178–184
95. Allen AM et al (2008) Pneumonectomy after chemoradiation: the Dana-Farber Cancer Institute/Brigham and Women's Hospital experience. Cancer 112(5):1106–1113
96. Gudbjartsson T et al (2008) Early surgical results after pneumonectomy for non-small cell lung cancer are not affected by preoperative radiotherapy and chemotherapy. Ann Thorac Surg 86(2):376–382
97. Doddoli C et al (2005) One hundred consecutive pneumonectomies after induction therapy for non-small cell lung cancer: an uncertain balance between risks and benefits. J Thorac Cardiovasc Surg 130(2):416–425
98. Martin J et al (2001) Morbidity and mortality after neoadjuvant therapy for lung cancer: the risks of right pneumonectomy. Ann Thorac Surg 72(4):1149–1154
99. Tedder M et al (1992) Current morbidity, mortality, and survival after bronchoplastic procedures for malignancy. Ann Thorac Surg 54(2):387–391
100. Kim YT et al (2005) Local control of disease related to lymph node involvement in non-small cell lung cancer after sleeve lobectomy compared with pneumonectomy. Ann Thorac Surg 79(4):1153–1161; discussion 1153–1161
101. Burfeind WR Jr et al (2005) Low morbidity and mortality for bronchoplastic procedures with and without induction therapy. Ann Thorac Surg 80(2):418–421; discussion 422
102. Jalal A, Jeyasingham K (2000) Bronchoplasty for malignant and benign conditions: a retrospective study of 44 cases. Eur J Cardiothorac Surg 17(4):370–376
103. Terzi A et al (2002) Sleeve lobectomy for non-small cell lung cancer and carcinoids: results in 160 cases. Eur J Cardiothorac Surg 21(5):888–893
104. Ferguson MK, Karrison T (2000) Does pneumonectomy for lung cancer adversely influence long-term survival? J Thorac Cardiovasc Surg 119(3):440–448
105. Khargi K et al (1994) Pulmonary function after sleeve lobectomy. Ann Thorac Surg 57 (5):1302–1304
106. Van Schil PE et al (1992) Second primary lung cancer after bronchial sleeve resection. Treatment and results in eleven patients. J Thorac Cardiovasc Surg 104(5):1451–1455
107. Bagan P et al (2005) Sleeve lobectomy versus pneumonectomy: tumor characteristics and comparative analysis of feasibility and results. Ann Thorac Surg 80(6):2046–2050
108. Yamamoto R et al (2000) Effects of preoperative chemotherapy and radiation therapy on human bronchial blood flow. J Thorac Cardiovasc Surg 119(5):939–945
109. Rendina EA et al (1997) Safety and efficacy of bronchovascular reconstruction after induction chemotherapy for lung cancer. J Thorac Cardiovasc Surg 114(5):830–835; discussion 835–837
110. Mentzer SJ, Myers DW, Sugarbaker DJ (1993) Sleeve lobectomy, segmentectomy, and thoracoscopy in the management of carcinoma of the lung. Chest 103(4 Suppl):415S–417S

111. Faber LP, Jensik RJ, Kittle CF (1984) Results of sleeve lobectomy for bronchogenic carcinoma in 101 patients. Ann Thorac Surg 37(4):279–285
112. Weisel RD et al (1979) Sleeve lobectomy for carcinoma of the lung. J Thorac Cardiovasc Surg 78(6):839–849
113. Sartori F et al (1986) Sleeve lobectomy in the treatment of bronchogenic carcinoma. Int Surg 71(4):233–236
114. Brusasco V et al (1988) Lung function following upper sleeve lobectomy for bronchogenic carcinoma. Scand J Thorac Cardiovasc Surg 22(1):73–78
115. Jensik RJ et al (1972) Sleeve lobectomy for carcinoma. A ten-year experience. J Thorac Cardiovasc Surg 64(3):400–412
116. Van Schil PE et al (1991) TNM staging and long-term follow-up after sleeve resection for bronchogenic tumors. Ann Thorac Surg 52(5):1096–1101
117. Firmin RK et al (1983) Sleeve lobectomy (lobectomy and bronchoplasty) for bronchial carcinoma. Ann Thorac Surg 35(4):442–449
118. Grillo HC (2004) Surgery of the trachea and bronchi (vol xvi). BC Decker, Hamilton, 872 p
119. Hollaus PH et al (2003) Risk factors for the development of postoperative complications after bronchial sleeve resection for malignancy: a univariate and multivariate analysis. Ann Thorac Surg 75(3):966–972
120. Fadel E et al (2002) Sleeve lobectomy for bronchogenic cancers: factors affecting survival. Ann Thorac Surg 74(3):851–858; discussion 858–859
121. Tsang V, Goldstraw P (1989) Endobronchial stenting for anastomotic stenosis after sleeve resection. Ann Thorac Surg 48(4):568–571
122. Grillo HC (1982) Carinal reconstruction. Ann Thorac Surg 34(4):356–373
123. Mitchell JD et al (1999) Clinical experience with carinal resection. J Thorac Cardiovasc Surg 117(1):39–52; discussion 52–53
124. Wood DE, Vallieres E (1997) Tracheobronchial resection and reconstruction. Arch Surg 132 (8):850–854; discussion 854–856
125. Mitchell JD et al (2001) Resection for bronchogenic carcinoma involving the carina: long-term results and effect of nodal status on outcome. J Thorac Cardiovasc Surg 121 (3):465–471
126. Jensik RJ et al (1982) Survival in patients undergoing tracheal sleeve pneumonectomy for bronchogenic carcinoma. J Thorac Cardiovasc Surg 84(4):489–496
127. Tsuchiya R et al (1990) Resection of tracheal carina for lung cancer. Procedure, complications, and mortality. J Thorac Cardiovasc Surg 99(5):779–787
128. Maeda M et al (1993) Operative approaches for left-sided carinoplasty. Ann Thorac Surg 56 (3):441–445; discussion 445–446
129. Roviaro GC et al (1994) Tracheal sleeve pneumonectomy for bronchogenic carcinoma. J Thorac Cardiovasc Surg 107(1):13–18
130. Dartevelle P, Macchiarini P (1996) Carinal resection for bronchogenic cancer. Semin Thorac Cardiovasc Surg 8(4):414–425
131. Kutlu CA et al (2000) Acute lung injury and acute respiratory distress syndrome after pulmonary resection. Ann Thorac Surg 69(2):376–380
132. Mathisen DJ et al (1998) Inhaled nitric oxide for adult respiratory distress syndrome after pulmonary resection. Ann Thorac Surg 66(6):1894–1902