Chapter 7
Surgery of Advanced Tumors

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Chest Wall Invasion

Five to 8 % of patients undergoing resection for NSCLC have involvement of the chest wall [1]. Patients' complaints are the most reliable indications of chest wall involvement, as infiltration between the ribs may result in false-negative bone or CT scans. It was claimed that CT scan could be inaccurate in assessing direct parietal pleura invasion of lung cancer [2]. Rendina et al. [3] reported that thickening of the pleura is not useful and obliteration of the extrapleural fat pad is the most sensitive and specific finding in CT scan. Furthermore, visible rib destruction from direct invasion is a very specific sign for chest wall invasion. Although MRI is not routinely used, it has the theoretic advantage of being able to determine if the muscle layers are involved. Positron emission tomography (PET) is useful for detecting distant metastases but is not useful for determining local invasion because the resolution is not adequate to determine chest wall invasion. McCaughan et al. [4] reported an elevated serum alkaline phosphatase level in 34 % of the patients; however, this abnormality is not a specific finding. Pulmonary function tests and quantitative perfusion lung scan are necessary to assess the patient's ability to withstand operation and whether the paradox motion of the residual wall requires stabilization.

The goals of surgery are to completely resect the primary tumors with clear surgical margins and maintain a normal respiratory physiology by restoring the rigidity of the chest wall and resected soft tissue. Knowledge of chest wall invasion preoperatively is important because entering the chest at a site remote from the chest wall invasion lessens the risk of tumor spillage, allows the surgeon to assess the extent of involvement, and avoids placement of the prosthetic material directly beneath the

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S. Peters, B. Besse (eds.), *New Therapeutic Strategies in Lung Cancers*,
DOI 10.1007/978-3-319-06062-0_7

incision. As a general rule, all tumors except those invading the thoracic inlet or the anterior thoracic cage are approached through a standard posterolateral thoracotomy. Resection should include at least one segment of the rib (with the related intercostal muscle) above and below the involved rib(s) and 3–5 cm laterally and medially. To prevent tumor spillage, the entire tumor-bearing area should be resected en bloc, and it is frequently easier to do the chest wall resection initially (small involvements) and then proceed with the pulmonary resection. For large involvements, it is easier to do a wedge excision of the tumor-bearing area with a mechanical stapler and to resect the remainder of the collapsed lobe later. Frozen sections on the soft-tissue margins are mandatory to confirm completeness of the resection.

Majority of the chest wall resections do not require prosthetic reconstruction. Resection of a portion of three or fewer ribs posteriorly rarely requires prosthetic replacement, as the scapula lessens the cosmetic and functional impact of the chest wall resection. Resection of larger defect, especially when located at the anterolateral aspects of the lower ribs, may require prosthetic replacement, yet the risks of infection should be balanced against the cosmetic and functional benefit of prosthetic replacement.

Reconstruction can be accomplished using nonreinforced materials like PTFE patch. With larger and unsupported defects, the chest wall rigidity can be obtained by utilizing titanium rib bridge [5]. Presently, chest wall reconstruction rarely requires the interposition of a myocutaneous flap [6]. As with all other prosthetic substitutes, absolute sterility is required, and the amount of air leaks should be minimal.

All T3 tumors are resectable, but the prognosis varies according to the involved site. A T3 tumor involving the chest wall provides the most favorable prognosis among the resected T3 lesions. If completely excised, T3 (chest wall) N0 lung cancers provide a 5-year survival in excess of 50 % (Table 7.1). The strongest determinants of 5-year survival, by far, are completeness of resection, depth of chest wall invasion, and nodal status. Patients with incomplete resection may survive less than 2.5 years [4, 7–19]. Likewise, the depth of chest wall invasion affects prognosis, as extension to the parietal pleura only is associated with twofold increase of 5-year survival (62 vs. 35 %) when compared to deeper involvements [4]. Different opinions exist as to whether tumors confined to the parietal pleura can be resected by simple extrapleural mobilization, without resecting en bloc the adjacent soft and bony tissues, as long as the resection margins are negative. While McCaughan et al. [4] showed that extrapleural mobilization was sufficient for a significant number of patients whose tumors invaded the parietal pleura only, Piehler et al. [8] reported a high incidence of local recurrence after extrapleural dissection for tumors invading the parietal pleura. Chapelier et al. [16] also found that patients with a tumor infiltration confined to the parietal pleura had a significantly better 5-year survival than those with chest wall infiltration. Most if not all series report no 5-year survivors with positive N2, compared to 5-year survival exceeding 50 % for N0 patients. In this sense, both positron emission tomography (PET) scan and mediastinoscopy are advocated for patients with chest wall involvement and enlarged lymph nodes. If patients are found to have N2 disease before thoracotomy, they should

