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Pancoast Tumors: Surgical Approaches and Techniques

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1. Introduction

1.1 History

Tumors of the superior sulcus represent less than 5% of lung malignancies. The distinctive symptomatology was first described by Edwin Hare in 1838 [1], and it has been nearly 80 years since clinical and radiographic features of this tumor were described by Dr Henry Pancoast, a radiologist, in 1924 [2]. As a radiologist, he noted the difficulty in detecting the tumor on a plain chest radiograph. He initially thought that these tumors arose from epithelial crest cells from the fifth brachial cleft. These tumors have been named Pancoast tumors or Pancoast-Tobias tumors after further descriptions of their features by these authors in 1932 [3, 4]. This was the first time that bronchogenic carcinoma was recognised as the primary cause of this syndrome.

Prior to the 1950s, superior sulcus tumors were uniformly fatal. Chardack and McCallum reported a long-term survival after surgical resection and postoperative irradiation therapy [5]. Paulson, using preoperative irradiation followed by surgical resection, published the first series, which included 18 patients, in 1966 [6]. Shaw and Paulson identified that preoperative irradiation and a well-defined resection were associated with a 5-year survival of 34% [7]. Based upon these studies, preoperative irradiation and an extended posterolateral paravertebral thoracotomy (Shaw Paulson approach) has been the “standard of care” over the last 5 decades. However surgical resection remained limited to tumors invading the ribs only, and any further involvement of vascular or neural structures was still considered to remain a contraindication for an operation. This was changed by Darteville who was the first to develop an anterior transcervical approach for the resection of tumors involving subclavian vessels. Later on several other modifications of this technique were reported but with no remarkable improvement on overall survival.

In the last century, the management of the superior sulcus tumor changed from inoperability and incurability to the current regimen of preoperative chemoradiation therapy, with an attempt at complete resection. Interest in trimodality treatment led to the South-West Oncology Group (SWOG) 8805 study of induction chemoradiotherapy (cisplatin, etoposide, 45Gy) followed by surgery that resulted in a complete response rate of 22% and encouraging results [8]. A recent prospective phase II study (SWOG 9416) suggests that preoperative concurrent chemoradiation (cisplatin, etoposide, 45Gy) improves the rate of complete resection, intermediate survival and decreases the rate of local or distal recurrence [9]. The 2-year survival was 55% for all eligible patients and 70% for patients who had a complete resection.

The superior sulcus tumor is a rare tumor posing a unique challenge to thoracic surgeons. The current regimen of preoperative chemoradiation with complete surgical resection leads to reasonable long term survival. Progress is being made in the understanding of the anatomy and biology of this disease. A choice of incisions provides options that have the potential to increase the rate of complete resection. New techniques allow resection of structures that were previously considered unresectable. Future efforts to improve the results will entail not only multidisciplinary approach to en bloc extended resection of adjacent structures but also preoperative therapy (chemotherapy or biologic agents) that yields greater tumor regression, thereby improving complete resection rates that are so critical to long-term survival in this form of non-small cell lung cancer (NSCLC).

2. Definition and surgical anatomy

Pancoast tumor is a cancer of the apex of the lung with no intervening lung tissue between tumor and chest wall. Subsequently, there is involvement of structures of the apical chest wall above the level of the second rib. The chest wall involvement may be limited to invasion of parietal pleura or may extend deeper to involve the periosteum or the bone of the first rib or apical vertebral bodies, or it may include invasion of subclavian vessels, the nerve roots of the brachial plexus or the stellate ganglion. Involvement of the chest wall only at the level of the second rib or lower should not be considered to meet the criteria for Pancoast tumor [10]. An apical tumor involving only the visceral pleura and not the chest wall by clinical staging should not be classified as a Pancoast tumor. However, it seems reasonable to include tumors that are thought to involve chest wall by clinical criteria.

Superior sulcus tumors may occur in the three compartments of the thoracic inlet and symptoms are related to the location. The anterior compartment lies anterior to the insertion of the anterior scalene muscle onto the first rib, the middle compartment extends from there to the posterior border of the middle scalene muscle, whereas the posterior compartment lies behind the middle scalene muscle [11]. Tumors located in the anterior component may invade the subclavian vessels, whereas those in the middle mainly invade the brachial plexus (Figures 1, 2). Posterior Pancoast tumors usually invade the stellate ganglion or vertebral bodies (Figure 3).