Table 7.1 Results after complete resection of NSCLC invading the chest wall

Author (ref)	Year	No. of patients	Operative mortality %	Survival rates, 5 years (%)			
				Overall	NO	N1	N2
Piehler [8]	1982	66	15.2	32.9	54.0	7.4[a]	7.4[a]
Patterson [9]	1982	35	8.5	38.0	NS	NS	0.0
McCaughan [4]	1985	125	4.0	40.0	56.0	21.0[a]	21.0[a]
Ratto [93]	1991	112	1.7	NS	50.0	25.0	0.0
Allen [10]	1991	52	3.8	26.3	29.0	11.0	NS
Shah and Goldstraw [11]	1995	58	3.4	37.2	45.0	38.0	0.0
Downey [12]	1999	175	6.0	36.0	56.0	13.0	29.0
Facciolo [13]	2001	104	0.0	61.4	67.0	100.0	17.0
Magdeleinat [14]	2001	201	7.0	21.0	25.0	21.0	20.0
Burkhart [15]	2002	94	6.3	38.7	44.0	26[a]	26.0[a]
Chapelier [16]	2000	100	1.8	18	22	9	0
Riquet [17]	2002	125	7	22.5	30.7	0	11.5
Roviaro [18]	2003	146	0.7	NS	78.5	7.2[a]	7.2[a]
Matsuoka [19]	2004	97	NS	34.2[b]	44.2	40.0	6.2

NS not stated
[a]N1 and N2 patients combined
[b]Complete resection

receive either preoperative chemotherapy or chemoradiotherapy, either as induction or definitive treatment.

The final area of controversy is whether radiation therapy, administered either pre- or postoperatively, is indicated in patients who have lung cancer that invade the chest wall. Potential benefits of preoperative therapy include the following: downstaging the tumor, allowing potentially unresectable tumors to be resected, decreasing the rate of close margins, and decreasing the risk of tumor spillage at the time of resection [20]. However, recent reports showed decreased survival rates in those patients who received radiation therapy [10, 14]. Currently, radiotherapy is proposed to reduce the incidence of local recurrence and should be reserved for patients with close surgical margins or those with hilar or mediastinal nodal involvement. Adjuvant chemotherapy had no apparent effect on survival, but the number of patients was too small to obtain statistically meaningful data.

Superior Sulcus Tumors

Superior sulcus lesions include a constellation of benign or malignant tumors extending to the superior thoracic inlet. They cause steady, severe, and unrelenting shoulder and arm pain along the distribution of the eighth cervical nerve trunk and first and second thoracic nerve trunks. They also cause Horner's syndrome and

weakness and atrophy of the intrinsic muscles of the hand, a clinical entity known as Pancoast-Tobias syndrome. Bronchial carcinoma represents the most frequent cause of superior sulcus lesions. Superior sulcus lesions of non-small cell histology account for less than 5 % of all bronchial carcinomas. These tumors may arise from either upper lobe and tend to invade the parietal pleura, endothoracic fascia, subclavian vessels, brachial plexus, vertebral bodies, and first ribs. However, their clinical features are influenced by their location. Tumors located anterior to the anterior scalene muscle may invade the platysma and sternocleidomastoid muscles, external and anterior jugular veins, inferior belly of the omohyoid muscle, subclavian and internal jugular veins and their major branches, and the scalene fat pad. They invade the first intercostal nerve and first rib more frequently than the phrenic nerve or superior vena cava, and patients usually complain of pain distributed to the upper anterior chest wall.

Tumors located between the anterior and middle scalene muscles may invade the anterior scalene muscle with the phrenic nerve lying on its anterior aspect; the subclavian artery with its primary branches, except the posterior scapular artery; and the trunks of the brachial plexus and middle scalene muscle (Fig. 7.1). As the tumor involves the brachial plexus, symptoms develop in the distribution of T1 (ulnar distribution of the arm and elbow) and C8 nerve roots (ulnar surface of the forearm and small and ring fingers).

Tumors lying posterior to the middle scalene muscles are usually located in the costovertebral groove and invade the nerve roots of T1, the posterior aspect of the subclavian and vertebral arteries, paravertebral sympathetic chain, inferior cervical (stellate) ganglion, and prevertebral muscles. These posterior tumors can invade the transverse process and the vertebral bodies (only abutting the

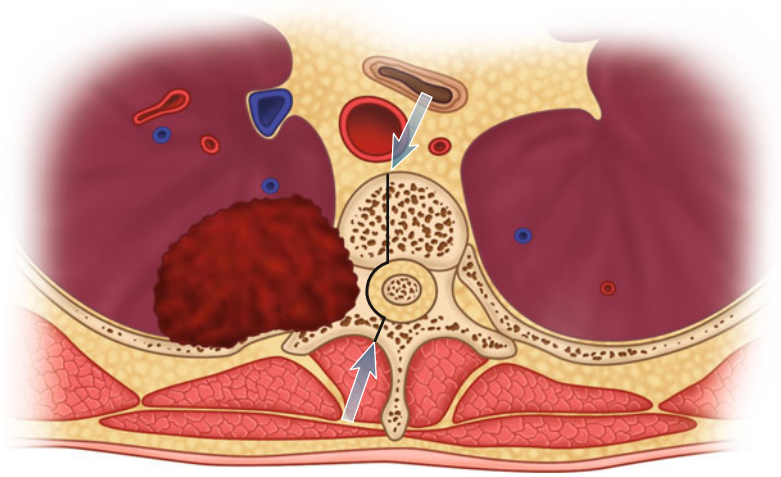

Fig. 7.1 Schematic drawing of a left superior sulcus bronchial carcinoma invading the middle thoracic inlet, including the subclavian artery. The *arrows* show the limits of the orthopedical resection to have R0 margins

costovertebral angle or extending into the intraspinal foramen without intraspinal extension may yet be resected). Because of the peripheral location of these lesions, pulmonary symptoms, such as cough, hemoptysis, and dyspnea, are uncommon in the initial stages of the disease. Abnormal sensation and pain in the axilla and medial aspect of the upper arm in the distribution of the intercostobrachial (T2) nerve are more frequently observed in the early stage of the disease process. With further tumor growth, patients may present with full-blown Pancoast syndrome.

Superior sulcus tumors are extremely difficult to diagnose at initial presentation. The time elapsed between the onset of the Pancoast-Tobias syndrome and diagnosis is still around 6 months. These patients usually present with small apical tumors that are hidden behind the clavicle and the first rib on routine chest radiographs. The diagnosis is established by history and physical examination, biochemical profile, chest radiographs, bronchoscopy and sputum cytology, fine-needle transthoracic or transcutaneous biopsy and aspiration, and computed tomography of the chest. If there is evidence of mediastinal adenopathy on chest radiographs, computed tomographic scanning, or positron emission tomography (PET) scan, histologic proof is mandatory because patients with clinical N_2 disease are not suitable for operation. Neurologic examination, magnetic resonance imaging, and electromyography delineate the tumor's extension to the brachial plexus, phrenic nerve, and epidural space. Vascular invasion is evaluated by venous angiography, subclavian arteriography, Doppler ultrasonography (cerebrovascular disorders may contraindicate sacrifice of the vertebral artery), and magnetic resonance imaging. Magnetic resonance imaging has to be performed routinely when tumors approach the intervertebral foramina to rule out invasion of the extradural space.

The initial evaluation also includes all preoperative cardiopulmonary functional tests routinely performed before any major lung resection and investigative procedures to identify the presence of any metastatic disease.

Although it is now established that radical surgery represents the only hope for long-term survival and cure, optimal management for superior sulcus tumors continues to be a major challenge. The traditional approach to superior sulcus tumors has been preoperative radiotherapy followed by resection, although this standard was established 45 years ago solely on the basis of encouraging short-term survival as compared with historical controls [21]. Then, high-dose curative primary radiotherapy [22], "sandwich" preoperative and postoperative radiotherapy [23], postoperative radiotherapy alone [24], and intraoperative brachytherapy combined with preoperative radiation therapy and operation [25] have been reported as the treatment modalities of superior sulcus tumors. In 2001, SWOG 9416 (Intergroup 0160) [26] evaluated the role of induction chemoradiotherapy and surgery for patients with superior sulcus tumors in multi-institutional setting and updated their results in 2003 [27] for the treatment of these tumors. And then, preoperative concurrent chemotherapy and radiotherapy have been explored by several other groups [28, 29]. The rate of complete resection was 92 % as opposed to an average of 66 % among historical series of conventional treatment [26, 30]. The consistency of the data regarding preoperative chemoradiotherapy and regarding

preoperative radiotherapy alone is convincing that preoperative chemoradiotherapy represents a new standard of care for patients with Pancoast tumors, although no randomized data are available comparing these approaches [31]. As to whether surgery should proceed or follow radiation therapy in newly diagnosed superior sulcus tumors, our strong opinion is to first resect, because dissecting on a previously (chemo)irradiated thoracic inlet unquestionably increases the technical difficulties and postoperative morbidity. Radiation therapy is to be discussed in the postoperative course.

Absolute surgical contraindications in the management of superior sulcus tumors are the presence of extrathoracic sites of metastasis, histologically confirmed N2 disease, and extensive invasion of the cervical trachea, esophagus, and the brachial plexus above the T1 nerve root; this is because it indicates that the tumor is locally too extensive to achieve a complete resection or that limb amputation is necessary. Invasion of the subclavian vessels should no longer be considered a surgical contraindication. Massive vertebral invasion, diagnosed preoperatively, is synonymous with unresectability. Invasions limited to the intervertebral foramen without extension into the spinal canal are resectable.

As a general rule, superior sulcus tumors not invading the thoracic inlet are completely resectable through the classic posterior approach of Shaw et al. [21] alone. Because the posterior approach does not allow direct and safe visualization, manipulation, and complete oncologic clearance of all anatomic structures that compose the thoracic inlet, superior sulcus lesions extending to the thoracic inlet should be resected by the anterior transcervical approach as described by Dartevelle et al. [24, 32]. This operative procedure is nowadays accepted as a standard approach for all benign and malignant lesions of the thoracic inlet structures, including nonbronchial cancers (e.g., osteosarcomas of the first rib and tumors of the brachial plexus), and for exposing the anterolateral aspects of the upper thoracic vertebrae. Contraindications to this approach include extrathoracic metastasis, invasion of the brachial plexus above the T1 nerve root, invasion of the vertebral canal and sheath of the medulla, massive invasion of the scalene muscles and extrathoracic muscles, mediastinal lymph node metastasis, and significant cardiopulmonary disease.

We also developed a technique for resecting posteriorly located superior sulcus tumors extending into the intervertebral foramen without intraspinal extension in collaboration with a spinal surgeon [33]. The underlying principle is that one can perform a radical procedure by resecting the intervertebral foramen and dividing the nerve roots inside the spinal canal by a combined anterior transcervical and posterior midline approach (Fig. 7.2). The reported surgical morbidity ranges from 7 to 38 % with surgical mortality generally around 5–10 % [34–48].