Fig. 1. Pancoast tumor located in the anterior component (anterior Pancoast tumor).

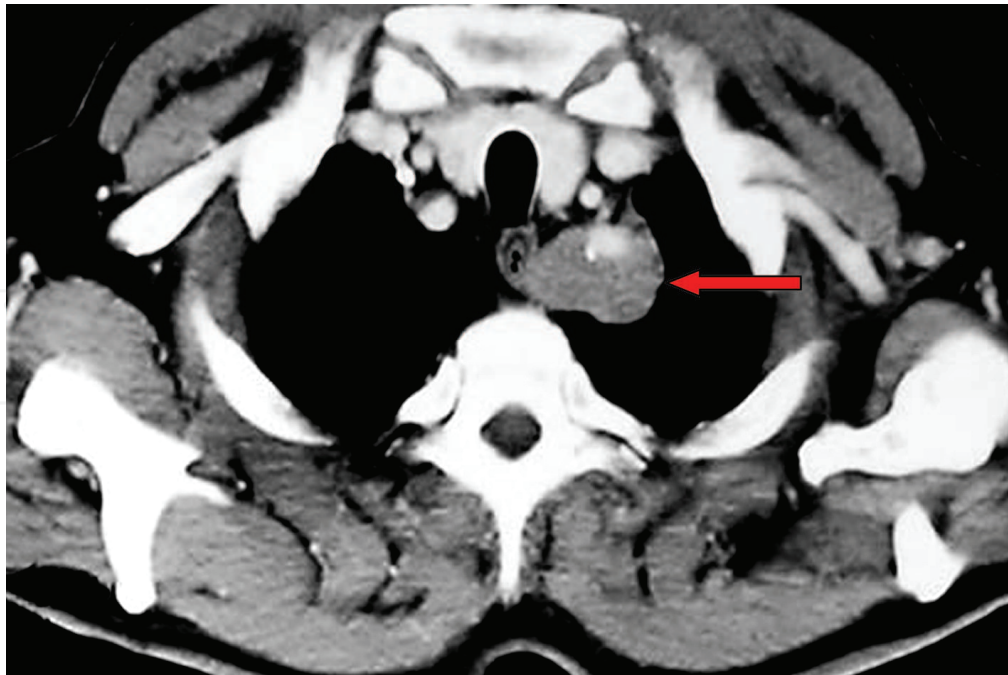


Fig. 2. Pancoast tumor occupying the middle component (median Pancoast tumor).