The overall 5-year survival rates after combined radiosurgical (posterior approach) treatment of superior sulcus tumors due to bronchial carcinoma range from 18 to 56 % (Table 7.2). The best prognosis is found in patients without nodal involvement who have had a complete resection.

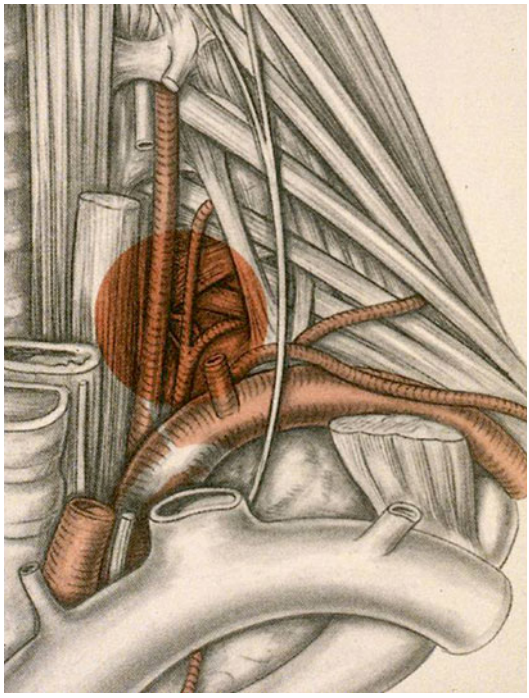

Fig. 7.2 Right-sided apical tumor involving the costotransverse space and intervertebral foramen and part of the ipsilateral vertebral body; this tumor is first approached anteriorly and then the operation is completed through an hemivertebrectomy performed through the posterior midline approach

Table 7.2 Results of patients treated surgically for superior sulcus tumors

Author, year	No. of cases	5-year survival (%)	Mortality (%)
Paulson, 1985 [35]	79	35	3
Anderson, 1986 [36]	28	34	7
Devine, 1986 [37]	40	10	8
Miller, 1987 [38]	36	31	NS
Wright, 1987 [39]	21	27	–
Shahian, 1987 [23]	18	56	–
McKneally, 1987 [40]	25	51	NS
Komaki, 1990 [22]	25	40	NS
Sartori, 1992 [41]	42	25	2.3
Maggi, 1994 [42]	60	17.4	5
Ginsberg, 1994 [43]	100	26	4
Okubo 1995 [44]	18	38.5	5.6
Dartevelle, 1997 [45]	70	34	–
Martinod, 2002 [46]	139	35	7.2
Alifano, 2003 [47]	67	36.2	8.9
Goldberg, 2005 [48]	39	47.9	5 %
Total	807	34.5 ± 11.7[a]	5.6 ± 2.2[a]

NS not stated

[a]Values are number ± standard deviation

Carinal Resections

Refinement in techniques of tracheal surgery and bronchial sleeve lobectomy has made carinal resection and reconstruction possible. However, the potential for complications remains high and few centers only have cumulated sufficient expertise to safely perform the operation. Surgery is still infrequently proposed because of its complexity and the paucity of data demonstrating benefit in the long term. However, results from recent series demonstrate that carinal resection is safe in experienced centers with an operative mortality of less than 10 % and can be associated with good to excellent long-term survival in selected patients. The current results are considerably better than those from earlier reported series and likely account for the improvement in surgical and anesthetic techniques.

Careful patient selection and detailed evaluation of the lesion is a key component to good surgical results in carinal resection. All patients should be evaluated to ascertain that they can tolerate the operation and withstand the necessary removal of pulmonary parenchyma. The preoperative workup consists of chest radiography, chest computed tomography (CT) scan, pulmonary function tests, arterial blood gas, ventilation/perfusion scan, electrocardiography, and echocardiography. Stress thallium studies, maximum oxygen uptake, and exercise testing are used when indicated. The operation is an elective procedure and efforts should be made to prepare the patients for surgery with chest physiotherapy, deep breathing, and cessation of smoking. Airway obstruction, bronchospasm, and intercurrent pulmonary infection should be reversed. Steroids should be discontinued before surgery.

Flexible or rigid bronchoscopy is crucial to evaluate the overall length of the tumor, the adequacy of the remaining airway, and the feasibility of a tension-free anastomosis. Besides routine investigation to rule out extrathoracic metastasis for patients with bronchogenic carcinoma, we also routinely perform a mediastinoscopy at the time of surgery in patients presenting with bronchogenic carcinoma to exclude N2 or N3 disease.

Pulmonary angiography is performed for carinal tumors arising from the anterior segment of the right upper lobe, because invasion of right upper lobe (mediastinal) artery usually indirectly reveals invasion of the posterior aspect of the superior vena cava (SVC). Superior cavography is performed if the SVC is potentially involved. Transesophageal echography is occasionally performed to evaluate tumor extension to the posterior mediastinum, especially the esophagus or the left atrium.

Indications and Contraindications

The safe limit of resection between the lower trachea and the contralateral main bronchus is usually considered to be 4 cm. This is particularly important if a right carinal pneumonectomy is performed and the left mainstem bronchus is to be reanastomosed end to end to the distal trachea. Upward mobilization of the left

mainstem bronchus is limited because of the aortic arch and can easily result in excessive anastomotic tension.

In patients with bronchogenic carcinoma, carinal resection should be considered for tumors invading the first centimeter of the ipsilateral main bronchus, the lateral aspect of the lower trachea, the carina, or the contralateral main bronchus. This applies usually for right-sided tumor, since left-sided tumor rarely extends up to the carina without massively invading structures situated in the subaortic space. The long-term results of carinal resection for patients with bronchogenic carcinoma and N2 or N3 disease are poor, and therefore, the findings of positive mediastinal nodes at the time of mediastinoscopy are usually considered a contraindication to surgery. Induction therapy may be offered for these patients, but we have found that this increases the technical difficulty of the operation and is associated with greater operative mortality, particularly if carinal pneumonectomy is required

Surgical Technique

Our technique of carinal resection has been reviewed in detail elsewhere [49, 50]. Only some specific points are presented herein. Ventilation during carinal resection has always been a major concern. Our technique is similar to Grillo et al. [51]. The patient is initially intubated with an extra-long armored oral endotracheal tube that can be advanced into the opposite bronchus if one-lung ventilation is desired. Once the carina has been resected, the opposite main bronchus is intubated with a cross-field sterile endotracheal tube connected to a sterile tubing system. The tube can be safely removed intermittently to place the sutures precisely.

Approaches

The incision varies according to the type of carinal resection.

Carinal resection without sacrifice of pulmonary parenchyma is approached through a median sternotomy. As previously reported by Pearson et al. [51–53], we find that this approach allows any type of pulmonary resection, including a left pneumonectomy.

For carinal resection with sacrifice of pulmonary parenchyma, the approach depends on the lung concerned by resection. On the right side, a right posterolateral thoracotomy in the fifth intercostal space gives perfect exposure of the lower trachea and the origin of both main bronchi. On the left side, exposure of the lower trachea and right main bronchus is hindered by the aortic arch; that is why the median sternotomy is our preferred approach for left carinal pneumonectomy.

Type of Carinal Resection

1. *Carinal resection without pulmonary resection*
   Carinal resection without pulmonary resection is limited to the tumors located at the carina or at the origin of the right or left main bronchus. Depending on the extent of invasion, different modes of reconstruction exist. For very small tumors implanted on the carina only, the medial wall of both main bronchi can be approximated together to fashion a new carina that is then anastomosed to the trachea (Fig. 7.3). When the tumor is more extensive, requiring a larger portion of the trachea to be resected, end-to-end plus end-to-side anastomosis is the method of choice.
2. *Right carinal pneumonectomy*
   Right carinal pneumonectomy is the most frequent type of carinal resection for bronchogenic carcinoma.
3. *Carinal resection with lobar resection*
   This has to be done when the bronchogenic tumor can extend from the right upper lobe to the carina and lower tract.
4. *Left carinal pneumonectomy*
   The aortic arch greatly hinders performance of the anastomosis in left carinal pneumonectomy. In our experience, we have favored a median sternotomy over a left thoracotomy in the past few years if a left carinal pneumonectomy is anticipated [54].

The results of carinal resection for bronchogenic carcinoma have improved over time. Recent series have shown that carinal resection is relatively safe in experienced centers and can be associated with good long-term survival in selected patients [54–65]. The median operative mortality is less than 7 % and the median 5-year survival is 43.3 % in our experience (Table 7.3).

Patients with positive mediastinal lymph node metastasis have a dismal prognosis; therefore, carinal resection should be considered a potential contraindication. Further studies should determine the role of induction therapy in patients presenting with bronchogenic carcinoma and N2 disease. Induction therapy seems to improve survival if the mediastinal nodes can be sterilized prior to the lung resection. However, induction therapy could potentially be associated with increased operative morbidity and mortality in patients requiring right carinal pneumonectomy. Recently, we reported that operative mortality increased from 6.7 to 13 % after induction therapy in patients undergoing right carinal pneumonectomy [54]. Martin et al. [66] also reported an operative mortality as high as 24 % after right pneumonectomy following induction therapy.

Superior Vena Cava Invasion

Superior vena cava (SVC) syndrome is a distressing manifestation of benign and malignant diseases obstructing venous return through the superior vena cava. Invasion of the superior vena cava (SVC) by the right-sided bronchogenic