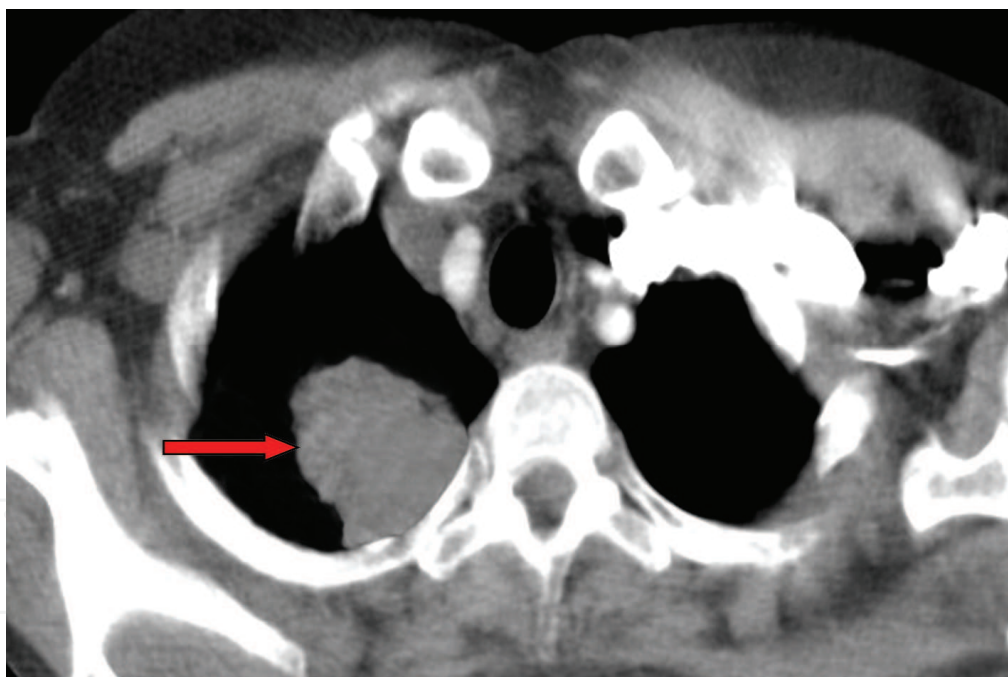


Fig. 3. Pancoast tumor located in the posterior component (posterior Pancoast tumor).

In case of invasion of the brachial plexus, patients often present with intense pain that begins in the shoulder and scapular region and extends down to the ulnar aspect of the arm (T1 dermatome) onto the small and ring fingers (C8 dermatome). Due to increasing pressure on the nerve roots, muscle atrophy of the ulnar aspect of the hand and loss of the triceps reflex can occur. In about 20-30% of patients, tumor invasion of the sympathetic chain and the stellate ganglion causes Horner's syndrome (ipsilateral ptosis, miosis and anhidrosis) [12].

COMPARTMENT	BOUNDARIES	included STRUCTURES	SIGNS AND SYMPTOMS
Anterior	Between sternum and anterior edge of anterior scalene muscle.	Platysma, sternocleidomastoid and omohyoid muscles, jugular and subclavian veins, scalene fat pad.	Pain radiating to the upper anterior chest wall, venous thrombosis.
Middle	Between anterior and posterior border of middle scalene muscle	Anterior and middle scalene muscles, subclavian artery and primary branches, phrenic nerve, trunks of brachial plexus	Pain and parasthesia radiating to the shoulder and upper limb, arterial thrombosis, diaphragmatic paralysis
Posterior	Behind middle scalene muscle	Posterior scalene muscle, posterior scapular artery, posterior aspect of subclavian and vertebral artery, paravertebral sympathetic chain, stellate ganglion, nerve roots of brachial plexus, long thoracic and spinal accessory nerves, neural foramina, vertebral bodies and prevertebral muscles.	Pain in the axilla and in the medial part of the upper arm, Horner's syndrome.

Table 1. Anatomical definition of the thoracic inlet and main clinical features in case of superior sulcus tumor invasion [13].

3. Biological behaviour

Advanced molecular biology techniques have accelerated the understanding of cancer biology. It is well established that the application of such technology has led to the recognition of lung cancer as a molecularly diverse set of tumor types whose only commonality is their origination in the lung [14]. Lung cancer classification is far more complex than the simplistic grouping into small cell and non-small cell variants with a comparable outcome when treated in a similar fashion [15]. Histologic subdivision of lung cancer uses only one of many phenotypic manifestations of the genetic changes that underlie lung cancer development.

Lung cancer development is a result of a stepwise progression of malignant transformation of normal respiratory epithelium. This transformation is driven by the cumulative effect of genetic alterations induced predominantly by inhaled carcinogens from tobacco smoke [16]. The Noguchi classification of lung adenocarcinoma is a pioneering effort to relate tumor