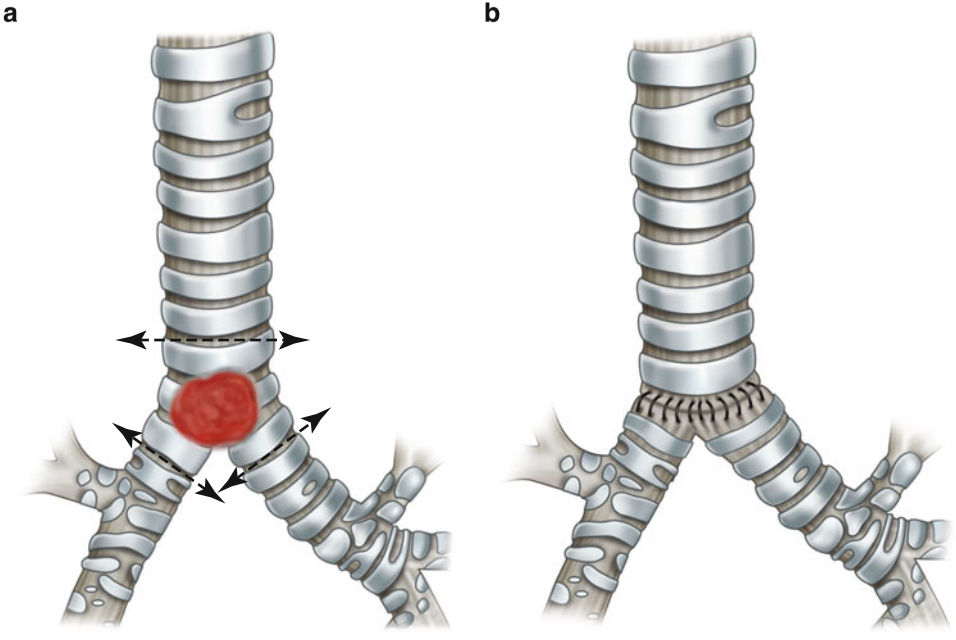

Fig. 7.3 Carinal resection with "neo-carina" reconstruction. (*1*) Carinal lesion involving little of the trachea. Resection lines are indicated (*1*). The medial walls of the right and left main bronchi are approximated with interrupted 4-0 PDS sutures to form a new carina (*2*)

Table 7.3 Mortality and 5-year survival rates after carinal pneumonectomy

Author, year	Number of patients	Operative mortality (%)	5-year survival (%)
Jensik, 1982 [55]	34	29	15
Deslauriers, 1989 [56]	38	29	13
Tsuchiya, 1990 [57]	20	40	59 (2 years)
Mathisen, 1991 [58]	37	18.9	19
Roviaro, 1994 [59]	28	4	20
Dartevelle,1995 [60]	60	6.6	43.3
Mitchell, 1999 [61]	143	12.7	42
Roviaro, 2001 [62]	49	8.2	24.5
Porhanov, 2002 [63]	231	16	24.7
Regnard, 2005 [64]	65	7.7	26.5
de Perrot, 2006 [54]	119	7.6	44
Macchiarini, 2006 [65]	50	4	51
Total	874	10.4 ± 11.6	25.6 ± 15.2

carcinomas occurs in less than 1 % of operable patients [67] and is usually regarded as an absolute surgical contraindication because of the dismal prognosis, absence of suitable graft material for reconstruction, and technical fear concerning the effects of SVC clampage, graft thrombosis, and infection. However, recent experimental and clinical advances increased the popularity of SVC replacement and expanded its therapeutic role in the management of patients with thoracic neoplasm [66–78]. Although SVC resection and revascularization is a technically demanding procedure, a favorable outcome is possible for selected patients with advanced lung cancer.

The clinical picture of a patient with SVC syndrome is routinely simple because the symptoms and signs are typical and unmistakable. The most common symptoms in descending order are dyspnea, suffusion, cough, and arm or facial swelling. Less common symptoms include chest pain, dysphagia, syncope, obtundation, hemoptysis, and headache. The most common signs are facial and extremity edema, engorged neck and chest veins, cyanosis, and plethora. In most patients, the syndrome is insidious, with slow development of symptoms. A short interval to presentation is highly correlated with either an underlying malignancy or catheter-induced thrombotic occlusion, whereas nonmalignant etiologies other than catheters are associated with long-standing symptoms. In this group of patients, the median time from onset of first symptom to actual presentation ranged from 3.2 to 6.5 weeks for patients with malignant disease.

These patients usually present with a mediastinal mass as noted by a widened superior mediastinum on routine chest radiographs. Computed tomography of the chest provides a detailed radiographic analysis of SVC, its tributaries, and critical anatomic structures. Magnetic resonance imaging provides multiplanar anatomic

detail that allows for easy visualization of the extrinsic mass in transverse, sagittal, and coronal planes. Superior vena cavography (simultaneous injection through both upper limbs) is an essential procedure when surgical intervention is contemplated. Echocardiography eliminates thrombosis extension into the right atrium and detects the patency of the jugular and axillary veins. Brain CT scan should always be performed to eliminate brain diseases that may increase brain edema during SVC clamping. Histologic diagnosis can be established by sputum histology, bronchoscopy, supraclavicular lymph node biopsy, thoracentesis, mediastinoscopy, bone marrow biopsy, and thoracotomy.

To perform an adequate and safe SVC resection and reconstruction, the greatest emphasis should be directed to adequately evaluate the tumoral and vascular indications, keep in mind the hemodynamic effects of venous clamping, and select the material for SVC revascularization.

Vascular Indications

Graft thrombosis may develop in the postoperative period and has deleterious consequences because of the risk of pulmonary embolism. SVC revascularization can be done only if there is an excellent patency at the level of the cephalic venous bed.

Hemodynamic Effects of SVC Clampage

The effects of SVC clampage are different according to the degree of obstruction of the SVC, but in fact Dartevelle et al. [69] have proven that it is not difficult to reverse the hemodynamic effects of SVC clamping by using fluid supplementation and pharmacologic agents, reducing the venous clamping time, and giving adequate anticoagulation therapy.

Spaggiari et al. [79] reported an analysis of the literature review regarding 109 patients who underwent SVC resection to identify the prognostic factors for patients with SVC invasion. This study has shown that SVC resection for lung cancer results in 30 % major postoperative morbidity and 12 % mortality rates. Five-year survival is 21 %, with median survival at 11 months. Patients who had an induction treatment presented with an increased risk of major complications. The type of pulmonary resection (i.e., pneumonectomy) and the type of SVC resection [80] (i.e., complete resection with prosthetic replacement) are the prognostic factors with the greatest adverse effect on survival.

Recently, Suzuki et al. [77] and Shargall et al. [78] reported a total of 55 patients with 12 % of mortality rate. Morbidity and mortality are linked with the association of a carinal pneumonectomy; excision of the SVC alone does not change anything.

Invasion of the Left Atrium, Aorta, and Main Pulmonary Trunk

Complete resections in patients with tumors invading the left atrium, aorta, and main pulmonary trunk are often not possible and are associated with a high mortality. There are no consistent data regarding these resections of T4 lung cancers. Systemic arterial invasion of T4 lung cancer carries the poorest long-term outcome. Limited local invasion of the intrapericardial pulmonary artery or left atrium can be resected completely with expected 5-year survival rates of ~20 to 30 % [81]. In general, if there is less than 1–1.5 cm of intrapericardial involvement of these structures, they can usually be resected with negative margins and a safe vascular closure. Although most authorities have viewed the need for more complex reconstructions that require cardiopulmonary bypass (CPB) as a contraindication to resection, recent reports encourage the application of CPB in extended pulmonary resection to achieve complete resection [70, 82–90]. It had been estimated that less than 0.1 % of all thoracic resections were done with CPB.

The indication for the surgical radical therapy is based on the individual situation of the patients after interdisciplinary evaluation and discussion of treatment options. Distant metastatic disease or extrathoracic sites of disease have to be excluded. All elective procedures are to be done in curative intention; no palliative indication is considered acceptable in these advanced tumors.

In most patients, locally advanced bronchogenic carcinoma can be resected without the need of CPB. Cardiopulmonary bypass is used to resect carcinoma invading the aortic arch, the descending aorta, the pulmonary artery bifurcation, the left atrium, and the carina. The potential side effects of CPB on lung function and other organ function are well described in the literature, but the oncologic side effect is less known. The observation that some patients with carcinomas, sarcoma, and other tumors are disease-free survivors over many years, despite the resection which occurs on CPB, indicates that the use of CB does not necessarily increase the risk of tumor dissemination although it has been observed occasionally [82]. The key issue for a favorable outcome justifying extended resection of advanced thoracic malignancies on CPB is patient selection.

Preoperative Evaluation

For preoperative workup, chest computed tomography (CT) is the primary mode of evaluation for all patients. A full biologic and radiographic workup is to be performed to exclude brain, abdominal, and bone metastasis. An angiography of the aortic arch and supraaortic trunks as well as a transesophageal ultrasound should be performed to demonstrate the presence of any invasion of the left subclavian artery and the esophageal wall. Duplex scan of both carotid and vertebral arteries has to be performed to assure good patency of all four vessels. Magnetic resonance imaging (MRI) is necessary to exclude an invasion of the intervertebral foramen.

The invasion of the left atrium by NSCLC is typically discovered at thoracotomy in less than 4 % of patients undergoing curative resection for NSCLC. The left atrium is usually invaded more frequently by direct extension rather than by tumor emboli protruding from the pulmonary veins. In most cases, resection of the left atrium can be achieved by apposing a vascular clamp on the left atrium to remove the tumor along with both pulmonary veins and by directly suturing the defect. If a larger portion of the left atrium is invaded, the tumor is often not completely resectable because of prolonged microscopic infiltration of the myocardium. Thus, CPB has rarely been used for left atrial resection in our experience. Some authors have found that CPB could be useful if the tumor extends into the lumen of the left atrium with a risk of systemic tumor embolization. Cardiopulmonary bypass allowed opening the left atrium after aortic cross-clamping and instillation of cardioplegia or after the induction of hypothermic ventricular fibrillation to avoid air embolism. Complete resection of tumors with partial invasion of the left atrial wall should not be denied because this procedure represents the only hope for cure [7, 70, 86–89].

The results of invasion of the aorta by NSCLC are limited to scattered reports, mainly because tumors are so locally extensive that resection is often impossible. Aortic invasion by NSCLC is usually limited to the adventitia. However, in rare instances, the media of the aorta is also invaded and resection requires cross-clamping of the aorta proximally and distally to remove the infiltrated wall. A shunt prosthesis between the ascending and descending aorta in order to resect and reconstruct the infiltrated portion of the aorta has been suggested. However, we believe that CPB was the easiest way to achieve perfusion of the upper and lower part of the body during aortic cross-clamping.

Complications

There is considerable evidence that CPB is associated with deterioration of pulmonary function as assessed by measuring the alveolar–arterial oxygenation gradient, intrapulmonary shunt, degree of pulmonary edema, pulmonary compliance, and pulmonary vascular resistance. More frequent and more severe complications with extended periods of mechanical ventilation are expected, if CPB is applied. In our experience [82], pulmonary edema, acute respiratory distress syndrome, and atelectasis associated with recurrent nerve palsy were the most common complications observed following T4 lung cancer resection with CPB. Bleeding is another frequent complication following CPB-assisted procedures. In a series of lung resection during cardiac operations with CPB, bleeding complications were reported to affect 21 % of patients.