histology with clinical and radiologic characteristics. This has resulted in the identification of atypical adenomatous hyperplasia and adenocarcinoma in situ as preinvasive neoplastic lung lesions that serve as precursors to invasive lung adenocarcinoma through a progressive transformation into the type A, B, and C adenocarcinomas with lepidic growth (referring to growth along alveolar structures) characterized by an increasing component of invasive carcinoma but showing excellent survival outcome, and the type D, E, and F solid-type adenocarcinomas with a well-recognized poor prognosis [17]. The most frequently described acquired genetic aberrations within the tumor involve the tumor protein p53 (TP53), KRAS, fragile histidine triad (FHIT), epidermal growth factor receptor (EGFR), cyclin-dependent kinase 2a (CDKN2), LKB1, retinoblastoma (RB), and Myc genes. Larger genomic mishaps such as chromosomal deletions involving the short arms of chromosomes 1, 3, and 9 (del 1p36, del 3p, and del 9p, respectively) are also frequently observed in different lung cancer histologic subtypes and stages. More recently, inversion translocation of the echinoderm microtubule-associated protein-like 4 (EML4) and anaplastic lymphoma kinase (ALK) genes on chromosome 2 (2p21 and 2p23) was shown to characterize a small subset of NSCLC with a characteristic clinical and histologic profile. The discovery of other molecularly defined lung cancer subsets is likely to be hastened by this finding [18].

The treatment options for patients with lung cancer have improved considerably in recent years. Improvements in survival have been noted for patients with every stage of the disease with the integration of new systemic therapy options, improvements to local therapy, and supportive care measures. A number of molecularly targeted agents that modulate a wide array of cell signaling pathways are currently under development. The remarkable success achieved with the use of EGFR tyrosine kinase inhibitors and the ALK inhibitors are the initial steps toward an era of individualized treatment options for patients with NSCLC. Several groups are now involved in screening tumor specimens for dominant oncogenic drivers in individual patients to guide treatment selection. A total of 13 known molecular abnormalities including 8 mutations are evaluated in the tumor specimens. By developing novel clinical trials across institutions to target each of these molecular events, the oncologist is evaluating a variety of individualized treatment approaches for patients with NSCLC. Because these molecular changes are noted in much smaller subsets of patients, such clinical trials are unlikely to complete accrual within a single institution in a reasonable time and therefore require such collaborative efforts to accelerate research.

The tremendous increase in the knowledge of lung cancer biology notwithstanding, a number of important questions remain unanswered. With lung cancer in never-smokers having been recognized as a unique entity, insights into the underlying mechanism and etiological factors will help in the development of novel therapies for this group of patients. The differences in lung cancer biology based on gender are another important area of research that will hopefully lead to the development of gender-driven therapeutic approaches. As newer therapeutic options are developed, participation of patients in clinical trials must be encouraged and supported by health care delivery systems. Currently, fewer than 5% of the patients diagnosed with cancer participate in therapeutic clinical trials [19].

Concerning Pancoast tumors it was traditionally believed that the biology was different from that of other non-small cell lung cancers and in that these tumors had a strong propensity to local invasion and a diminished incidence of spread through lymphatic or hematogenous routes. However, recent data does not support this belief [20]. Additionally the incidence of pathologic N2 disease, is similar to that of other peripheral stage I or II lung tumors and survival is better following a formal lobectomy rather than a wedge resection

alone. The unique feature of Pancoast tumors appears not to lie in the tumor biology but rather in the anatomy of the region in which these tumors occur.

Ipsilateral supraclavicular nodal involvement is classified as N3 disease. However, there is some evidence that such involvement in patients with a Pancoast tumor may not preclude long-term survival. Ipsilateral supraclavicular node involvement in these patients may have a prognostic importance more akin to that of N1 disease [21].

4. Surgical approaches

4.1 Posterior approach

The ideal tumor for the posterolateral approach is situated posteriorly in the superior sulcus and does not invade the anterior structures of the thoracic inlet. It may however invade the vertebral bodies or the brachial plexus. The C8 and T1 nerve roots are most commonly invaded. It is important to assess the patient's neurologic function preoperatively and to inform him properly concerning postoperative neurological morbidity [22].