Surgical reports dealing with tumors invading the pulmonary artery trunk are limited. Ricci et al. [90] reported pulmonary angioplasty under CPB in three patients whose NSCLC invaded the main pulmonary trunk; however, all patients died within 25 months following operation. Tsuchiya et al. [70] replaced the bifurcation of the

Table 7.4 Results of patients treated surgically for NSCLC involving the left atrium

Author, year	Number of patients	Operative mortality (%)	5-year survival (%)
Shirakusa, 1991 [87]	12	8.3	NS
Martini, 1994 [88]	8	NS	12.5
Tsuchiya, 1994 [70]	44	NS	22
Macchiarini, 1997 [7]	31	3.2	21.6
Ratto, 2004 [89]	19	0	14
Bobbio, 2004 [86]	23	9	10
Total	137	5.75 ± 4.2	14.0 ± 5.4

NS not stated

pulmonary artery on CPB in six patients. Because all patients died within 30 months from operation, invasion of the pulmonary artery trunk was considered technically resectable but incurable biologically.

Vascular resection and reconstruction of the aorta and left atrium have been safely described with 5-year survival rates more than 20 % (Table 7.4). Combined pulmonary and aorta resection is described by Fukuse et al. [85], with 5-year survival rates of 31 % ($n = 15$). Combined pulmonary and left atrial resection has been described most recently by Bobbio et al. [86] with 5-year survival rates of 10 % ($n = 23$). Recently, Ohta et al. [91] reported that 16 patients underwent thoracic aorta resection along with a lung resection with the mortality rate 12.5 % and 5-year survival rates were 70 % for patients with N0 disease and 16.7 % for patients with N2 or N3 disease.

We have recently reported our CPB experience in resecting NSCLC [82]. We operated on 7 patients with 0 % mortality and 28 % ($n = 2$) morbidity. Among the 7 patients, one died of pulmonary emboli 6 months after surgery, three patients are alive without recurrences, and the remaining three patients are alive with recurrences.

The use of CPB does not appear to increase the risk of cancer dissemination. Several series have reported combining lung resection for bronchogenic carcinoma with aortocoronary bypass surgery during the same operative procedure with good early and long-term results despite the use of CPB.

Long-term outcome of patients with locally advanced lung cancer depends primarily on completeness of resection. Martini et al. [88] have reported a series of lung cancer invading the mediastinum and observed that the 5-year survival rate was 30 % if the tumor was completely resected, whereas it was only 14 % if it was incompletely resected. Similar observations were reported in a series of lung cancer invading the heart or great vessels with 5-year survival ranging between 23 and 40 % if the tumor was completely resected, whereas no patients survived greater than 3 years if the tumor was incompletely resected.

Further studies will be necessary to confirm these findings in patients undergoing resection of locally advanced NSCLC under CPB. Patients with locally advanced NSCLC should be treated with aggressive multidisciplinary therapy in a manner that maximizes the chance for long-term cure while minimizing the overall risks of treatment.

Invasion of the Vertebral Body

Direct invasion of the vertebral body or the costovertebral angle by an NSCLC other than a superior sulcus tumor is rarely observed. Treatment options vary among the radiation therapy alone, resection by shaving off the bone, and tangential or hemivertebrectomy. DeMeester et al. [92] provide evidence that for tumors limited invasion of periosteum below the third vertebral body, long-term survival (5-year survival, 42 %) and cure for selected patients can be anticipated by combining a preoperative radiation therapy (30 Gy) and en bloc resection of the primary tumor and involved vertebral body. Resectability was based on the preoperative radiological absence of bony erosion and intraoperative absence of invasion into costotransverse foramen. For tumors with more extensive invasion, McCormack [67] reported a 10 % survival at 5 years by performing a total vertebrectomy and spinal stabilization; however, no conclusions were drawn as to its value.

Conclusion

Improved surgical techniques have increased the feasibility and radicality of extended operations for patients with potentially resectable but locally invasive NSCLC. Advances in the perioperative management and postoperative care, along with a careful patient selection, will likely make the operative mortality and morbidity less prohibitive and a more favorable prognosis.

It has been well demonstrated that the prognosis after operations for T3/T4 tumors mainly depends on the N stage. Patients with N0 or minimal N1 disease do significantly better after radical resection, a finding that clearly justifies operative therapy in these patients. On the other hand, both the technical complexity of the operation and its rare occurrence therefore suggest centralization of the procedure to departments that express profound and continuous interest in such problems and that at the same time have a high degree of experience with both general thoracic and vascular procedures.

Our policy regarding locally advanced lung cancer patients is to perform surgery on first intention, whenever a complete resection is thought to be technically possible. Complete resection resulting in good mean 5-year survival is possible, especially for tumors invading the trachea or carina (5-year survival is 40 %). In our opinion, any attempt to downstage the disease in these particular patients introduced a new dilemma for the surgeon concerning the type of resection to be performed: the one that was required initially to remove all the disease or the one dictated by the residual disease.

The thoracic medical and surgical community should promote all efforts to extend the surgical indications for locally advanced NSCLC, making these operations available whenever possible to patients in whom a cure can be achieved.

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