The patient is placed in the lateral decubitus position. The incision starts anteriorly, allowing exploration of the chest cavity (usually through the fourth/fifth interspace) to assess resectability. The extension of the tumor onto the thoracic chest wall, thoracic inlet, lung, and mediastinum should be assessed. The incision is then extended posteriorly around the tip of the scapula and vertically upward between the spinous processes and posterior edge of the scapula, up to C7 (Figure 4). The division of muscle layers starts from the latissimus dorsi and trapezius to expose and subsequently divide the serratus anterior, rhomboidius major and minor, and levator scapulae muscles. The dorsal scapular nerve and scapular artery branches should be avoided when dividing the rhomboids at their insertion into the medial border of the scapula. These muscles will all be meticulously reapproximated at the end of the case. The chest wall resection is carried out first, in order to release the involved chest wall into the pleural cavity allowing for a safer lobectomy. En bloc resection of the chest wall and lung is preferred to extrapleural dissection without rib sacrifice, which often leads to incomplete resection. In most cases, the first two or three ribs are removed, although more ribs may be resected if required. The resection should guarantee large free margins, resecting 3-4 cm of uninvolved rib anteriorly and one rib and the intercostal muscle below the tumor inferiorly.

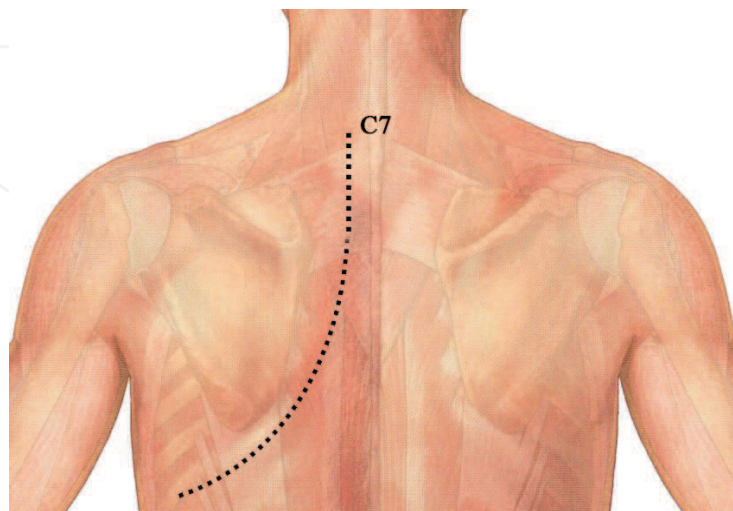


Fig. 4. Posterior approach for Pancoast tumors (Shaw Paulson thoracotomy). The incision extends up to the 7th cervical vertebrae.

First, the anterior and inferior dissection is started along the established resection margins beginning with the healthy rib. The invaded ribs and intercostal muscles are divided using rib shears and electrocautery, in succession from below to above, and the intercostal neurovascular pedicles are ligated. When the first rib is reached, the anterior and middle scalenus insertions to the second and first rib are divided with cautery, exposing the structures of the thoracic inlet crossing above the first rib. It is very important to note the insertions of the anterior and middle scalene on the first rib. Also of note is the phrenic nerve lying on the anterior surface of the anterior scalene. This, as well as the subclavian vein and artery should be identified before dividing the anterior scalene.

The posterior phase of the dissection starts by incising the erector spinae muscle along its anterior border from T1 to T5 and retracting it outward to expose the costotransverse joint. If the tumor involves the parietal pleura only, with no rib or vertebral erosion, the ribs may be disarticulated from the transverse processes, preserving the latter structures. The intercostal nerve and vessel originating from the intervertebral foramen are identified and divided between clips or sutured with 3-0 Prolene. This manoeuvre is repeated for each rib, until the first rib is reached. If the tumor involves the ribs posteriorly, the transverse processes are removed along with the adjacent lateral cortex of the vertebrae using an osteotome.

The lower trunk of the brachial plexus is identified by retracting the first rib downward and can be dissected posteriorly until it splits into the C8 (above the neck of the first rib) and T1 (below the neck of the first rib) nerve roots. Most commonly, the neoplastic invasion is limited to the first thoracic nerve root, which may be divided medial to its entry into the lower trunk and lateral to tumor involvement, keeping the C8 nerve root intact. This is very important in order to avoid the morbidity of loss of function of the intrinsic muscles of the hand [23]. When the tumor involves the C8 nerve, the lower trunk of the brachial plexus should be divided medially, at its origin from the spine. When the T1 nerve root is divided there is usually only a sensory deficit along the medial aspect of the hand.

With a hand inside the chest, the first rib is cut either at its neck if the head is not involved with tumor or beyond the attachment of its tubercle to the transverse process. The chest wall is then released from the apex of the chest en bloc by sequentially dividing the lower portion of the stellate ganglion and first intercostal artery.

Then a formal upper lobectomy with systematic lymph node dissection is the final step. The tumor attached to the chest wall is removed as one specimen. At this time a routine evaluation of the margins is done, obtaining biopsies and placing clips for helping postoperative irradiation.

It is not usually necessary to reconstitute the posterior defect in the chest wall, as it is covered by the scapula. A defect of three or more ribs or over the tip of the scapula should be closed with synthetic mesh. It is well established that meticulous reapproximation and closure with mesh prevents major morbidity in respiratory chest wall motion.

The posterior approach allows excellent exposure of the posterior chest wall including the transverse processes and thoracic nerve roots. It also allows standard exposure of the pulmonary hilum. However, surgical manipulation of the subclavian vessels is very difficult. Furthermore, visualization of the apex is poor making assessment of the appropriate extent of resection problematic.

4.2 Anterior approach

The anterior surgical approach to Pancoast tumors is modified to optimize exposure. Depending on location and size of the tumor there are two basic incisions: 1) a transclavicular incision and 2) a hemi-clamshell incision with supraclavicular extension.

The transclavicular incision (Dartevelle approach) is used with the patient in the supine position with the neck hyperextended and the head turned toward the uninvolved side [24]. The skin is prepared from the mastoid process to the xyphoid process and from the midaxillary line to the contralateral midclavicular line. The cervicotomy uses an L-shaped incision that follows the anterior border of sternocleidomastoid muscle and the inferior border of the clavicle to the deltopectoral groove (Figure 5). In first reports, a standard clavicular resection was included but this was associated with functional disability and suboptimal cosmetic results. An alternative approach involves bisecting the manubrium to preserve the claviculomanubrial junction (Grunenwald approach) (Figure 6) [25].

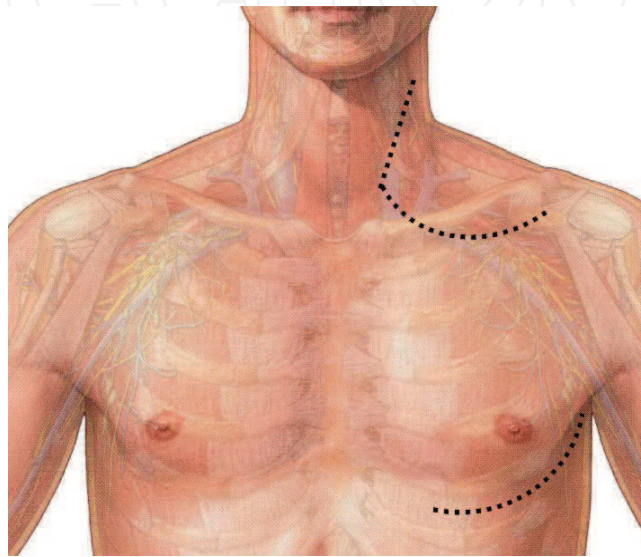


Fig. 5. Anterior transclavicular approach for Pancoast tumors (Dartevelle approach).



Fig. 6. Anterior approach for Pancoast tumors (Grunenwald approach).

The hemi-clamshell incision is a clavicular-sparing approach [23]. The patient is in full lateral position with slight posterior rotation. The skin is prepared in the same manner as described for the transclavicular approach. In patients requiring a supraclavicular extension, the ipsilateral arm is incorporated in the skin preparation.

The sternocleidomastoid muscle is divided and the medial half of the clavicle is resected. Variations of this approach include simple division of the mid-portion of the clavicle and

subsequent reconstruction with plates and screws, or disarticulation of the sternoclavicular joint and lateral retraction of the clavicle.

The sequential steps involve dissection of the jugular veins, dissection of the arteries and exposure of the brachial plexus. Dissection of the jugular veins is important for adequate exposure. Ligation of the internal jugular vein is well tolerated. Especially on the left side, the thoracic duct is ligated with care.

The anterior scalene muscle is divided either at its insertion on the scalene tubercle of the first rib, or as close as it gets to its origin at the transverse processes of C3-C5. The anterior scalene muscle is well defined in 2/3 of patients and may be located behind the subclavian artery or split into two with the artery passing between the bundles [26]. The subclavian artery is mobilized by dividing most of its branches. Care is taken to preserve the vertebral artery and resection of the vessel is done only if it is involved with the tumor. A preoperative Doppler ultrasound is important to detect any extracranial occlusive disease. If the subclavian artery is invaded by the tumor, the affected portion is resected and reconstructed with a PTFE vascular graft. A small dose of heparin is administered during vascular clamping. Following anterior traction of the subclavian artery, the middle scalene muscle comes into good view.

The middle scalene muscle originates from the transverse processes of C2-C7 and inserts onto the first rib between the subclavian groove and the posterior tubercle of the transverse process. In tumors invading the middle compartment of the thoracic inlet, the middle scalene muscle may be extensively involved. In these cases resection of the middle scalene muscle requires mobilization along its origin from the lower cervical vertebrae.

At this stage the cords of the brachial plexus are identified laterally. The anterior surface of vertebral bodies C7 and T1 are in view. The sympathetic chain and the stellate ganglion are lying in front of the vertebral bodies of C7 and T1. C8 and T1 nerve roots are visualized and dissected medially up to the lower trunk of the brachial plexus. The C8 nerve component of the plexus is preserved for better functional outcome of the upper limb. For carcinomas affecting the spine a multilevel unilateral laminectomy, nerve root division inside the spinal canal and vertebral body division can be performed by neurosurgeons.

The chest wall resection is performed with progressive resection of the first, second and third ribs. The ribs are resected from the costochondral junction anteriorly to the articulation with the transverse process. To facilitate mobility of the en bloc mass, resection of a short segment of rib (1-2 cm), may create a "mobile" chest wall. Resection of lower ribs is difficult and pulmonary resection by means of a conventional lobectomy is difficult. It may sometimes be necessary to perform a separate posterior thoracotomy to complete the resection and lymph node dissection.

The anterior approach facilitates direct visualization of vascular structures and provides excellent exposure of brachial plexus, sympathetic chain and stellate ganglion. There is freedom for hemi-vertebrectomy for tumors invading anterior parts of the vertebrae. Oncological clearance seems to be optimal due to the fact that the tumor is the last structure to be encountered. Finally the anterior approach seems to offer less morbidity than the posterior one.

A relative disadvantage of the anterior approach is the difficulty in removing the transverse processes and the head of the ribs in order to disarticulate them. The need to perform an additional posterior thoracotomy for the lobectomy and systematic mediastinal lymph node dissection could be seen as a factor that negates the routine use of anterior approach.

4.3 Future perspectives

Although the understanding of the biology and treatment of Pancoast tumors has evolved significantly, it is clear that more progress is needed. When considering that a large randomized trial may not be performed due to the relative rarity of the disease, the present clinical evidence from several phase II studies suggests that induction chemoradiotherapy and surgery be recommended as modern standard of care for Pancoast tumors. However, there are many issues still remaining for debate or are under discussion [27].

1. Recruitment of patients with N2 disease for surgery.
2. Ipsilateral supraclavicular lymph node disease should be considered as N1 disease.
3. The role of high dose preoperative radiotherapy (6000 cGy).
4. The role of prophylactic cranial irradiation.
5. The role of adjuvant postoperative chemotherapy.
6. The role of more aggressive surgery in cases of extensive involvement of the brachial plexus.

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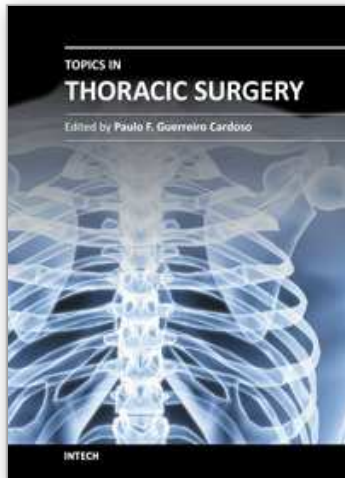
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